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MR Angiographic and Sonographic Indications for Endarterectomy

John Huston, Douglas A. Nichols, Patrick H. Luetmer, Charlotte H. Rydberg, Bradley D. Lewis, Fredric B. Meyer, Robert D. Brown, and Cathy D. Schleck

PURPOSE: **Our objective was to determine whether appropriate criteria could be developed for performing an endarterectomy on the basis of sonographic and MR angiographic findings.**

METHODS: **Fifty patients were examined prospectively with sonography, MR angiography, and conventional angiography. All three imaging studies were performed within 2 weeks of one another, and conventional angiography served as the reference standard.**

RESULTS: **All 10 carotid occlusions were detected with sonography and MR angiography. Sonography accurately showed flow in two arteries, and MR angiography showed flow in one of three nearly occluded arteries with extremely slow flow. Multislab three-dimensional time-of-flight MR angiographic sequences underestimated the degree of stenosis in 12 arteries, and in two cases this resulted from high T1 signal within the atherosclerotic plaque. With conventional angiography as the reference standard for 70% to 99% stenosis, sonography had a sensitivity of 96%, a specificity of 91%, and a positive predictive value of 90%, while concordant sonographic findings and the presence of a signal void on multislab 3-D time-of-flight sequences had a sensitivity of 72%, a specificity of 98%, and a positive predictive value of 97%.**

CONCLUSION: **Endarterectomy performed on the basis of sonographic findings of 70% to 99% stenosis and of a signal void on multislab 3-D time-of-flight MR angiographic sequences is appropriate.**

Cerebral infarction is the third leading cause of death in the United States, with an estimated 500 000 new cases each year. Atherosclerotic disease involving the carotid bifurcation with associated shedding of emboli or clots accounts for a substantial percentage of infarcts. The North American Symptomatic Carotid Endarterectomy Trial (NASCET) (1) and the European Carotid Surgery Trial (2) demonstrated a therapeutic benefit of carotid endarterectomy in symptomatic patients in whom stenosis of the internal carotid artery is greater than or equal to 70%. Effort has turned to finding noninvasive techniques to identify appropriate patients for endarterectomy accurately in lieu of the more expensive conventional angiography, with its known risks. Initial studies have shown clinical utility for magnetic resonance (MR) angiography, typically performed with axial two-dimensional time-of-flight (TOF) (3–5) and sagittal slab three-dimensional TOF (6, 7) techniques. More recently developed, optimized MR angiographic protocols have led to a proposed strategy of operating on patients after sonography and MR angiography produce concordant findings (8–12). Our hypothesis was that with concordant sonographic and MR angiographic results, a subgroup of patients could appropriately undergo carotid endarterectomy without undergoing conventional angiography.

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From the Departments of Diagnostic Radiology (J.H., D.A.N., P.H.L., C.H.R., B.D.L.), Neurologic Surgery (F.B.M.), and Neurology (R.D.B.) and the Section of Biostatistics (C.D.S.), Mayo Clinic, Rochester, Minn.

Address reprint requests to J. Huston, MD, Department of Diagnostic Radiology, Mayo Clinic, 200 1st St SW, Rochester, MN 55950.

Methods

During a 5-month period, 51 consecutive patients believed to have clinically significant carotid stenosis and who were scheduled for cerebral angiography were recruited after informed consent was obtained. All patients had previously undergone carotid sonography within 2 weeks of the time MR angiography and conventional angiography would be performed. Although attempts were made to randomize the order in which the MR angiogram and the conventional angiogram were obtained, most patients had the MR angiogram the afternoon following the conventional angiographic study. One patient was unable to complete MR angiography, leaving 50 patients available for analysis. The study group included 34 men and 16 women, ranging in age from 42 to 87 years (median age, 70 years).

Patients were examined with a 1.5-T superconducting imaging system. MR angiography included a coronal 2-D phase-contrast scout image, a 2-D TOF sequence, and multislab 3-D TOF sequences. The 2-D TOF sequence comprised 80 axial sections 1.5-mm thick with a moving superior saturation band

TABLE 1: Sonographic criteria for assessing carotid artery stenosis

Degree of Stenosis, %	Velocity Criteria, cm/s		Ratio of Internal Carotid Artery to Common Carotid Artery
<40	<125	PSV	<1.6
40–69	125–229	PSV	>1.6–3.1
70–99	≥230	PSV	≥3.2
	≥70	EDV	

Note.—PSV indicates peak systolic velocity; EDV, end diastolic velocity.

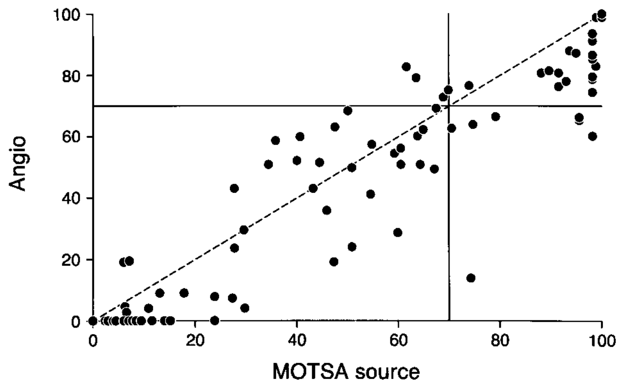

FIG 1. Internal carotid artery diameter stenosis measured on a conventional angiogram by blinded interpretation (*Angio*) versus that measured on multislab 3-D TOF MR angiogram (*MOTSA source*), with each dot representing a single carotid artery. The degree of stenosis was both overestimated and underestimated by the multislab 3-D TOF source technique.

and parameters of 40/8.7/1 (repetition time/echo time/excitations), a 256 × 128 matrix, a 60° flip angle, and a 16 × 16-cm field of view. The sequence was prescribed from superior to inferior, with the first section at the level of the petrous internal carotid artery as determined by the 2-D phase-contrast scout image. The multislab 3-D TOF sequence comprised seven slabs, each with 24 axial sections, 1-mm thick, and an overlap of four sections, with a superior saturation band and parameters of 35/6.9/1, a 256 × 192 matrix, a 30° flip angle with an inferior to superior variable sequence, and a 22 × 16-cm field of view. The sequence was centered such that the most superior slab was just inferior to the petrous portion of the internal carotid arteries. Postprocessing maximum-intensity-projection subvolumes were created to isolate each carotid artery on both the 2-D TOF and the multislab 3-D TOF sequences. Both carotid bifurcations were included on all MR angiograms. Mild motion was evident on the studies of a few patients, but did not result in nondiagnostic examinations.

Sonographic evaluation of the extracranial carotid system and vertebral arteries included both color Doppler and duplex spectral analysis with either a 5- or 7.5-MHz linear array transducer. First the common carotid artery and the extracranial internal and external carotid arteries were examined with color Doppler imaging. This examination allowed rapid identification of atherosclerotic plaque and associated areas of flow disturbance. Whenever a region of flow disturbance or visible evidence of stenosis was identified by color Doppler sonography, duplex spectral analysis was performed to quantify the degree of stenosis. Criteria for quantification of carotid stenoses by sonography was based on a study of 236 patients at our institution who had both sonography and cerebral angiography from January 1995 to February 1996 (Table 1) (13). Sonograms were reviewed by a single observer who was blinded to clinical information and results of other imaging studies.

Selective cerebral angiography was performed in all 51 patients via a femoral artery approach. Both biplane cut film and digital subtraction techniques were used. At least two and as many as four projections of the carotid bifurcations were obtained with conventional angiography.

Three experienced neuroradiologists reviewed the MR angiograms and the conventional angiograms blinded to clinical history and results of other diagnostic tests. The percentage of diametric stenosis was determined using the NASCET (14) measurement technique and a jeweler's eyepiece having 0.1-mm demarcations. Special conditions included defining a signal void on MR angiograms as 98% stenosis and near occlusion with collapse of the internal carotid artery (slim sign) on either the MR angiogram or the conventional angiogram as 99% diametric stenosis.

The conventional angiograms were randomized, and measurement of the right side was completed before the left side was reviewed. The multislab 3-D TOF studies were randomized, and the maximum-intensity-projection subvolume and source images were measured separately. The presence of a signal void was also recorded. Because it is the most sensitive sequence for detecting slow flow, occlusion, or patency of the internal carotid artery, the 2-D TOF sequence was used for these determinations. Previous work had shown considerable overestimation of the degree of stenosis with the 2-D TOF technique, and therefore direct measurements were not obtained (15).

The degree of stenosis for the conventional angiogram, the multislab 3-D TOF maximum-intensity-projection subvolumes, and the multislab 3-D TOF source images was defined as the average measurement recorded by the three blinded readers. A signal void was considered present on the 2-D TOF sequence when one was identified by at least two of the three blinded readers. The same criterion was used to identify occlusion. Blinded readings of the conventional angiograms were compared with the measurements of stenosis obtained at the time the examination was performed (clinical readings). The clinical measurements were typically made with the use of a ruler with 1-mm demarcations.

Receiver operating characteristic (ROC) analysis was used to assess the readers' ability to discriminate between diseased and normal arteries with each diagnostic technique. Results of conventional angiography were considered to represent the true disease state for each artery. An artery with a stenosis of 70% or greater was considered to be diseased; otherwise, the artery was considered normal. For each test, sensitivity (true-positive fraction) and 1 minus specificity (1 minus false-positive fraction) were calculated at several cut points. Two-sided 95% confidence intervals at a threshold of 70% stenosis were calculated exactly from the cumulative binomial distribution. The estimates of areas under the ROC curves, their standard errors, and the paired comparisons of areas were made with nonparametric techniques based on the work of Hanley and McNeil (16, 17).

Results

Using conventional angiograms as the reference standard, multislab 3-D TOF MR angiography tended to overestimate the degree of carotid stenosis; however, it underestimated stenoses by more than 5% in 12 arteries (Fig 1). Source images were more specific than maximum-intensity-projection subvolumes (Table 2). The coefficients for interobserver variation for the three blinded readers were as follows: conventional angiogram, κ = .97; multislab 3-D TOF maximum intensity projection, κ = .93; and multislab 3-D TOF source images, κ = .91. All 10 internal carotid artery occlusions

TABLE 2: Comparison of sensitivity, specificity, negative predictive value, positive predictive value, and accuracy (95% confidence interval) for blinded versus clinical readings of angiograms showing 70% or more stenosis

	Sensitivity	Specificity	Negative Predictive Value	Positive Predictive Value	Accuracy
Blinded interpretation					
Sonography	97.1 (84.7, 99.9)	75.4 (63.1, 85.2)	98.0 (89.4, 100.0)	67.4 (52.5, 80.1)	82.8 (73.9, 89.7)
3-D TOF MIP image	94.1 (80.3, 99.3)	84.1 (72.7, 92.1)	96.4 (87.5, 99.6)	76.2 (60.6, 88.0)	87.6 (79.4, 93.4)
3-D TOF source image	88.2 (72.6, 96.7)	88.9 (78.4, 95.4)	93.3 (83.8, 98.2)	81.1 (64.8, 92.0)	88.7 (80.6, 94.2)
3-D TOF signal void	88.2 (72.6, 96.7)	92.1 (82.4, 97.4)	93.6 (84.3, 98.2)	85.7 (69.7, 95.2)	90.7 (83.1, 95.7)
2-D TOF signal void	88.2 (72.6, 96.7)	78.5 (66.5, 87.7)	92.7 (82.4, 98.0)	68.2 (52.4, 81.4)	81.8 (72.8, 88.9)
Clinical reading					
Sonography	95.7 (85.2, 99.5)	90.7 (79.7, 96.9)	96.1 (86.5, 99.5)	89.8 (77.8, 96.6)	93.0 (86.1, 97.1)
3-D TOF MIP image	82.6 (68.6, 92.2)	92.3 (81.5, 97.9)	85.7 (73.8, 93.6)	90.5 (77.4, 97.3)	87.8 (79.6, 93.5)
3-D TOF source image	73.9 (58.9, 85.7)	94.2 (84.1, 98.8)	80.3 (68.2, 89.4)	91.9 (78.1, 98.3)	84.7 (76.0, 91.2)
3-D TOF signal void	73.9 (58.9, 85.7)	98.1 (89.7, 100.0)	81.0 (69.1, 89.8)	97.1 (85.1, 99.9)	86.7 (78.4, 92.7)
2-D TOF signal void	89.1 (76.4, 96.4)	94.4 (84.6, 98.8)	91.1 (80.4, 97.0)	93.2 (81.3, 98.6)	92.0 (84.8, 96.5)

Note.—MIP indicates maximum-intensity projection; TOF, time of flight.

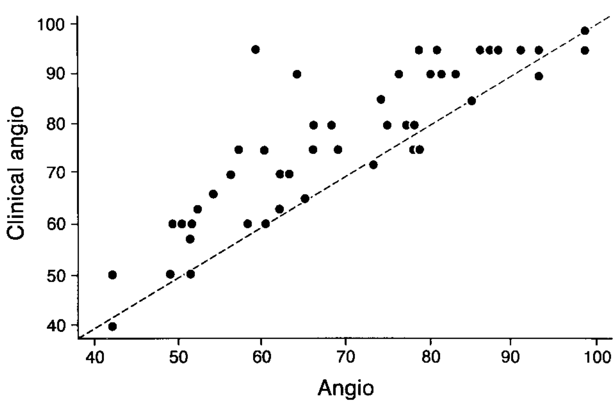

FIG 2. Internal carotid artery diameter stenosis measured on a conventional angiogram by clinical interpretation (*Clinical angio*) versus that measured on a conventional angiogram via blinded interpretation (*Angio*), with each dot representing a single carotid artery. The degree of stenosis was found on average to be 7% greater at the time of the clinical interpretation, which typically involved use of a ruler, as compared with the average of three blinded readers using a jeweler's eyepiece.

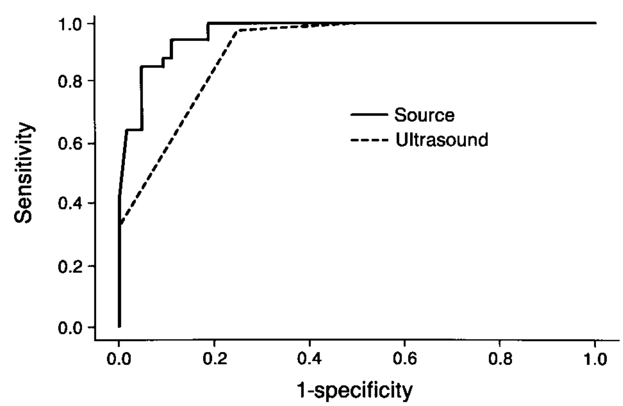

FIG 3. ROC curve for multislab 3-D TOF MR angiographic source images (*solid line*) and sonograms (*dotted line*) shows a significant difference in area under the curve, with superior performance by MR angiography (P = .0052).

were identified at sonography and 2-D TOF MR angiography.

The percentage of stenosis determined by a blinded reading was compared with the percentage of stenosis reported at the time angiography was performed. The blinded interpretation was determined by using a jeweler's eyepiece with 0.1-mm demarcations, and the clinical reading was typically obtained with a ruler having 1-mm demarcations. For carotid arteries with stenoses between 40% and 99%, the mean percentage of stenosis for the blinded reading was 70% and the mean percentage for the clinical reading was 77%, which was a statistically significant difference ($P <$ .0001) (Fig 2).

Sonography identified a total of 39 arteries with stenoses between 70% and 99%. When the angiograms of these 39 arteries were reviewed blindly, 23 of them were classified as having stenoses between 70% and 99%. The average of the three measurements for the blinded readers was less than 70% for the remaining 16 arteries. When the same 39 arteries were evaluated with the measurements made clinically at the time angiography was performed, quite different results were obtained. Thirty-four of the arteries were clinically interpreted as between 70% and 99% stenosed, while five were measured as less than 70%. This correlates with the significantly different measurements obtained between the blinded and the clinical readings of the conventional angiograms (Fig 2). The criteria for the sonographic interpretations were based on the clinical interpretation of conventional angiograms and therefore one would expect the superior correlation found with the clinical readings.

ROC curves were constructed for multislab 3-D TOF maximum-intensity-projection and source images. Although the source images showed superior performance, with 0.0054 difference in areas under the curve, the difference was not significant (P = .51). When multislab 3-D TOF source images were compared with sonograms, the MR angiographic technique showed superior performance, with 0.061 difference in the area under the curve, which was statistically significant (P = .0052) (Fig 3). Because of the categorical nature of the sonographic variables

TABLE 3: Comparison of sensitivity, specificity, negative predictive value, positive predictive value, and accuracy (95% confidence interval) for blinded versus clinical readings of angiograms showing 70% or more stenosis

	Sensitivity	Specificity	Negative Predictive Value	Positive Predictive Value	Accuracy
Blinded interpretation					
Sonography + MIP	91.2 (76.3, 98.1)	87.7 (77.2, 94.5)	95.0 (86.1, 99.0)	79.5 (63.5, 90.7)	88.9 (81.0, 94.3)
Sonography + source image	85.3 (68.9, 95.1)	90.8 (81.0, 96.5)	92.2 (82.7, 97.4)	82.9 (66.4, 93.4)	88.9 (81.0, 94.3)
Sonography + 3-D TOF signal void	85.3 (68.9, 95.1)	92.3 (83.0, 97.5)	92.3 (83.0, 97.5)	85.3 (68.9, 95.1)	89.9 (82.2, 95.1)
Sonography + 2-D TOF signal void	85.3 (68.9, 95.1)	80.0 (68.2, 88.9)	91.2 (80.7, 97.1)	69.1 (52.9, 82.4)	81.8 (72.8, 88.9)
Clinical reading					
Sonography + MIP	80.4 (66.1, 90.6)	96.3 (87.3, 99.6)	85.3 (73.8, 93.0)	94.9 (82.7, 99.4)	89.0 (81.2, 94.4)
Sonography + source image	71.7 (56.5, 84.0)	96.3 (87.3, 99.6)	80.0 (68.2, 88.9)	94.3 (80.8, 99.3)	85.0 (76.5, 91.4)
Sonography + 3-D TOF signal void	71.7 (56.5, 84.0)	98.2 (90.1, 100.0)	80.3 (68.7, 89.1)	97.1 (84.7, 99.9)	86.0 (77.6, 92.1)
Sonography + 2-D TOF signal void	87.0 (73.7, 95.1)	96.3 (87.3, 99.6)	89.7 (78.8, 96.1)	95.2 (83.8, 99.4)	82.0 (73.1, 89.0)

versus the continuous nature of the source variable, the trapezoidal rule used for investigating ROC area nonparametrically may have artificially accentuated the difference in the areas. Another way to do the ROC analysis is by using the binomial method. With this method, the area for the sonogram was 0.97 and there was no significant difference. The two statistical methods, nonparametric and binomial, yielded very different results, and further studies may be necessary to determine whether MR angiography or sonography is superior.

Three arteries with severe atherosclerotic changes had near occlusions, with extremely slow flow shown at angiography. One of these arteries was correctly categorized sonographically as between 70% and 99% stenosed, but was determined at MR angiography to be occluded. Another artery had such slow flow through the stenotic segment that it was categorized by sonography as 40% to 69% stenosed, while MR angiography showed a slim sign, and therefore the artery was defined as 99% stenotic. The third artery was incorrectly classified as occluded by both sonography and MR angiography.

Imaging results were analyzed on the basis of concordant sonographic and MR angiographic interpretations of carotid stenosis between 70% and 99%. This included the direct measurements from the maximum-intensity-projection and source images as well as the presence of a signal void on the multislab 3-D TOF and 2-D TOF sequences. Both the blinded and clinical interpretations of conventional angiograms were used as reference standards (Table 3).

Discussion

With the proved benefit of carotid endarterectomy, interest has grown in developing an alternative to conventional angiography for the accurate, preoperative identification of patients with clinically significant carotid stenosis. Noninvasive techniques, such as sonography, MR angiography, and CT angiography, offer less risk and lower cost. A strategy has been proposed to screen patients with sonography and then to confirm the presence of a 70% to 99% stenosis with MR angiography prior to endarterectomy (8–12). Conventional angiography would be reserved for patients with disparate sonographic and MR angiographic findings. Our hope was that an optimized multislab 3-D TOF technique would allow direct measurements from the MR angiograms.

In this study we were surprised by the number of times multislab 3-D TOF sequences underestimated the degree of stenosis as compared with conventional angiograms. Three conditions were associated with this underestimation, including high T1 signal within the atherosclerotic plaque, a high-velocity jet through the stenotic segment resulting in "ballooning" of signal, and a stenosis at the origin in association with a transverse orientation of the proximal internal carotid artery. Two arteries had such high T1 signal in the atherosclerotic plaque that portions of the plaque were confused with the patent lumen (Fig 4). Yaun et al (18) have shown that increased T1 signal in carotid atherosclerotic plaques can result from foam cells, fibrous plaque, and organized thrombus. Two arteries had intense MR angiographic signal at the site of a high-grade stenosis that measured less than that on the conventional angiogram (Fig 5). Presumably, the high-velocity coherent flow pattern yields a very high signal that is associated with partial-volume effects. Subtle pulsatility of the artery may increase the number of voxels that are included in the partial volume. Increasing the spatial resolution and cardiac gating might address this problem by offering smaller voxel sizes and fewer underestimations of stenosis. In two arteries with stenosis at the origin of the internal carotid artery, stenosis was underestimated owing to the transverse orientation of the proximal artery. When reviewing the source images of these arteries, the maximal stenosis was not appreciated because the orientation of the section was not perpendicular to the vessel lumen. Perhaps multiplanar reconstruction would be useful for evaluating arteries with these morphological characteristics (19).

The significant difference in the average measurement of stenosis for the three blinded readers as compared with that obtained by clinical interpretation most likely results from the different methods of measurement used. When arteries between 40% and 99% stenosis were reviewed, the clinical reading produced an average of 7% greater stenosis than did the blinded reading. Clinical measurements were typi-

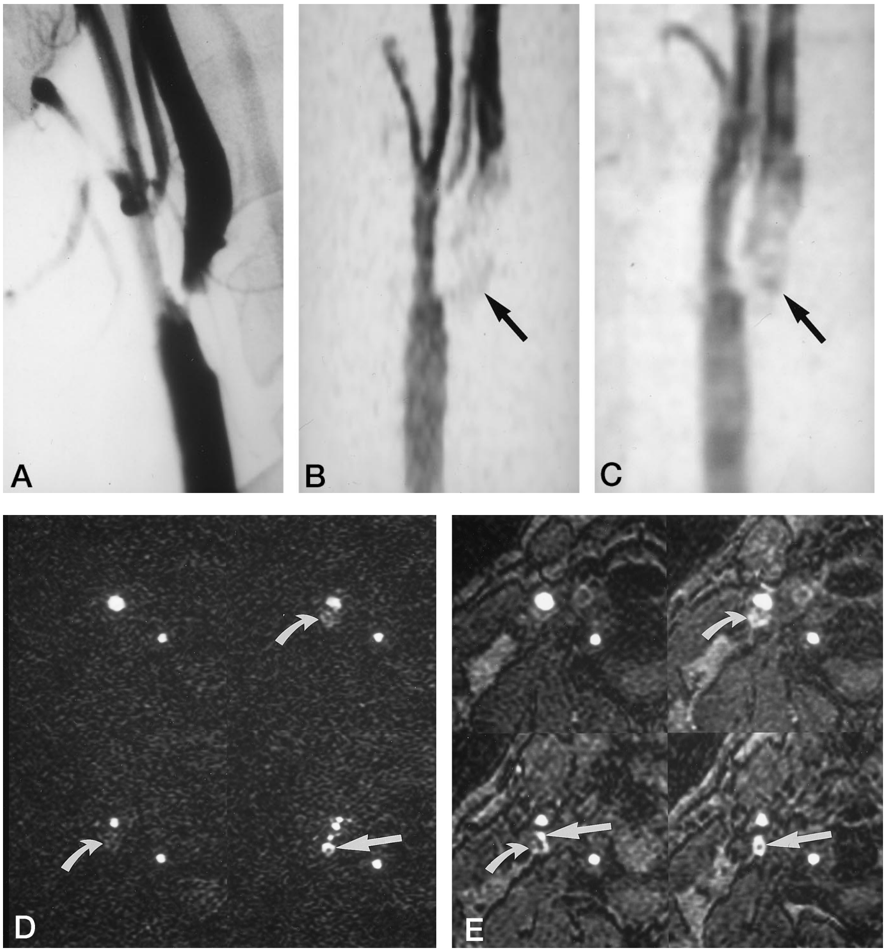

FIG 4. Underestimation of carotid stenosis owing to plaque with high T1 signal in a 48-year-old man.

Conventional angiogram (*A*) interpreted at the clinical reading as 90% stenosis and at the blinded readings as 81% stenosis. Two-dimensional TOF MR angiogram (*B*) and multislab 3-D TOF maximum-intensity-projection image (*C*) show how the plaque simulates a vascular lumen (*arrows*). A set of four source images shows the high-signal plaque (*curved arrows*) and internal carotid artery lumen (*straight arrows*) on the 2-D TOF (*D*) and the multislab 3-D TOF (*E*) sequences.

FIG 5. Underestimation of carotid stenosis caused by "ballooning" of MR angiographic signal through the stenotic segment in an 87-year-old man.

Conventional angiogram (*A*) interpreted at the clinical reading as 75% stenosis and at the blinded reading as 79% stenosis. Two dimensional TOF MR angiogram (*B*) shows a signal void (*arrow*). Multislab 3-D TOF image (*C*) shows intense signal at the stenosis (*arrow*) resulting in a measured stenosis less than that found at the conventional or blinded reading. Both the multislab 3-D TOF maximum-intensity-projection and source images showed 63% stenosis.

cally made with a ruler having 1-mm demarcations, whereas the blinded readings were made with a jeweler's eyepiece with 0.1-mm demarcations. However, Young et al (20) found no important differences among techniques widely used for measuring carotid stenosis, including visual impression (eyeballing) and use of calipers. The clinical interpretation could have been influenced by either the clinical setting or the results of previous sonograms, and existing studies support a contextual bias in radiologic interpretation (21, 22). One artery was determined to have a 90% stenosis by clinical measurement and a 28% stenosis on blinded review. This internal carotid artery had a signal void on 2-D TOF sequences, and a high-grade

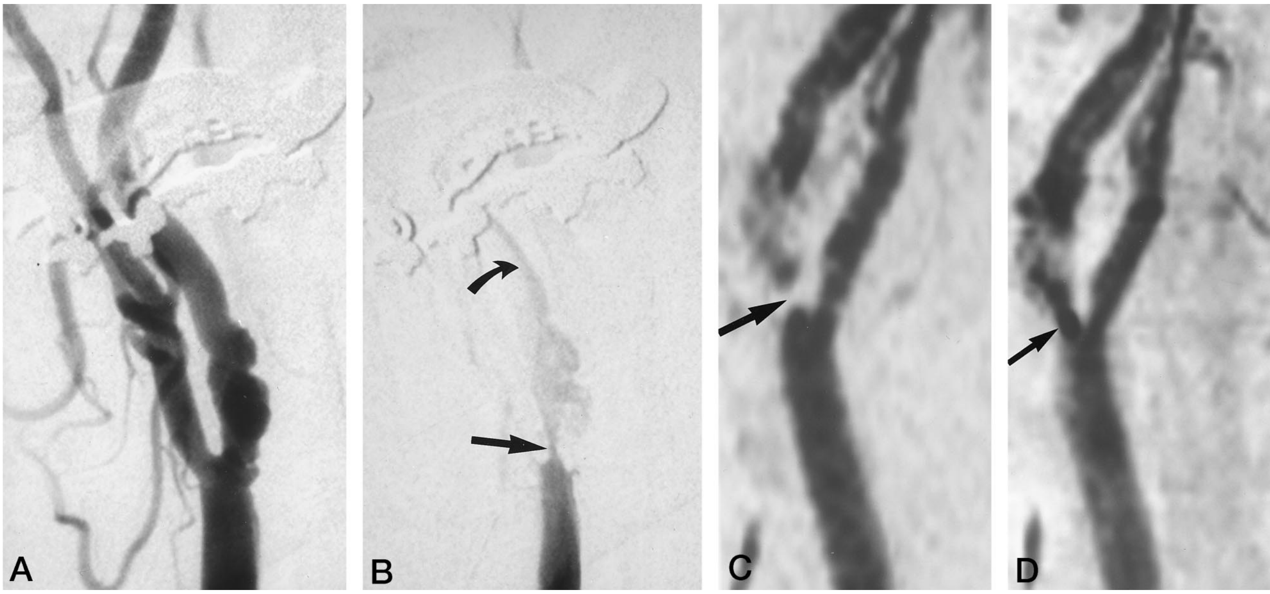

FIG 6. Significant discrepancy between the clinical and blinded interpretations of the conventional angiogram in a 64-year-old man. The ulcerated complex plaque (*A*) was interpreted as a 90% stenosis on the clinical reading and as a 28% stenosis on the blinded reading. Review of the first angiogram image with contrast (*B*) shows a narrow channel (*straight arrow*) proximal to faint filling of the internal carotid artery (*curved arrow*). Sonogram showed high-velocity flow corresponding to a 70% to 99% stenosis, and a high-grade stenosis was noted at endarterectomy. A signal void was present on the 2-D TOF maximum-intensity-projection image (*arrow*, *C*). Multislab 3-D TOF image shows a residual lumen that measured 58% on both the maximum-intensity-projection and source images (*arrow*, *D*). This may be an additional example of "ballooning" of MR angiographic signal associated with a high-velocity jet through the stenotic segment.

stenosis was found at surgery (Fig 6). On review, it appeared that a high-grade stenosis seen initially was quickly obscured by a complex ulcerated plaque. Perhaps the combining of imaging results is essential in some problematic cases.

Depending on which reference standard is used, the clinical or blinded reading, sensitivity and specificity for the MR angiographic techniques vary considerably (Table 2). Perhaps that difference can be explained in part by the large number of vessels clustered about the 70% stenosis level in this study. The 7% difference shifted a large number of arteries between categories (less than 70% compared with more than 70%) when the clinical reading was compared with the blinded reading reference. Unfortunately, the investigators are not certain which reference standard is more consistent with the measurement technique used in major clinical trials, and more investigation is required. The key point will be to determine a measurement technique that allows results to be in line with the major prospective studies, including NASCET.

In summary, we identified a subgroup of patients in whom we believe it is appropriate to proceed from sonography and MR angiography to carotid endarterectomy. This group consists of patients with sonographic findings of 70% to 99% stenosis and a signal void on multislab 3-D TOF MR angiograms. Sonography as the initial screening technique offers high sensitivity, ranging from 97% (blinded angiographic reading reference) to 96% (clinical angiographic reading reference). The addition of the signal void criterion increases the specificity and positive predictive value. Depending on the method of analysis used, this strategy offers a specificity ranging from 98% (clinical angiographic reading reference) to 92% (blinded angiographic reading reference) and a positive predictive value ranging from 97% (clinical angiographic reading reference) to 85% (blinded angiographic reading reference). This more restrictive use of MR angiographic findings has been adopted in part because of the recent availability of markedly improved MR angiographic techniques now offered with stronger MR gradients. These new techniques have demonstrated that both short echo times and tridirectional flow-compensated multislab 3-D TOF sequences more accurately depict the arterial lumen at points of stenosis than do the MR angiographic techniques used in this study. Also, contrast-enhanced MR angiography of the carotid arteries may play an important role in the future (23). Additional trials will be required to determine if stronger-gradient MR angiography, possibly with the addition of bolus contrast techniques, will allow direct measurement of stenoses on MR angiograms. For standard-gradient MR angiography, the presence of a signal void on 3-D multislab sequences obtained after sonography that shows a 70% to 99% stenosis indicates the presence of a surgically significant lesion.

Acknowledgments

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