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### Assessment of Carotid Artery Stenosis by MR Angiography

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Anderson et al in this issue of AJNR compare magnetic resonance angiography (MRA), x-ray angiography (XRA), and carotid ultrasound (US) in the examination of atheromatous disease of the common carotid bifurcation. The innovation they introduce is the use in all patients of paired 2D and 3D time-of-flight (TOF) MRA imaging. The 2D images are more sensitive to slow flow but of lower resolution and are subject to in-plane flow artifacts. The 3D images offer higher resolution and sensitivity to flow in any direction, but exhibit poor contrast in slow velocity situations.

They conclude: 1) that such MRA studies of the common carotid bifurcation "may be used to clarify equivocal findings of US, or replace XRA in presurgical planning," and 2) that MRA and XRA provide redundant information for grading stenotic disease. They anticipate that findings such as theirs might permit MRA "to replace the expense and risk of XRA." Their study is limited to imaging of the common carotid bifurcation; given this narrow focus, shorn of clinical context, their data may indeed suggest that MRA is as good as XRA. But the study of carotid territory ischemic disease is more than "bifurcationology." Their article raises problems not uncommonly found in reports on the relative clinical utility of two or more technological tools, in which it is not necessarily evident that appropriate comparisons have been made or to what populations the findings may be generalized.

Ideally, each technique should be applied in a uniform, objective manner, preferably in a prospective design that permits near-equal sample sizes for each methodology, a common population for each technique, and a uniform set of indications for the different studies. The current paper uses a retrospective study design, which is necessary in most real situations and acceptable

if variables that cannot be controlled are accounted for.

The objectives of such a study should be made clear and the conclusions should reach no further than the limits imposed by these objectives. If the study is designed, for example, to assess the capability of detecting stenosis and ulcerations of the common carotid bifurcation, the conclusions should not be extrapolated to patients with other potential causes of ischemic events, unless incidental findings justify this.

How the study population was selected should be made clear. In the report of Anderson et al, the cases had a "high suspicion for stenotic carotid artery disease." Does this mean the sample represented 61 consecutive patients who presented with asymptomatic bruits and/or symptoms? Symptoms potentially implicate other causes of ischemic events, in addition to those at the common carotid bifurcation.

If comparisons between technologies are being made in different populations, the size and composition (age, sex, risk factors) of the subset tested with each technology should be similar and representative of patients at risk for the disease under surveillance. In other words, the probable prevalence of the disease should be similar in each group. Anderson et al nicely get around this problem by having a large subset of patients who underwent all three tests. Of the 61 patients, MRA was done in all, US in 50, XRA in 36, and all three studies in 31. Sixty-one carotids were studied by MRA/XRA, 93 by MRA/US, 50 by XRA/US, and 50 by all three tests. The authors are able to minimize the potential disparity between the former three sets by demonstrating that their Spearman and Pearson correlations are similar to those obtained for the patients who had all three studies. However, contingency tables based on stenosis grades were constructed only

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for the former (see Fig. 3 of Anderson et al), although the latter group is statistically more meaningful.

When technologies are compared, the indications for each test and the timing of the studies relative to each other need to be stated, so that one can assess for (inadvertent) bias. For example, because the prerequisite for entry into this study was an MRA, it is likely that in some cases MRA was done to clarify confounding US data, whereas in some situations MRA may not have been done if the US was definitive. This would unfavorably prejudice the quality of the US data. MRA was done after arteriography in some cases, when the lesion characteristics could have been known to the physician planning the MRA (although not necessarily to the one interpreting the study). This would favorably prejudice the MRA results.

The technique(s) with which a new technology is compared should be performed and interpreted with similar degrees of precision. In this paper, the angiographic data, for example, are not of uniform quality. Not all patients (how many?) had two neck projections. Did the patient in whom arteriography missed a stenosis because of an overlapping external carotid artery have the benefit of both projections? Five patients had only arch injections, which can provide bifurcation images of quite varying quality. In the cases of "occlusion" we do not know if a prolonged neck run (a "tricklogram") was done to assess for hairline patency. In the selective studies, were intracranial runs done? Did these show relevant abnormalities that would have been missed by a method that studies only the bifurcation? The interpretation of the arteriographic and MRA studies was agreed upon by a "consensus" vote of a panel of four persons expert in interpretation of these techniques. No information is given as to how the US data were managed. Presumably the studies were done by vascular surgical technologists and interpreted by the surgeons who were included as authors.

Inter-observer variability should be assessed, as the authors have done, showing good correlation between readers. Methods of analysis should ultimately account for all cases entered into the study and should be comparable for each technique. The applicability of each technique should be made evident, including the number of, and reasons for, failed studies. In this article, six patients had "failed" MRA studies; we are told that eight XRAs were "unsatisfactory," but not

why, nor are we given the US failure rates. Were confounding US studies treated differently and included in the statistical analysis? How many patients refused studies by each technique? Sensitivity, specificity, and predictive value data are useful ways to assess technology and require the failed cases to be included in the denominators. As the authors point out, the definition of stenosis was different for the US than for the MRA and XRA groups.

For the above reasons, some of the findings in this investigation, as thorough as it is, may be a function of the study methods and applicable only to the authors' population. At best, the results might be relevant to the evaluation of nonacute patients who have asymptomatic bruits in whom the diagnostic objective is to determine whether advanced common carotid bifurcation disease is present or absent. The findings cannot be generalized to patients with transient monocular or hemispheric ischemic events. The study of the bifurcation alone gives us no information about lesions more distal to the proximal internal carotid that might put the patient at risk for ocular or hemispheric stroke. Ocular and/or hemispheric transient ischemic attacks (TIAs) and stroke may result from distal cervical carotid dissection, fibromuscular disease, siphon atheromatous stenosis, and giant cell arteritis, in addition to atheromatous stenosis of the common carotid bifurcation. Hemispheric TIAs and strokes that are of primary cerebrovascular origin may be due to supraclinoid carotid artery disease, middle cerebral artery stenosis, or clot from an intracranial aneurysm, as well as extracranial carotid artery disease.

Any methodology that is designed to assess symptomatic patients must reliably evaluate the carotid/ophthalmic system in cases of transient monocular visual disturbances, and the carotid/middle cerebral system in cases of transient hemispheric attacks. This means not only that MRA studies must include more than the bifurcation and that XRA should include head films, but that appropriate noninvasive evaluation should include both direct and indirect tests. The direct tests monitor the carotid directly in the neck; the indirect tests monitor the carotid through distal circulatory beds, such as the periorbital circulation, for evidence of hemodynamic change caused by a bifurcation lesion. In addition to facilitating identification of more distal disease, the indirect tests improve the accuracy of the noninvasive battery in detecting bifurcation dis-



ease per se: for example, where tortuosity of the neck vessels, acoustical shadowing, or a high bifurcation limits the application of the direct tests. The finding of normal direct tests and abnormal indirect tests in patients who present with transient monocular visual disturbances suggests the diagnosis of giant-cell arteritis, as well as siphon or ophthalmic artery atheromatous disease. We make the diagnosis of giant-cell arteritis de novo several times a year, based on such findings and subsequent confirmatory blood work.

Two major issues in carotid disease relate to the need to characterize ulcers and to demonstrate degrees of severity of advanced stenosis. Arteriography is not reliable in identifying carotid ulcers (1). Noninvasive studies also are not useful for demonstrating ulceration (2). Whether MRA will be more reliable is unclear. An ulceration is an erosion of the single cell-layer intima. Only a microscopic examination can show us that. In some cases, the outpouchings that are called ulcerations represent normal residual lumens between two atheromatous plaques or reendothelialized "ulcer" craters. Severe true ulcerations typically are associated with very tight stenosis of the internal carotid and are found proximal to the stenosis. Identification of tight stenosis, therefore, might be sufficient in identifying the patient at risk for stroke from carotid disease, whether or not ulceration contributes to the pathophysiology of stroke.

The North American Symptomatic Carotid Endarterectomy Trial (3) has clearly demonstrated the efficacy of carotid endarterectomy in patients with 70% stenosis, but the efficacy was even more marked the greater the degree of stenosis. In the future, it may become critical to differentiate a 90% from a 70% or 80% stenosis in deciding upon surgical or medical management and to follow patients frequently for evidence of progression within these ranges. MRA tends to overestimate the degree of stenosis and, with current techniques, may be of limited application for identification of precise residual lumen diameter; moreover, it is not the most cost-effective method for following patients for progression. A full battery of noninvasive studies can document 0.25–0.5 mm increments of progression of stenotic disease with a 90% accuracy once the residual lumen diameter reaches 2 mm.

Carotid noninvasive and transcranial Doppler studies should be used, for the present time, to complement MRA neck and head studies. The

latter should not typically stand alone until they have the capability to assess the entire carotid/ophthalmic system or the carotid/intracranial circulation in symptomatic patients, measure precise degrees of stenosis, be practical for following patients for progression of disease, and be free of signal drop-out artifacts, such as those due to turbulence and in-plane flow. In patients being followed for progression of disease, only a baseline MRA would be needed.

Prior to surgery, x-ray carotid arteriography is desirable. In general, MRAs (just as noninvasive studies before them (4)) are best used to rule in an x-ray arteriogram, rather than to rule one out. X-ray arteriography remains the definitive test for documenting lumen size, intraluminal thrombus, tandem lesions, and the adequacy of collateral flow (5). It is the only procedure that has been proved to be able to differentiate a very tight stenosis ("virtual occlusion") from a complete occlusion. Color flow Doppler cannot. Whether MRA can differentiate the two remains inconclusive. We have a case examined with head MR (T1/T2) and 3D TOF MRA that showed no evidence of flow from the internal carotid bifurcation through the siphon on angiographic or axial head images. At arteriography, a hairline lumen persisted; it took 8 seconds for the contrast to fill from the internal carotid origin to the siphon. In our laboratory we find that 25%–33% of patients who have no evidence of flow on color flow, duplex, and/or continuous wave examinations have open carotid arteries. Until proved otherwise in a study with a large sampling of patients with hairline lumens, arteriography remains the only method that can reliably distinguish virtual from complete occlusion. In the presence of a complete occlusion, arteriography is the most reliable tool for determining whether there is retrograde flow from the reconstituted siphon to the cervical carotid. This situation indicates a short segment lesion that represents a risk for recurrent ischemia, but one that can be opened safely. The exceptions to doing x-ray arteriography prior to surgery are in patients with crescendo TIAs or stroke-in-evolution in whom the noninvasives (and/or MRA) are diagnostic, or in patients with medical contraindications to an invasive or contrast study.

Arteriography is basically a safe procedure. The complication rate is 0.5% or less for severe complications. In the VA Cooperative Study on carotid endarterectomy, in which two thirds of 188 patients demonstrated stenosis greater than



70%, no major complications occurred; 4% had transient neurologic events (6). We do not know the morbidity produced by lesions missed by MRA studies. The fact that some neuroradiologists in training today feel more comfortable doing an MR study than an x-ray arteriogram (or, for different reasons, a US study) should not prejudice our concepts of the proper evaluation of patients with operable carotid disease. It was only a few years ago that neuroradiologists considered an arch study or retrograde brachial inadequate for assessment of the stroke-prone or acute-stroke patient because of the limited extent of the vascular axis studied or because the resolution was not sufficient.

MRA is the ultimate example of a polymodal technology, one that can be done in many different ways. Between 2D/3D, TOF/phase contrast and multiple pulse sequence alternatives, the technical permutations are remarkable. Anderson et al have nicely explored a sensible combination of techniques. Even given their limited US battery, their results indicate the complementary value of MRA and US in screening patients for common carotid bifurcation disease. But by focusing on the common carotid bifurcation and not dissecting out the clinical contexts of their cases, they have not proven that their findings (that MRA and XRA provide redundant information) can be extrapolated to the universe of patients who present with a transient neurologic syndrome or with stroke. If MRA assessment is not appropriately structured and the conclusions not appropriately targeted, false expectations may arise among referring physicians, who subsequently will be disappointed; this valuable tool

then may be clouded with the reputation of "another IV-DSA" (intravenous digital subtraction angiography).

The choice of tests for patients with suspected carotid disease depends on the clinical objective, the equipment available, the neuroradiologist's expertise, the patient's indulgence, and the payer's financial resources. Even as technological advances improve its clinical applicability, the question is whether MRA will become accessible, practical, and cheap enough to replace US as the initial test in stroke-prone and acute-stroke patients, in whom MRA might best be used to provide complementary information "to clarify equivocal findings of US." Some day MRA may supplant XRA in the work-up of stroke disease. But, especially for patients who become considerations for surgical therapy, x-ray arteriography, at the present time, remains the definitive test for cerebrovascular lesions.

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