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Preoperative Evaluation of Carotid Artery Stenosis: Comparison of Contrast-Enhanced MR Angiography and Duplex Sonography with Digital Subtraction Angiography

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BACKGROUND AND PURPOSE: Contrast-enhanced MR angiography and extracranial color-coded duplex sonography are noninvasive, preoperative imaging modalities for evaluation of carotid artery stenosis. Innovative techniques and improvements in image quality require frequent reassessment of accuracy, reliability, and diagnostic value compared with those of digital subtraction angiography (DSA). We evaluated contrast-enhanced MR angiography and duplex sonography compared with DSA for detection of high-grade carotid artery stenoses.

METHODS: Four readers, blinded to clinical symptoms and the outcome of other studies, independently evaluated stenoses on contrast-enhanced MR angiograms in 71 vessels of 39 symptomatic patients. Duplex sonography was also performed in all vessels. The severity of stenosis was defined according to North American Symptomatic Carotid Endarterectomy Trial criteria (0–29%, 30–69%, 70–99%, 100%). Results of both modalities were compared with the corresponding DSA findings.

RESULTS: Contrast-enhanced MR angiography had a sensitivity and specificity of 94.9% and 79.1%, respectively, for the identification of carotid artery stenoses of 70% or greater. Sensitivity and specificity of duplex sonography were 92.9% and 81.9%, respectively. Combining data from both tests revealed a sensitivity and specificity of 100% and 81.4%, respectively, for concordant results (80% of vessels).

CONCLUSION: Concordant results of contrast-enhanced MR angiography and duplex sonography increase the diagnostic sensitivity to 100%. The reliability of MR angiography is comparable to that of DSA. The combination of contrast-enhanced MR angiography and duplex sonography might be preferable over DSA for preoperative evaluation in most patients, thus reducing the risk of perioperative morbidity and improving the overall outcome.

Contrast-enhanced MR angiography and color-coded duplex sonography are the most important noninvasive tools for determining the degree of stenosis of the carotid artery bifurcation. Numerous recent studies have evaluated both tests with regard to their potential to replace selective digital subtraction angiography (DSA) in the preoperative assessment of carotid disease (1–9). There are many controversies regarding the accuracy and reliability of both modal-

ities. Because of ongoing improvement in imaging techniques, assessment of diagnostic accuracy is essential for appropriate patient care.

This prospective study was designed to compare contrast-enhanced MR angiography and duplex sonography with DSA with regard to the evaluation of carotid artery bifurcations in patients with symptomatic carotid artery stenoses. Attention was focused on the concept of combining these two noninvasive tests, and therefore we sought to determine whether concordant results can improve diagnostic accuracy to a level that eliminates the need for DSA.

Methods

Thirty-nine consecutive patients (seven women, 32 men; age range, 41–80 years; mean age, 67.4 ± 8.4 years) with clinically suspected symptomatic carotid artery stenoses, referred to our institution for preoperative imaging, were included in this pro-

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TABLE 1: Imaging parameters for contrast-enhanced MR angiography

Parameter	Time Resolved	Bolus Timing
TR (ms)	4	6
TE (ms)	1.65	2.16
Flip angle (degrees)	25	30
Slab thickness (mm)	64	70
Number of partitions	64	80
Field of view (mm)	300	300
Pixel size (mm)	2.13×1.17	1.17×0.59
Pixel matrix	88×256	160×512
Acquisition time (s)	9	30.98

spective study that was conducted between August 1999 and July 2002. Indications for imaging were amaurosis fugax ($n = 10$), single or recurrent transient ischemic attack ($n = 14$), and stroke in the previous 8 weeks ($n = 15$).

Written informed consent was obtained from all patients. The study was approved by the institutional ethics board. Patients with known contraindications for contrast-enhanced MR angiography or DSA were excluded.

Both carotid artery bifurcations were examined with contrast-enhanced MR angiography, duplex sonography, and selective DSA within 10 days.

Transfemoral arteriograms with the digital subtraction technique (Angiostar Plus; Siemens, Erlangen, Germany), aortic arch injection, and selective catheterization of both common carotid arteries, with documentation of three different views (posteroanterior, lateral, and 45° oblique), were obtained in all patients and served as the standard of reference. Iopromid 120–200 mL (Ultravist 300 or Ultravist 370; Schering, Berlin, Germany) was used as the contrast agent.

Contrast-enhanced MR angiography of the carotid arteries was performed with a 1.5-T magnet (Magnetom Symphony; Siemens Medical Systems) by using a combined head and neck coil. The first 19 patients were examined with a time-resolved technique, whereas the next 20 patients were examined with an improved examination protocol with use of a bolus-timing technique. Gadopentetate dimeglumine 25–35 mL (Magnevist; Schering) was intravenously injected by using a power injector (Spectris MR injector; Medrad, Pittsburgh, PA) at a flow rate of 3.0 mL/s and flushed with 20 mL of saline. Fast gradient-echo images (fast low-angle shot) were obtained with a 3D data acquisition (Table 1).

The source coronal images were postprocessed with a standard maximum intensity projection algorithm. Each carotid artery was segmented individually at 15° rotational intervals around the cephalocaudal axis. Maximum intensity projections and individual coronal partitions were analyzed.

According to a current literature review (10), vessels with a complete signal void on contrast-enhanced MR angiograms and evidence of flow in the internal carotid artery distal to the bifurcation were considered patent and the stenosis was defined as high-grade (70–99%).

The degree of stenosis, determined by MR angiography and DSA, was evaluated independently by four radiologists (BB, NZ, JL, IB), blinded to clinical symptoms and the outcome of other studies. The diameter of the vessel was obtained by direct measurement with a magnifying lens with a 0.1-mm graduation scale. The degree of stenosis of the internal carotid artery was determined and classified into four categories, based on the North American Symptomatic Carotid Endarterectomy Trial (NASCET) criteria (11, 12): 0–29%, 30–69%, 70–99%, and 100%.

Duplex sonography was performed with a Sonoline Elegra 5.0 system (Siemens), with a 7.5-MHz linear array transducer. Following a standard protocol, longitudinal and transverse im-

ages of the common carotid artery, the carotid bulb, and the internal carotid artery on both sides were obtained. Pre- and poststenotic peak systolic, end-diastolic, and mean velocity were measured. These criteria were used to assign stenosis categories, corresponding to those from the NASCET study. As defined by these data, vessels with an internal carotid artery-to-common carotid artery peak systolic velocity ratio of more than 3.0 were classified as having stenoses of greater than 70%, according to the existing laboratory protocol, which was based on published criteria (13).

Statistical analysis was performed with SPSS for Windows 8.0 (SPSS, Chicago, IL) and Excel 2000 (Microsoft, Redmond, WA). Statistical tests were calculated based on the classifications of each observer and the pooled data for assessment of the reliability to identify a stenosis of 70% or greater: 1) sensitivity and specificity of contrast-enhanced MR angiography, with DSA as the reference standard; 2) sensitivity and specificity of duplex sonography, with DSA as the reference standard; 3) correlation of MR angiography with DSA; 4) correlation of sonography with DSA. For calculation of the correlation of sonography with DSA and MR angiography with DSA, the Spearman rank correlation coefficient was used. To assess the diagnostic reliability of MR angiography, the interobserver variability of MR angiography and DSA was tested by using κ statistics. The degree of agreement between different readers was defined by the scale of Landis and Koch (14): <0.00, poor; 0.00–0.20, slight; 0.21–0.40, fair; 0.41–0.60, moderate; 0.61–0.80, substantial; 0.81–1.0, almost perfect.

Results

No neurologic events occurred in the 39 patients during or after any of the performed imaging procedures. Seventy-one of 78 carotid bifurcations were examined adequately with all three modalities. Seven carotid bifurcations had to be excluded from statistical analysis because of diagnostically nonuseful images: in three patients, the carotid artery could not be visualized selectively on DSA images; in four patients, the insonation of the stenosis was not possible because of sonographic attenuation due to echogenic plaque in the artery wall. No noteworthy artifacts from patient movement were noted on any MR angiograms. All MR angiograms were considered to be of sufficient quality.

Assessment of Stenosis with DSA

Evaluation of 71 carotid artery bifurcations with DSA revealed 35 (49%) high-grade stenoses ($\geq 70\%$), of which three (4%) were occluded; 16 bifurcations (23%) with 30–69% stenosis; and 20 bifurcations (28%) with a 0–29% stenosis. Interobserver agreement between the readers was substantial ($\kappa = 0.78$).

MR Angiography versus DSA

Evaluation of stenosis yielded 80% concordant gradings with contrast-enhanced MR angiography compared with DSA (Table 2). Of 284 evaluations (four observers \times 71 vessels), there were 37 overestimations (13.0%) and 19 underestimations (6.7%). For identification of a 70% or greater stenosis, as determined by DSA, the mean values for sensitivity and specificity of contrast-enhanced MR angiography

TABLE 2: Comparison of estimates of internal carotid artery stenoses with contrast-enhanced MR angiography versus DSA

Percentage Stenosis with MR Angiography	Percentage Stenosis with DSA			
	0–29	30–69	70–99	100
0–29	64	12	—	—
30–69	7	30	7	—
70–99	3	27	122	—
100	—	—	—	12

Note.—Numbers are pooled data (4 observers \times 71 vessels = 284 evaluations).

TABLE 3: Results for detecting a 70–99% stenosis with contrast-enhanced MR angiography and duplex sonography

Parameter	MR Angiography (n = 4 \times 71)	Sonography (n = 71)
Sensitivity (%)*	94.9 (91–100)	92.9 (91–94)
Specificity (%)*	79.1 (76–84)	81.9 (74–86)
False-negative†	7 (2.5)	10 (3.5)
False-positive†	30 (10.6)	26 (9.2)

* Numbers in parentheses are 95% confidence intervals.

† Data are number (%) of evaluations.

were 94.9% and 79.1%, respectively (Table 3). Thirty (10.6%) false-positive evaluations occurred with MR angiography for identification of a 70% or greater DSA-evidenced stenosis, with DSA-evidenced stenoses ranging from 57% to 65% (mean \pm SD, 63 \pm 2.6%). In six false-positive estimations, the reason for overestimation was a signal void. No obvious explanation was found for the discrepancy in the remaining arteries. Seven (2.5%) false-negative evaluations occurred with contrast-enhanced MR angiography, each manifesting a DSA-evidenced stenosis of 80%. All three occlusions were correctly identified by all readers. The correlation of contrast-enhanced MR angiography with DSA was high ($P = .894$), and the interobserver agreement was substantial ($\kappa = 0.76$).

Duplex Sonography versus DSA

Stenosis evaluation with duplex sonography (determined by one neurologist [BD]) resulted in 78% concordant gradings compared with DSA (Table 4). There were 44 overestimations (15.5%) and 18 (6.3%) underestimations of stenosis degree. For the identification of a 70% or greater stenosis, as determined by DSA, the mean values for sensitivity and specificity were 92.9% and 81.9%, respectively (Table 3). Twenty-six overestimations were false-positive evaluations for detecting a 70% or greater stenosis, with DSA-evidenced stenoses ranging from 60% to 66% (mean \pm SD, 64 \pm 2.4%). Ten underestimations were false-negative evaluations, with degrees of DSA-evidenced stenoses of 84% to 88%. All three vessel occlusions were identified correctly. Correlation of duplex sonography with DSA was high ($P = .880$).

TABLE 4: Comparison of estimates of internal carotid artery stenosis with duplex sonography versus DSA

Percentage Stenosis with Sonography	Percentage Stenosis with DSA			
	0–29	30–69	70–99	100
0–29	56	8	—	—
30–69	18	36	10	—
70–99	—	26	118	—
100	—	—	—	12

Note.—Numbers are pooled data (4 observers \times 71 vessels = 284 evaluations).

TABLE 5: Results for detecting a 70–99% stenosis in 227 cases (79.9%) with concordant grading with contrast-enhanced MR angiography and duplex sonography

Parameter	Value
Sensitivity	100 (100)
Specificity	81.4 (80–89)
False-negative	0
False-positive	8.4

Note.—Data are percentages. Numbers in parentheses are 95% confidence intervals.

Stenosis Assessment with MR Angiography and Sonography

Agreement between MR angiography and duplex sonography was found in 227 evaluations (80%). Considering only these data, the mean values for sensitivity and specificity for the identification of a 70% or greater stenosis were 100% and 81.4%, respectively (Table 5). There were no cases in which both modalities concurred but underestimated a 70% or greater stenosis. The rate of false-positive results was decreased from 10.6% for MR angiography and 9.2% for sonography to 8.4% for concordant readings. The concordant DSA-evidenced stenoses ranged from 60% to 65%.

Signal Void at MR Angiography

In 83 MR angiographic evaluations (29%), all readers identified a complete signal void at the site of stenosis. The degree of stenosis, determined by DSA, for these carotid arteries ranged from 60% to 99% (mean \pm SD, 84 \pm 9.5%). The classification into high-grade (70–99%) stenosis by MR angiography was 93% concordant with DSA. Nevertheless, six short signal voids were detected with stenoses of 60–65% by DSA, thus leading to MR angiographic overestimation of the stenosis degree.

Discussion

Large randomized studies have indicated the benefit of carotid endarterectomy in patients with a high-grade stenosis of the internal carotid artery (15–17). The desire to precisely characterize these patients has increased the need for reliable and exact diagnostic tools to evaluate the degree of carotid artery stenosis. In the past, DSA has been regarded as the only

reliable test for preoperative evaluation of stenosis. However, the intervention-related stroke rate ranges from 0.5% to 1.0% (18–20). Noninvasive imaging tools, including MR angiography and duplex sonography, have been considered as potential substitutes for DSA (21–28). The problems so far are less accuracy and reliability, with a potential for resultant inappropriate treatment. Although contrast-enhanced MR angiography has been performed since 1996, the quality of these sequences has been improved since, leading to an ongoing need for critical reassessment of the diagnostic power.

This study includes a prospective and direct comparison of contrast-enhanced MR angiography and duplex sonography with the standard method DSA for evaluation of stenoses of the carotid bifurcation in symptomatic patients. A recent retrospective evaluation of the records of patients who underwent duplex sonography and contrast-enhanced MR angiography showed a reduction of misclassification by combining the two tests (29). For this reason, we focused additionally on the concordant results of contrast-enhanced MR angiography and duplex sonography to determine the potential of these two noninvasive tests in combination to replace selective DSA.

Our data show that both contrast-enhanced MR angiography and duplex sonography are sensitive tests for the detection of clinically relevant carotid artery stenosis. The sensitivities of MR angiography and duplex sonography were similar (94.9% and 92.9%) when identifying a stenosis of 70% or greater. In 79.9% of the evaluated carotid arteries in this study, contrast-enhanced MR angiography and duplex sonography revealed identical degrees of stenoses. Regarding these concordant results of both tests, only the sensitivity could be improved to 100%, with all patients who required therapy being classified correctly.

The specificities of contrast-enhanced MR angiography and duplex sonography and the specificity of the combination of both modalities were similar, with a slight improvement in duplex sonography and contrast-enhanced MR angiography concordant results in comparison to contrast-enhanced MR angiography alone. False-positive results with the combined tests occurred in 8.4% of cases, leading to surgical treatment of carotid arteries manifesting with a 60–65% stenosis as visualized with DSA. Although it is unclear how severe a patient would be harmed by such a small error in stenosis measurement, it seems to be a minor drawback considering the results of studies, other than NASCET, that identified a benefit from operative treatment in stenoses of 60% or greater (17). The sensitivity and specificity for contrast-enhanced MR angiography and duplex sonography in our study are similar to those of previous studies that used 3D and 2D time-of-flight (TOF) MR techniques (1, 2, 10, 29). Our data regarding the concordant results of contrast-enhanced MR angiography and duplex sonography are also in agreement with previous data (3, 29) of studies that used nonenhanced MR angiography, except for the value of specificity not being substantially improved by combining both tests.

However, the number of false-positive results could be decreased. The same conclusion resulted from a retrospective comparison by Johnston and Goldstein (9) of radiology reports from 569 patients, in which they demonstrated a reduction of misclassification from 28% (duplex sonography) and 18% (contrast-enhanced MR angiography) to 7.9% for concordant results of both tests. In contrast, Mittl et al (10) did not find a close correlation between MR angiography and duplex sonography owing to low sensitivity of both tests. A possible explanation could be the use of the 2D TOF technique, which is known to be less accurate than 3D TOF and contrast-enhanced MR angiography (30).

Both imaging tests, contrast-enhanced MR angiography and duplex sonography, show a tendency to overestimate carotid stenoses. Six of 30 false-positive evaluations with contrast-enhanced MR angiography were due to short signal voids, resulting in less specificity compared with that of duplex sonography. This is a known problem of MR angiography (4) that results from signal intensity loss due to an increase in velocity at the point of a high-grade stenosis. The use of a contrast agent reduces this signal intensity loss substantially, because of a reduction of TE and a minimalization of saturation effects, which results in improved imaging of the stenoses delineation (5, 30). Nevertheless, the combination of limited spatial resolution and intravoxel dephasing still results in signal intensity loss in high-grade stenoses, leading to an overestimation of the degree of stenosis and signal voids at very small residual vessel lumina. This fact can be confirmed by our study and indicates that contrast-enhanced MR angiography is unlikely to achieve a specificity of 100%. Such results (6, 7, 31) might be explained only by a nonblinded evaluation or few patients included ($n = 21$ [31]) or many stenoses less than 70%. The data of other studies comparing contrast-enhanced MR angiography with DSA reveal sensitivities and specificities of 94–98% and 85–96%, respectively (8, 32), which agree with our results.

In accordance with a recent prospective study (21), our results do not justify the exclusive use of extracranial duplex sonography as a preoperative imaging test of carotid stenoses, as suggested by other studies (33, 34). In our study, 5.7% of carotid arteries with a stenosis of 70% or greater would have been treated incorrectly (using the average stenosis readings of all four readers for this calculation). Besides increased sensitivity, an important advantage of contrast-enhanced MR angiography is the possibility to assess the carotid artery from the aortic arch to the circle of Willis. Thus, tandem stenoses might be detectable with contrast-enhanced MR angiography, which may be relevant for surgical procedures and can be expected in up to 9% of patients (35). Reliability of contrast-enhanced MR angiography seems to be another advantage in comparison to duplex sonography. In contrast to duplex sonography, contrast-enhanced MR angiography is operator independent when following a standard protocol. The interobserver agree-

ment in our study was high for contrast-enhanced MR angiography and comparable to that of DSA (0.76 vs 0.78), indicating a good reproducibility of contrast-enhanced MR angiography, which is important in routine clinical use. In contrast, duplex sonography is influenced by considerable interobserver differences (36). Apart from well-known contraindications, motion artifacts in less cooperative patients represent the most relevant limitation of contrast-enhanced MR angiography. However, owing to a short acquisition time, motion artifacts were only a minor problem in this study, and all contrast-enhanced MR angiographic studies led to a sufficient diagnostic quality.

A limitation of this study was the low statistical power due to the small number of patients. However, today it is difficult to obtain a larger series, since DSA is no longer used routinely in the evaluation of patients suspected of having carotid artery stenosis. The choice of DSA as the standard of reference in our study, resulting in a standard bias, may also be interpreted as a limitation of our study. However, DSA is known to be a reliable technique in preoperative carotid artery imaging. It has been used as the reference technique for definition of the degree of stenosis in all large international randomized trials that have demonstrated the benefit of surgical treatment of high-grade carotid stenoses (11, 16, 17).

A change in MR angiographic technique was performed after 19 patients to improve performance. Bolus-timing contrast-enhanced MR angiography has the potential to be more reliable when examining patients with differences in circulation time. There is no comparative evaluation of time-resolved and bolus-timing contrast-enhanced MR angiography. In our study, there were no differences in sensitivity and specificity for identifying a stenosis of 70% or greater between the stenosis readings of bolus-timing and time-resolved contrast-enhanced MR angiography, thus no bias was introduced.

Conclusion

The presented prospective study confirms duplex sonography and contrast-enhanced MR angiography to be effective noninvasive methods for the evaluation of carotid artery stenosis before carotid endarterectomy. Our data indicate that DSA may be dispensable when duplex sonography and contrast-enhanced MR angiography are combined and lead to concordant results, but do not support surgical decision making based on any of these methods alone. Following this concept, almost 80% of the assessed carotid arteries in this study underwent intraarterial DSA unnecessarily. Apart from reducing the DSA-associated risk of stroke, most of these patients would have been treated correctly, according to the NASCET study, and no patient with a high-grade stenosis would have missed the appropriate treatment. In those patients in whom duplex sonography and contrast-enhanced MR angiography are discordant, definite diagnosis should be obtained with DSA. With regard to the rapid technical progress and increase in reliability of noninvasive methods, it is justified to expect a further

reduction of the diagnostic failure rate in the next few years. Thus, the diagnostic value of noninvasive methods may eventually reach a standard comparable to that of DSA.

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