Assessment of carotid artery stenosis by ultrasonography, conventional angiography, and magnetic resonance angiography: Correlation with ex vivo measurement of plaque stenosis

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Purpose: Several studies have investigated the correlation between Doppler ultrasonography (DUS), angiography (CA), and magnetic resonance angiography (MRA) in the evaluation of stenosis of the carotid bifurcation. However, these studies suffer from the lack of a true control—the lesion itself—and therefore conclusions about the diagnostic accuracy of each method remain relative. To determine the absolute accuracy of these modalities, we have prospectively studied lesion size with DUS, MRA, and CA in 28 patients undergoing 31 elective carotid endarterectomies and compared the percent of carotid stenosis determined by each technique to the carotid atheroma resected en bloc.
Methods: All patients were evaluated by each modality within 1 month before the thromboendarterectomy. With DUS, stenosis size was determined by standard flow criteria. For angiography and MRA, stenosis was defined as residual lumenal diameter/estimated normal arterial diameter (European Carotid Surgery Trial criteria). At surgery the carotid atheroma was removed en bloc in all patients. Patients in whom the lesion could not be removed successfully without damage were excluded from the study. Stenosis of the atheroma was determined ex vivo with high-resolution (0.03 mm^3) magnetic resonance and confirmed by acrylic injection of the specimen under pressure and measurement of the atheroma wall and lumen.
Results: The measurements of the ex vivo stenosis by high-resolution magnetic resonance imaging correlated closely with the size of stenosis determined by the acrylic specimen casts ($r = 0.92$). By ex vivo measurement, the lesions were placed in the following size categories: 40% to 59% stenosis ($n = 2$), 60% to 79% stenosis ($n = 6$), 80% to 89% stenosis ($n = 7$), and 90% to 99% stenosis ($n = 16$).
Conclusions: In general, the correlation of measurements of ex vivo stenosis with all modalities was good in these severely diseased arteries, although it was better for DUS ($r = 0.80$; $p < 0.001$) and MRA ($r = 0.76$; $p < 0.001$) than for CA ($r = 0.56$; $p < 0.05$). (J VASC SURG 1995;21:82-9.)

Two recent multicenter clinical trials have established that carotid endarterectomy is effective in preventing stroke in patients with symptoms with an internal carotid artery (ICA) stenosis greater than 70 percent.[1-4] Both trials used x-ray angiography (XRA) to establish severity of stenosis. However, XRA is an inherently two-dimensional technique and the apparent degree of stenosis can depend on the viewing angle of a severely diseased arterial segment.[5] A more accurate determination of lumenal diameter would be expected from magnetic resonance angiography (MRA), which is an inherently three-dimensional technique, or from Doppler ultrasonography (DUS), which measures flow through the narrowed lumen.

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The relative ability of these techniques to assess carotid stenosis can be established by comparing them to the operative specimen providing that the morphologic manipulations required to measure the stenosis are minimized. In this study we have used high-resolution magnetic resonance imaging (MRI) (0.03 mm^3 voxels) to avoid sectioning or casting lesions. With this independent standard established on specimens removed en bloc at the time of surgery, we have compared the ability of XRA, MRA and DUS to categorize accurately carotid stenoses of patients undergoing carotid endarterectomy. Our data demonstrate that MRA and DUS are superior to XRA in categorizing lesions in these severely stenosed carotid arteries.

METHODS

Patient population

Between December 1990 and May 1994, 31 carotid endartectomy specimens, which could be removed en bloc during carotid endartectomy, were studied. These 31 specimens came from 28 patients: 30 from men and one from a woman. An additional three specimens removed from three patients were excluded from the study because the plaque was damaged during surgery. The patients ranged in age from 57 to 82 years. Thirty arteries were studied with XRA, 29 arteries were studied with MRA, 28 arteries were studied with DUS, and 27 arteries were studied with all three modalities. All studies were done less than 1 month before thromboendarterectomy. At surgery the carotid atheroma was removed en bloc in all patients.

Imaging studies

XRA was performed with digital subtraction angiography. Early studies were performed with a DF5000 LUA (GE Medical Systems, Milwaukee, Wis.) with an image intensifier matrix of 512 × 512. More recent studies were performed with an Integris V3000 (Philips Medical Systems, Best, The Netherlands) at 1024 × 1024 resolution.

MRA was performed on a 1.5 T Magnetom (Siemens, Erlangen, Germany) with a linearly polarized transmit-receive neck coil.[6] Assessment of stenosis was performed on the basis of three-dimensional image acquisition studies. Both sagittal and transverse three-dimensional studies were performed.[7,8] In the sagittal acquisition, the slab was centered on the carotid bifurcation and a three-dimensional gradient recalled echo sequence (fast imaging with steady-state precession [FISP]) was performed. The image resolution was 0.9 × 1.0 × 1.25 mm. After that, a three-dimensional transverse slab was performed at the level of the identified lesion with image resolution of 0.8 × 1.0 × 1.1 mm. The transverse acquisition was performed with parameters providing higher contrast of flow to stationary material than in the sagittal acquisition, because flow saturation is less of a concern in axial studies. In MRA studies, projection images can be calculated by postprocessing without requiring additional image acquisition. Maximum intensity projection images were calculated at 15-degree rotational intervals about the longitudinal axis of the patient.

Color-flow Doppler imaging was performed in earlier studies with either a 7.5 or 5 MHz transducer (Quantum Quad-1; Quantum Medical Systems, Issaquah, Wash.) and in later studies with a 7.0 or 5 MHz transducer (Acuson XP; Acuson, Mountain View, Calif.). Flow measurements were obtained with the Doppler angle at 60 degrees or less to the course of the vessel. Longitudinal and transverse imaging of the carotid arteries was performed. Peak systolic and end-diastolic velocities in the common carotid artery (CCA), ICA, and external carotid artery were recorded and ICA/CCA velocity ratios were determined.

In vivo assessment of stenosis

The data for each modality were gathered independently. All images were read in a blinded fashion. The degree of stenosis shown by MRA, XRA, and MRI studies was graded according to the criteria of the European Carotid Surgery Trial.[3,4] The criteria of the European Carotid Surgery Trial determine the degree of stenosis by finding the minimum value of the ratio of the residual ICA lumen to the estimated normal ICA lumen at the same level. This was chosen rather than the North American Symptomatic Carotid Endarterectomy Trial criteria because the North American Symptomatic Carotid Endarterectomy Trial criteria require determination of the "normal" ICA just distal to the lesion, bulb, and poststenotic dilation. That information is not available from the specimen, whereas it is straightforward to determine both the lumenal diameter of the stenosed channel and the normal lumen of the ICA from the specimen.

All available views in the x-ray studies were reviewed to determine which view showed the greatest apparent stenosis. On the image showing the greatest degree of stenosis, contours were drawn of the estimated lumen of the normal vessels. Measurements were made with a 7X jeweler's magnifying loupe with 0.1 mm divisions of the residual ICA

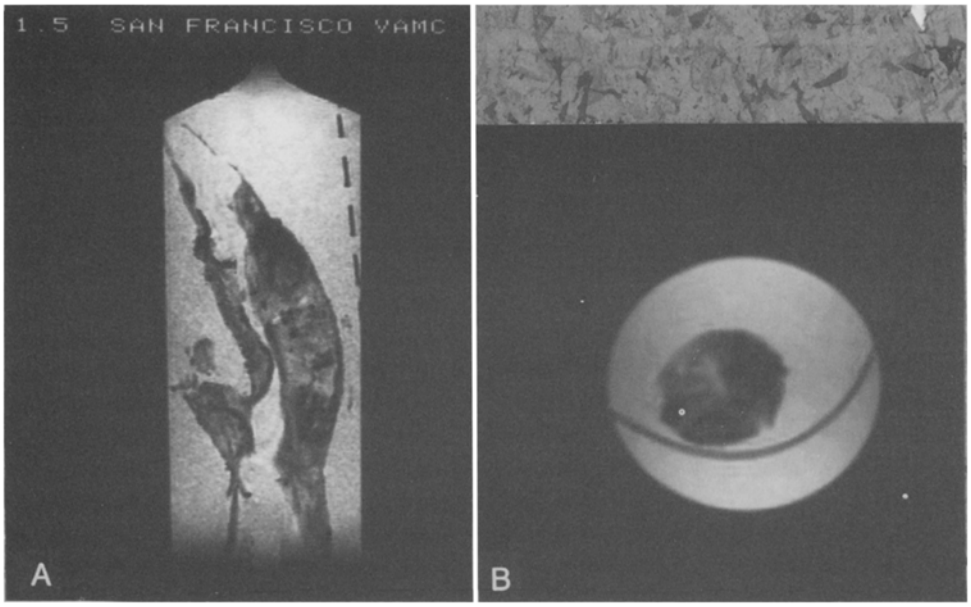

Fig. 1. High-resolution MRIs of endarterectomy specimen. **A,** One slice through ICA and ECA, in longitudinal axis of specimen. **B,** Transverse slice through specimen.

lumenal diameter and the diameter of the estimated normal ICA lumen at the level of the maximal degree of stenosis. The ratio of those two values was the percent stenosis assessed by XRA.

A similar procedure was adopted for the MRA study. The maximum intensity projection images were reviewed to determine the view that demonstrated the maximum apparent stenosis. Lumenal contours of the estimated normal lumen were drawn, as for the x-ray study, and the degree of stenosis was measured. It is not uncommon for there to be complete interruption of the intralumenal signal in MRA studies of high-grade stenosis.[8] Complete occlusion is differentiated from high-grade stenosis on MRA by determining the presence of cranial-directed flow in the carotid canal at the level of the intrapetrous carotid artery. In the nine cases in which there was signal interruption but the vessel was shown to be patent by the detection of distal flow, a stenosis grade of 99% was assigned.

Carotid artery stenosis was assessed from DUS on the basis of hemodynamic changes. A diameter stenosis was assigned on the basis of the measured peak systolic velocities, end-diastolic velocities, and the ICA/CCA velocity ratio.[9] Other ultrasonographic indicators of significant carotid artery disease, such as a markedly narrowed lumen, poststenotic dilation with turbulence, absent diastole in the common carotid artery, or a tardus parvus waveform, were also considered in the determination of the extent of disease.

Specimen evaluation

The endarterectomy specimen was placed in a syringe of saline solution, to which a small amount of gadolinium diethylenetriaminepentaacetic acid, a magnetic contrast agent, had been added and imaged within 8 hours of surgery. Care was taken to flush the specimen to remove all air bubbles. Three-dimensional data sets were obtained that were postprocessed to provide images in the longitudinal and transverse planes (Fig. 1). The longitudinal images were reviewed to serve as a "roadmap" of the overall lumenal configuration and to help identify the region of maximal stenosis. Maximum stenosis was ultimately determined from images transverse to the ICA lumen. The inner and outer boundaries of the plaque were evaluated and the minimum and maximum lumenal diameters, lumenal area, plaque diameter, and plaque area were measured. In seven cases the patent lumen could not be detected and a stenosis value of 99% was assigned to those specimens.

All three in vivo modalities are intended to provide a measure of the reduction in cross-sectional area of the vessel lumen but on a scale referenced to the lumenal diameter. XRA and MRA evaluate reduction of lumenal diameter by measuring diameter stenosis from projection images with the implicit

assumption that the lumen is circular. DUS measurements, which are sensitive to variations in hemodynamic flow and hence to area stenosis, are typically converted to a scale that determines the diameter reduction, again assuming a circular lumen. To provide a consistent reference parameter with which to compare all three modalities, the "effective diameter" of the lumen was determined by calculating the diameter of a circle with the same area as that of the lumen of the specimen. The degree of diameter stenosis was then calculated from the ratio of the effective lumenal diameter to the diameter of the plaque.

Because we were concerned about the extent to which the specimens retained their luminal dimensions ex vivo, we examined three of the specimens while varying the intraluminal pressure. Tubes were placed around each branch of the specimen and the whole system was enbedded in epoxy. Pressure was then applied through the CCA branch while the other two branches were occluded. Pressure was varied between 50 and 200 mm Hg. The specimens were imaged at all pressure levels and no variation in the intraluminal areas could be detected. Although it is probable that plaque that has different compositions might respond differently to variation in intraluminal pressure, this small study indicates that in some cases the lumen of the ex vivo specimen closely matches that of the lumen before endarterectomy.

As a validity check on the MRI measurements of the specimen lumen, casts of six plaques were made. The specimens were injected with epoxy and the plaque was removed once the epoxy had set. Measurements of the minimum diameter and the orthogonal diameter in the stenotic region of the cast were measured with calipers. Similar measurements were made at locations that were clearly identifiable on both the cast and the imaging studies, such as at the origins of the internal and external carotid arteries.

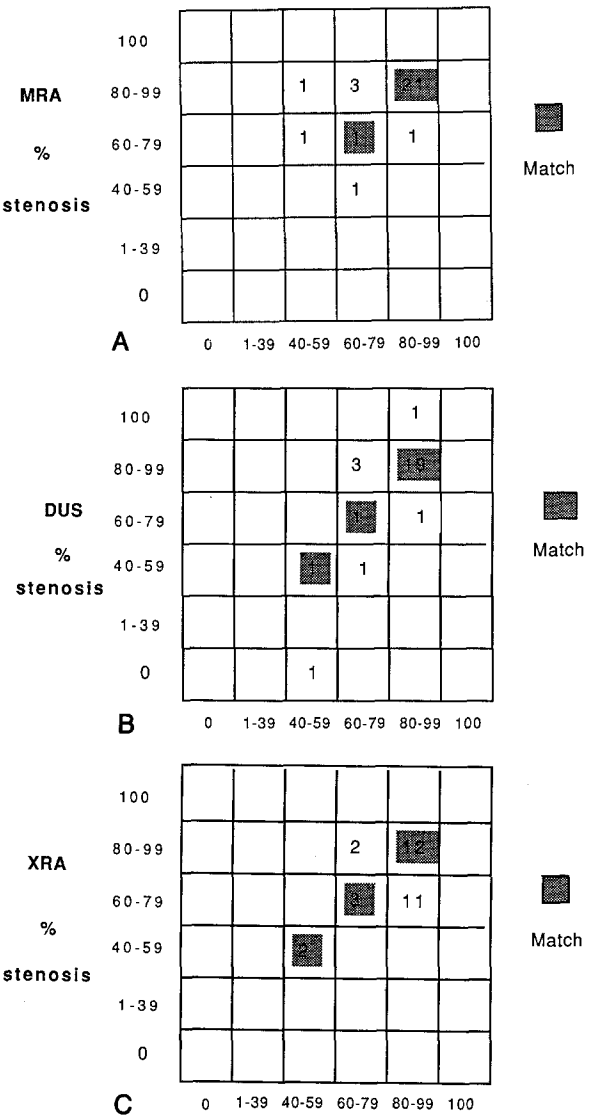

Fig. 2. Comparison by grade of stenosis of specimen with MRA ($r = 0.76$; $p < 0.001$) **(A)**, DUS ($r = 0.80$; $p < 0.001$) **(B)**, and XRA ($r = 0.56$; $p < 0.005$) **(C)**. All are Spearman rank correlation coefficients.

Data analysis

In each modality the reduction in diameter of the ICA was categorized as follows: mild (1% to 39%), moderate (40% to 59%), severe (60% to 79%), critical (80% to 99%), and occluded (100%). Comparisons between size of stenosis as determined by MRA, DUS, and XRA and ex vivo specimen stenosis determined by high-resolution MRI were made with the Spearman rank correlation coefficient. In the 27 specimens in which in vivo MRA and XRA studies were obtained, the mean value of the stenosis was calculated.

RESULTS

Ex vivo measurement of stenosis. By ex vivo measurement, the 31 endarterectomy specimens were placed in the following categories: two lesions were moderate, six were severe, and 23 were critical. Of the critical stenoses, seven were graded as 80% to 89% stenosis and 16 were graded as 90% to 99% stenosis.

The ex vivo measurements of specimen lumen size correlated closely with those determined from the acrylic specimen casts ($r = 0.92$).

Comparisons with imaging data. Overall, our

Table I. Agreement of stenosis with specimen

	MRA (%)	*DUS (%)*	*XRA (%)*
Overestimate	17	14	6
Match	76	75	57
Underestimate	7	11	37

study showed that the correlation of measurement of ex vivo stenosis with all three modalities was quite good in these severely diseased arteries, although the correlation was better for DUS ($r_s = 0.76$) than for XRA ($r_s = 0.56$). The agreement within categories of stenosis is summarized in Table I.

A comparison of the 29 MRA studies with measurements of the specimens revealed that the degree of stenosis agreed with the ex vivo data in 22 cases (76%). MRA overestimated the degree of stenosis in five cases (17%) and underestimated stenosis in two cases (7%) (Fig. 2, *A*). The degree of stenosis measured in the 28 DUS studies agreed with that measured from the specimen in 21 cases (75%). DUS overestimated the degree of stenosis in four cases (14%) and underestimated the degree of stenosis in three cases (11%) (Fig. 2, *B*). A comparison of the 30 XRA studies with measurements from the specimen found that the degree of stenosis agreed in 17 cases (57%). XRA depicted the stenosis as greater than that measured with the specimens in only two cases (6%). However, the stenosis was underestimated with XRA in 12 cases (37%) (Fig. 2, *C*).

Of the 23 specimens determined to have critical stenosis, MRA and DUS correctly determined the degree of stenosis in 95% (21/22) and 90% (19/21), respectively. The degree of stenosis assessed in both those modalities show better agreement with measurements made from the specimen in arteries graded as having critical stenosis than they do over all grades of stenosis. In contrast, XRA correctly determined the degree of stenosis in only 52% (12/23) of critical cases, which is the same rate of agreement as that of XRA with the ex vivo measurements for the entire group. In 11 (48%) of 23 arteries determined by ex vivo measurement of the specimen to have critical stenosis, XRA underestimated the degree of stenosis.

DISCUSSION

This study is consistent with previous reports that show that XRA tends to underestimate the degree of vascular stenosis.[10-12] However, an analysis of the relative correlations of the different modalities with measurement of the specimen lumen must take into account the unique data acquisitions of each modality. The degree of ICA stenosis assessed by XRA and MRA was determined from the apparent reduction in the lumenal diameter as measured from projection images. In XRA, two projection images were acquired and the degree of stenosis assigned was the maximum measured from the two views. In MRA, data were postprocessed to provide multiple views of the carotid arteries (in 15-degree increments) and the degree of stenosis was again the maximum measured from all projections. In DUS, flow velocities and flow indexes were used to determine diameter stenosis in cooperation with wave and spectral analysis. In principle, flow indexes are independent of viewing angle and reflect only the degree of area reduction of the insonated artery.

The accuracy of XRA in assessing arterial stenosis is known to depend on geometric considerations.[5] Evaluation of arterial stenosis from measurements of diameter width on projection XRA images is justified only for a circular lumen. On the axial, high-resolution MRIs of the specimens in this study sample, the lumenal cross sections were noted to have a wide variety of geometric shapes and were never circular. Projection images, particularly when only two views are obtained, are liable to large variations in the assessed degree of stenosis. In contrast, MRA data are inherently three-dimensional, allowing the creation of a relatively large number of views from one data set and providing a higher probability of detecting the maximal diameter narrowing.

Previous studies assessing the reliability of MRA to evaluate stenosis of the carotid bifurcation used XRA as the standard. These studies suggested that MRA tended to overestimate the degree of stenosis, particularly for more severe degrees of stenosis,[13,14] and attributed this overestimation by MRA to signal loss caused by disturbed flow patterns. We found that compared with ex vivo measurement of the lesion, there is only a slight tendency for MRA to overestimate the degree of stenosis in these severely diseased arteries, whereas XRA often underestimates the degree of lumenal stenosis.

As expected, DUS correlated closely with the measured degree of stenosis in our resected speci-

mens. DUS criteria for estimating the degree of stenosis of the ICA have been evaluated critically and shown to correlate with the clinical significance of carotid artery disease.[15,16] As in the case of MRA, when XRA was held as the standard, DUS appeared too variable to be used reliably.[17,18] Our data and those of Alexandrov et al.[12] indicate that the variability lies not with DUS but with XRA.

Because all patients were treated operatively, the lesions represented here were weighted toward those with more severe degrees of stenosis. This study therefore cannot address the question of the reliability of the various modalities in assessing more moderate degrees of stenosis.

The lumen could not be detected on high-resolution MRI in seven cases but was visible in all in vivo studies. For a typical ICA, a residual lumen of less than 0.3 mm would represent a stenosis of greater than 96%. One explanation for the discrepancy between the in vivo and specimen studies is that the high-contrast properties of MRA and XRA imply that a patent lumen on a digitized image will occupy at least one image pixel and possibly two image pixels independent of the true size of the lumen. Another possibility is that the lumen collapsed after resection and was therefore not visible on the specimen study.

In considering the utility of MRA, it should be emphasized that these results were obtained on one MRI system and at this relatively early stage in the evolution of this technology there is a range of hardware capabilities and a range of operator experience in obtaining and evaluating these studies. There is the potential, however, for substantial improvements in the accuracy that MRA has demonstrated in assessing carotid stenosis. These include improvements in resolution, reduction in sensitivity to flow disturbances, and improved assessment of the MRA data by review of individual slices transverse to the stenosed vessel. Research on the noninvasive characterization of atherosclerotic plaque with MRI is also being actively pursued.[19]

The results of this study show that measurement of stenosis in carotid endarterectomy specimens correlates better with noninvasive imaging than with XRA. This result supports the continued use of DUS as a screening technique. When an additional modality is needed for establishing the degree of stenosis at the carotid bifurcation, MRA is better than XRA in patients with severely diseased carotid arteries. The role of MRA in assessing lesser degrees of stenosis awaits further data. Current clinical trials have found that there is a correlation between XRA-determined stenosis and stroke risk. Our data suggest that imaging with DUS or MRA would define this correlation further and therefore the role of carotid endarterectomy in the prevention of stroke.

REFERENCES

1. North American Symptomatic Carotid Endarterectomy Trial (NASCET) Steering Committee. North American Symptomatic Carotid Endarterectomy Trial: methods, patient characteristics, and progress. Stroke 1991;22:711-20.
2. North American Symptomatic Carotid Endarterectomy Trial Collaborators. Beneficial effect of carotid endarterectomy in symptomatic patients with high grade carotid stenosis. N Engl J Med 1991;325:45-453.
3. European Carotid Surgery Trialist's Collaborative Group. MRC European Carotid Surgery Trial: interim results for symptomatic patients with severe (70-99%) or with mild (0-29%) carotid stenosis. Lancet 1991;337:1235-43.
4. Hankey G, Warlow C. Symptomatic carotid ischaemic events: safest and most cost effective way of selecting patients for angiography, before carotid endarterectomy. Br Med J 1990;300:1485-91.
5. Zwiebel W, Austin C, Sackett J, et al. Correlation of high-resolution, B-mode and continuous wave Doppler sonography with arteriography in the diagnosis of carotid stenosis. Radiology 1983;149:523-32.
6. Anderson C, Saloner D, Lee D, Fortner A. Dedicated coil for carotid MR angiography. Radiology 1990;176:868-72.
7. Masaryk AM, Ross JS, DiCello MC, Modic MT, Paranandi L, Masaryk TJ. 3DFT MR angiography of the carotid bifurcation: potential and limitations as a screening examination. Radiology 1991;179:797-804.
8. Anderson CM, Saloner D, Lee RE, et al. Assessment of carotid artery stenosis by MR angiography: comparison with x-ray angiography and color-coded Doppler ultrasound. AJNR Am J Neuroradiol 1992;13:989-1003.
9. Bluth E, Stavros A, Marich K, et al. Carotid duplex sonography: a multicenter recommendation for standardized imaging and Doppler criteria. Radiographics 1988;8:487-506.
10. Rubin J, Bondi J, Rhodes R. Duplex scanning versus conventional arteriography for the evaluation of carotid artery plaque morphology. Surgery 1987;4:749-54.
11. Ricotta J, Bryan F, Bond M, et al. Multicenter validation of real-time (B-mode) ultrasound, arteriography, and pathologic examination. J VASC SURG 1987;6:512-20.
12. Alexandrov A, Bladin C, Maggisano R, Norris J. Measuring carotid stenosis: time for a reappraisal. Stroke 1993;24: 1292-6.
13. Mittl RJ, Broderick M, Carpenter J, et al. Blinded-reader comparison of magnetic resonance angiography and duplex ultrasonography for carotid artery bifurcation stenosis. Stroke 1994;25:4-10.
14. Huston J III, Lewis B, Wiebers D, Meyer F, Riderer S, Weaver A. Carotid artery: prospective blinded comparison of two-dimensional time-of-flight MR angiography with conventional angiography and duplex US. Radiology 1993;186: 339-44.
15. Moneta G, Taylor D, Zierler R, Kazmers A, Beach K, Strandness D. Asymptomatic high-grade internal carotid artery stenosis: is stratification according to risk factors or duplex spectral analysis possible? J VASC SURG 1989;10:475-83.
16. Roederer G, Langlois Y, Jager K, et al. The natural history of

carotid arterial disease in asymptomatic patients with cervical bruits. Stroke 1984;15:605-13.
17. Haynes R, Taylor D, Sackett D, Fox A, Rankin R, Barnett H. Poor performance of Doppler in detecting high-grade carotid stenosis [Abstract]. Clin Res 1992;40:184A.
18. Barnett H, Barnes R, Robertson J. The uncertainties surrounding carotid endarterectomy. JAMA 1992;268:3120-1.
19. Yuan C, Tsuruda J, Beach K, et al. Techniques for high resolution MR imaging of atherosclerotic plaque. J Magn Reson Imaging 1994;4:43-50.

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DISCUSSION

Dr. D. Eugene Strandness, Jr. (Seattle, Wash.). This study emphasizes once again the problems that are associated with attempts to quantify by any means the degree of stenosis that will satisfy clinical needs. Unfortunately, as you have already heard, the North American Symptomatic Carotid Endarterectomy Trial (NASCET) and the European Carotid Surgery Trial use different methods of measurement that have confused the issue further. For example, in the European Carotid Trial, a 50% diameter reduction of the bulb is a 0% diameter reduction by the NASCET method. To complicate the problem further, Dr. Barnett has insisted that arteriography be used as the screening method. He claims that it is the only accurate method of determining a 70% stenosis. This stance is based on the poor performance of many of the centers in NASCET with ultrasound screening. Unfortunately, I must point out to you that the problem related to the NASCET trial has not been emphasized. In fact, the studies done in NASCET were not standardized and many of the systems and techniques used were not state of the art. This problem was brought to the attention of the NASCET investigators during the trial, and they ignored it.

This conclusion by Dr. Barnett leaves many surgeons in a difficult position, because if only arteriography is used for screening, large numbers of patients will undergo the dye study who do not need it.

I think this study brings into clear focus many of the problems associated with each of the modalities that are available. Clearly magnetic resonance angiography (MRA) cannot be used as a screening test for several reasons. First, it is too expensive. Second, most clinical MRA units are so busy with other testing procedures that they make it very difficult to use it for this purpose. This is certainly the case in our hospital. Third, there is a significant number of our patients who cannot be studied, because of either claustrophobia, the presence of metal such as pacemakers, or the inability to hold their breath. Also, as noted here, overestimation of the degree of stenosis for low-grade lesions could pose a serious problem. This deficiency of MRA may be overcome, but it is going to take time.

Although we could discuss at great length the problems associated with each of the modalities, I think there are more important questions that you might want to address: (1) You did not suggest an algorithm that might be used for the two large groups of patients (i.e., patients with and without symptoms); what do you propose? (2) You did not define any diagnostic criteria for a 70% diameter reduction. Would you accept and, perhaps more directly, do you use the criteria that were presented by Dr. Greg Moneta and the Oregon group (J VASC SURG 1993;17:152-9) before this Society in the stroke meeting last March? (3) Because ultrasonography and magnetic resonance imaging (MRI) seem to work for high-grade lesions, what is your experience with the lesser lesions? Do you think that MRI, which may overcall lesions in this category, should not be applied until further work has been done? (4) What would you do with a patient with symptoms who, by arteriography, had a 50% diameter–reducing lesion? (5) How would you handle a patient with symptoms who had a greater than 80% stenosis by duplex ultrasonography and a 60% diameter reduction by arteriography?

These are important questions because they are what we encounter in daily life. I asked these last two questions because Dr. Barnett has insisted that what we need is precision, and he is perfectly satisfied that a radiologist with a calibrated eyepiece represents true precision.

Dr. Xian M. Pan. We agree that MRA is not to be used as a screening technique. Not only is the cost too high but it is unproved technology in lesser degrees of stenosis.

I will respond to each of your questions in order:

First, our algorithm is to use ultrasonography as a screening technique and follow up symptom-free patients with known stenoses every 6 months. Before completing this study, we have obtained angiograms on all patients who have stenoses greater than 80% by screening ultrasonography.

Now we are planning to move toward using only ultrasonography and either head computed tomography or MRI, which in our institution would include MRA before surgery. Unfortunately, at our institution the neurologists have very little experience with ultrasonography and are going to continue doing angiograms on their patients.

Second, would we accept the Moneta criteria for Doppler ultrasonography, which compensates for the inaccuracies of the NASCET angiographic grading criteria? This may be an appropriate adjustment for patient management and your referring neurologists' peace of mind, but it avoids the real problem. If the decision to perform a

carotid endarterectomy is to be based on the degree of stenosis, we should have the most accurate estimate of the stenosis available. Doppler ultrasonography, as currently practiced, is excellent at predicting severity of stenosis. Why should we change it to match a modality that is potentially less accurate?

Third, what is our experience with MRA in the lesser degrees of stenosis? We have only five specimens in the 60% to 79% stenosis category and only two lesions of less than 60% stenosis. MRA appeared to overcall these lesions, but the numbers are too few to be certain.

Regarding your last two questions, what would we do with a patient with symptoms who has 50% stenosis by angiography and a symptom-free patient who has a disagreement between angiography and ultrasonography? A patient on our service with a single neurologic event and 50% stenosis by angiography would also have undergone ultrasonography. If the ultrasound examination verified 50% stenosis, this patient would not be operated on unless he had repetitive events. In cases of disagreement between angiography and Doppler ultrasonography, the decision to proceed with endarterectomy is made on the basis of Doppler ultrasonography.

Finally, we agree with you that Dr. Barnett is confusing the precise display of the lines representing the luminal edge of the arteries with accuracy. In fact, the fuzzy line of the MRA and the flow velocities of the Doppler ultrasound examination may be much more accurate.

Dr. Wesley S. Moore (Los Angeles, Calif.). This is the way a comparative analysis should be carried out. You have clearly identified that the angiogram is not the gold standard. It is the lesion that is the gold standard and therefore all other tests are to be compared to the lesion and not some other faulty examination.

My concern is that you have chosen to use the European Carotid Surgery Trial, or the European criteria, for measuring stenosis. I understand why you did that, and that is that you do not remove a normal portion of the internal carotid artery to carry out that comparison. I think that is all right when you compare the angiogram according to the European criteria and the specimen according to the European criteria. What I am concerned about is that the duplex ultrasound examination and the MRA appear to correlate well but with a faulty measurement. Had you used the NASCET or the Asymptomatic Carotid Atherosclerosis Study criteria for measuring carotid artery stenosis, how well would the ultrasound examination and the MRA correlate?

Dr. Joseph H. Rapp. As you pointed out, we cannot use the NASCET criteria. Therefore I cannot answer your question. The European criteria and the NASCET criteria are different measurements. The European criteria measure the total amount of atherosclerosis at a given point, and the NASCET criteria compare that degree of atherosclerosis and luminal narrowing with the distal internal carotid artery. The European criteria speak to the atherosclerotic burden. It is my bias that this is going to be a more accurate way of looking at the disease process. As to the accuracy of our ex vivo measurement, we were concerned about this, which is why we did the casts (i.e., to verify our ex vivo imaging). It worked very well, although no method may be perfect.

Dr. Strandness. The issue is pretty clear. We have two different worlds here, both claiming that a 70% diameter reduction is causing the problem, and when you get right down to it, neither one is 70%. I do not care how you define it, I think you have hit the nail right on the head: The NASCET criteria do not tell you about the total atherosclerotic role to the bifurcation, and basically all of our original ultrasound studies documenting the role of duplex ultrasonography were based on measurements from the bulb, which is something a lot of people do not realize. We did not use the NASCET criteria to verify duplex ultrasonography. I think you are right. We are in the real world, where precision is wonderful, but we are not there yet, regardless of any method.

Dr. Rapp. We presented these data last week to our neurologists, and although they would love not to do angiography, they essentially refuse to accept doing a carotid endarterectomy without the angiogram, because they are adhering to the data as presented by Dr. Barnett. The onus is on vascular surgeons to show that these procedures can be done on the basis of ultrasonography alone.

Dr. William C. Krupski (Denver, Colo.). I have a question with the methods. You are now using a gold standard as a specimen and the cast of the specimen. Yet that specimen shrinks after you remove it. It is not fixation perfused. Dr. Pan said that you did an experiment in four specimens under pressure; is that enough to decide that this is now the true size of the lumen? Exactly how would you maintain the pressure at 120/80 mm Hg or even higher? Did you use a perfusion system, or did you clamp both sides of the specimen? How did you do that to be sure that it did not just shrink and you were overestimating the degree of stenosis?

Dr. Rapp. First, we removed only lesions that could be removed en bloc (i.e., without cutting through the lesion and into the lumen). This is difficult unless the lesion is calcified. Lesions with a thin wall on one side were generally excluded by these criteria. Dr. Saloner cannulated each end and then coated each with rubberized silicone. This allowed him to perfuse them, plug off the other end, and pressurize them to 100 mm Hg. The lesions were then imaged. There is probably going to be some shrinkage; if you look at the study, there were several specimens in which the actual lumen could not be seen. However, we believe this is as good as we can do.