AJNR

Angiography in patients with occlusive cerebrovascular disease: views of a stroke neurologist and neuroradiologist.

L R Caplan and S M Wolpert

AJNR Am J Neuroradiol 1991, 12 (4) 593-601
http://www.ajnr.org/content/12/4/593.citation

Special Article

Angiography in Patients with Occlusive Cerebrovascular Disease: Views of a Stroke Neurologist and Neuroradiologist

L. R. Caplan[1] and S. M. Wolpert[2]

Even after four decades of use, cerebral angiography continues to be a focus of controversy and misunderstanding among neurologists, surgeons, and neuroradiologists. Cerebral angiography is, or at least should be, performed solely by neuroradiologists and should be requested solely by neurologists, neurosurgeons, or vascular or cardiac surgeons after neurologic consultation. Most often at issue are the indications for angiography, the timing of the procedure, the need for preliminary investigations, and the extent and sequence of opacifications and filming. Improvements in neuroimaging and sonography have definitely reduced the need for angiography. However, angiography is still critical in the evaluation of patients with suspected aneurysms, vascular malformations, and arteritis. Angiography remains the key investigative device to detect, localize, and quantify occlusive cerebrovascular lesions. Tumor, displacement of brain structures, and abnormalities of the ventricles and CSF pathways are now usually defined satisfactorily by CT and MR imaging. We, a stroke neurologist who works closely with neuroradiologists and an experienced neuroradiologist with a special interest in cerebrovascular disease, thought it might be useful to express our views on angiography in regard to patients with occlusive disease. The discussion for the most part is also relevant to MR angiography (MRA), which eventually may partially or completely replace arterial opacification with contrast material. Since the extracranial and all the intracranial arteries cannot be imaged in a reasonable interval by MRA, technology, personnel, and time considerations will limit the number of patients that can be studied and the time available for each patient. Neuroradiologists and neurologists will need to make decisions about which vessels should be studied in which sequence in which patients. Angiographic decisions will need to be individualized irrespective of whether MRA or arterial opacification angiography is performed.

MRA

We will begin by discussing MRA, clearly the most current topic in cerebrovascular imaging.

Method of Planning the Procedure

As in standard angiography by arterial catheterization, forethought and hypothesis generation should precede MRA in order to maximize the yield of the procedure. Clinicians should be able to place the patient into one of three groups: those with anterior circulation ischemia, those with posterior circulation ischemia, or those thought to have penetrating artery ischemic disease (lacunar infarction). The vascular occlusive lesions in patients in the lacunar infarct group should always be intracranial, but the vascular lesions in the anterior and posterior circulation groups might be intracranial or extracranial. The probability of extracranial disease can be estimated

Received February 6, 1991; accepted without revision February 6, 1991.
[1] Department of Neurology, New England Medical Center Hospital, 750 Washington St., Boston, MA 02111. Address reprint requests to L. R. Caplan.
[2] Department of Radiology, New England Medical Center Hospital, Boston, MA 02111.

AJNR **12:593–601, July/August 1991** 0195–6108/91/1204–0593

by using demographic variables, medical history, findings from clinical neurovascular examination, and the results of sonography. To place patients in one or another of these categories, the clinician and neuroradiologist use a variety of information enumerated in Table 1. Under ordinary, nonemergency situations we advocate performing CT or spin-echo MR imaging; sonography of the extra- and intracranial arteries; and, when indicated, cardiac echocardiography before MRA. Case examples should help illustrate the method.

Representative Case Reports

Case 1

A 53-year-old black woman had had two attacks of right arm weakness and numbness. During one attack, her speech was abnormal, but it was difficult from her description to determine whether the abnormality involved language (aphasia) or articulation (dysarthria). She had a history of hypertension, well controlled on medicines, but had never had angina pectoris or leg claudication. On examination, she had no bruits but did have slight residual weakness and hyperreflexia of the right limbs. CT showed a small wedge-shaped infarct involving the cortex and underlying white matter located on the convexity surface of the left lateral frontal lobe just anterior to the precentral gyrus. The cerebellum and brainstem were normal. A duplex scan showed no significant carotid artery stenosis in the neck. Transcranial Doppler (TCD) showed higher velocities in the left middle cerebral artery (MCA) compared with the right.

The right limb weakness could have been caused by a lesion in the left cerebral hemisphere or in the left brainstem. Aphasia would place the lesion within the hemisphere, but if the speech abnormality were dysarthria either locale would be common. Stroke risk factors in this patient (hypertension but no large artery systemic disease) also made lacunar infarction a clinical consideration. CT, by localizing the infarct to the paracentral region, a location quite compatible with the neurologic symptoms and signs, helped place the ischemia in the anterior circulation within the MCA territory. Furthermore, the superficial cortical location of the infarct excluded lacunar infarction caused by penetrating artery disease.

Once the lesion is located in the territory of the MCA anterior circulation, what are the probabilities of extracranial internal carotid artery (ICA) disease vs an intracranial ICA or MCA lesion? Demography can be very helpful. Black persons tend to have more extensive and severe intracranial occlusive disease, while white persons have more extracranial disease [1–3]. Sex is also an important predictor, since men have a striking preponderance of extracranial disease while women have somewhat more intracranial stenoses and occlusions [1]. Hypercholesterolemia and coronary artery and peripheral vascular occlusive disease (angina pectoris, myocardial infarction, or claudication) are found more often in patients with extracranial occlusive disease [4]. Knowing only that the patient was a black, hypertensive woman without coronary or peripheral vascular occlusive disease, the likelihood of an intracranial lesion would be high. Normal findings on sonography of the cervical ICA and abnormal results from TCD further increase the probability that the vascular occlusive process involved the intracranial MCA or, less likely, the ICA siphon.

In this case, the neuroradiologist should first be sure that films of the intracranial ICA and MCA are optimal. The lesion could be occlusive or stenotic in nature and involve the main stem of the MCA and its divisions or branches. If a lesion is found in the left MCA as expected, the right MCA should also be carefully examined, since bilateral lesions are common. Imaging of the cervical ICA has a very low yield. Had the patient been a white man with hypercholesterolemia and coronary artery disease, the odds would have strongly favored an occlusive lesion in the neck, especially if a duplex scan had shown abnormalities. In that case, a cervical MRA study emphasizing the ICAs would have been the first step, and intracranial imaging would have been less likely to yield important data.

TABLE 1: Information Used to Categorize Lesion Prior to MR Angiography

Source of Information	Information Obtained
Demographic data	Race, sex, age
General history	Hypertension, diabetes, coronary disease, peripheral vascular disease, hyperlipidemia
Neurologic history	Nature of symptoms
Vascular examination	Bruits, absent pulses
Neurologic examination	Brain localization
CT and MR imaging	Location of infarcts
Sonography	Findings on carotid and vertebral artery duplex and Doppler and transcranial Doppler

Case 2

A 26-year-old white woman developed severe headaches involving the left occiput and mastoid region 1 week earlier while on a skiing vacation. One day before admission, she felt dizzy and off balance, and tended to veer to the left when she walked. Neurologic examination showed slight left arm dysmetria and incoordination, horizontal nystagmus to the left, and gait ataxia. Standard spin-echo MR showed an infarct in the left posterior inferior cerebellum and no brainstem infarct. Continuous-wave Doppler showed no abnormalities at the origin of the vertebral arteries, but TCD showed a reduced intracranial vertebral artery signal on the left with reversal of flow and increased velocities in the right intracranial vertebral artery.

In this patient, the symptoms and signs clearly localize the lesion to posterior circulation structures. Dizziness, nystagmus, and ataxia localize the lesion to the vestibular-cerebellar system in the lateral brainstem tegmentum or cerebellum. Unlike the first patient, this patient was quite young and had absolutely no risk factors for atherosclerosis. The onset after physical activity and prominent headache suggest the diagnosis of dissection of one or both vertebral arteries, a process that usually involves the distal extracranial segments of the vertebral arteries and often is bilateral [5, 6]. Doppler sonography can be very helpful in studying posterior circulation ischemia as well as anterior circulation occlusive disease [7]. In this case, MRA should first concentrate on the distal extracranial left vertebral artery. The right extracranial vertebral artery should be studied also. If a dissection is found, either spread to the intracranial vertebral artery or intraarterial embolism might have occurred, so intracranial imaging of the vertebral artery, basilar artery, and posterior cerebral artery (PCA) would be useful. If neck imaging shows no lesion, the intracranial vertebral artery should be studied carefully since the lesion must involve this vessel proximal to the origin of the posterior inferior cerebellar artery.

In these two sample patients, the clinician has used clinical data from the neurologic history and examination plus the results of imaging with CT or MR to locate the lesion in either the anterior or posterior circulation. Then by using demographic and stroke risk factor data and the results of the vascular bedside examination and sonography, an estimate was made of the probability of extracranial vs intracranial disease. In patients with suspected penetrating artery (lacunar) disease, the aim of MRA is to exclude an occlusive lesion

of the major intracranial artery supplying the penetrating artery branches involved (MCA in lenticulostriate lesions, PCA in thalamic infarcts, basilar artery in pontine infarcts). At times, an occlusive lesion of the parent artery can lead to infarction predominantly in the territory of the deep penetrating artery [8, 9]. Occasionally, extracranial ICA lesions can produce syndromes not easily differentiated from lacunar infarcts (10], but sonography should detect these cases.

The findings on the first MRA images may help decide whether to pursue further imaging. Occlusion of the PCA dictates a search for an intraarterial source of embolization; most often the source is the intracranial vertebral artery or occlusion at the origin of the vertebral artery in the neck. To accurately diagnose most patients, information about both the extra- and intracranial components of the affected anterior or posterior circulation will be necessary. At times, the results of sonographic studies of the extracranial arteries may suffice without the need for MRA imaging of the neck.

What Information Do Clinicians Seek from MRA?

The major goal of imaging is to place the arterial lesion into one of three groups: complete vascular occlusion presumably by thrombotic formation, severe flow-reducing stenosis, or normal or minor stenosis of a vessel not impeding flow. The majority of atherosclerotic lesions occur in proximal arteries in the intra- and extracranial systems that should be visible on MRA. At present, we guide treatment differently depending on the category mentioned. For normal or nonstenosing lesions we prescribe aspirin or other medicines that alter platelet function. For tightly stenosed arteries, we prescribe Coumadin or surgery, depending on the locale and severity of the neurologic deficit. For occluded arteries, thrombolytic therapy or short- or long-term Coumadin is recommended depending on the recency of occlusion and whether occlusion is embolic or found locally in an area of preexisting tight stenosis. Aneurysms of the major basal arteries and lesions within the vascular walls such as dissections may also be well shown by MRA.

Venous occlusive disease is especially amenable to detection by MR imaging and MRA, but different strategies are needed for imaging. The clinical setting and results of CT or MR often suggest the possibility of venous occlusive disease when these studies are available prior to angiography.

Capabilities and Limitations of MRA

The location of lesions causing cerebrovascular disease of the carotid territory, while usually at the carotid bifurcation, can vary from the origin of the brachiocephalic arteries to the terminal branches of the intracerebral arteries. The lesions can consist of smooth atheromatous plaques, ulcerated plaques, or mural thrombi; stenoses or occlusions may occur. Not all patients with stroke have atheromatous thromboembolic disease; in some patients, carotid or vertebral dissections or aneurysms with emboli may be the cause of the ischemic event. Cut-film angiography can demonstrate these abnormalities and also focal alterations in cerebral blood flow such as retrograde collaterals, focal areas of slow flow, and reactive hyperemia. Such changes in flow may be seen in 40% of patients with focal cerebral infarction and in 25% of patients with episodes of transient cerebral ischemia [11]. Some of these changes may be present even without angiographic evidence of an occluded artery.

Almost all these secondary features of cerebral flow alteration, while seen on standard cut-film angiography, cannot be seen by MRA. However, current therapy, as already mentioned, depends on determining basic anatomic information about the carotid bifurcation such as patency, occlusion (presence and extent), and degree of stenosis. The ability of MRA to provide this information is promising. In studies of the carotid bifurcation, comparable evaluations of MRA with contrast-enhanced angiography has shown that MRA can reliably demonstrate normal carotid bifurcations and siphons, and indicate stenosis in most cases. In one study, 21 of 22 stenoses and occlusions were correctly diagnosed with time-of-flight techniques [12]. Unfortunately, moderate degrees of stenosis sometimes were overgraded as severe because signal loss occurred from both velocity changes in the artery and turbulence. An accurate estimate of the caliber of a stenotic carotid artery is critical. In patients with an angiographically apparent occluded artery, the angiographic trickle technique (12 ml of contrast material over 4 sec with delayed filming) may demonstrate the "slim" or "string" sign indicating slow flow through a patent artery. Such patients may benefit from endarterectomy, whereas patients with completely occluded arteries will not. By using time-of-flight techniques, Litt et al. [13] showed that regions of severe stenosis usually were not shown well by MRA, and sometimes areas of severe stenosis on enhanced angiography appeared occluded on MRA. Also, angiographically occluded arteries may be misinterpreted on MR images as patent. Plaque ulcerations are poorly seen on MRA [14].

Thus, with the present state of technology, the main role of MRA in the assessment of the carotid bifurcation suggests its use as a screening test in which patients with normal bifurcations need no further workup but those with apparent stenoses or occlusions still need cerebral angiography. Many of the criticisms of the use of MRA for carotid bifurcation disease are also applicable to atherosclerotic disease of the petrous and cavernous portions of the carotid artery. By using three-dimensional time-of-flight techniques for the intracranial circulation, Masaryk et al. [15] found MRA to be most advantageous for the evaluation of patent intracranial aneurysms, vessel displacement, and large-vessel disease. The disadvantages included limited field of view, persistent signal voids, limited spatial resolution, and inadequate depiction of lesions with slow flow. A limited field of view is a significant problem, and, since intracranial vascular occlusions may be cortically located, imaging of the complete intracranial circulation is necessary. It is unfortunate that the overall imaging time for such studies approaches the upper limits of patient tolerance.

MRA can detect aneurysms in the circle of Willis that are 3 mm or larger with a sensitivity of 86% (18 of 21 detected) [16]. However, a limited field of view may be a problem, since aneurysms causing embolic strokes may exist in the extracranial carotid artery, the circle of Willis, or more peripherally in the MCA. MRA is not suitable for the detection of thrombosed aneurysms or those containing slow flow, and it underestimates the size of aneurysms with turbulent flow [14]. The application of MRA to the diagnosis of vertebrobasilar disease

is largely unexplored. Current research with the use of very short TEs and time-of-flight techniques has significantly improved the images of intracranial vessels with rapid flow [17]. Phase-sensitive techniques appear to be more sensitive to the detection of slow flow than time-of-flight techniques are and also are not subject to the problem of differentiating the bright signal of flowing blood from that of adjacent hemorrhages, as may occur with a dissecting aneurysm [18]. Unfortunately, three-dimensional phase-sensitive techniques are more time-consuming than three-dimensional time-of-flight techniques.

A critical question is to what degree will MRA affect patient care decisions and at what cost [19]. The technology is improving, but at the moment MRA does not have the spatial resolution, selectivity, or dynamic character of conventional angiography.

Myths Surrounding Standard Angiography

Because of the limitations of MRA, standard angiography will continue to play a strong role in the evaluation of patients with brain ischemia. Unfortunately, we believe myths and unsubstantiated dogma have colored the use of angiography and have stood in the way of its optimal use. This section will consider these myths.

Myth 1

Angiography is indicated only as a prelude to surgery. If surgery is not considered, angiography should not be performed.—A recent position paper [20] and background article [21] from the American College of Physicians on the diagnostic evaluation of the carotid arteries made the assumption [21]: "Diagnostic evaluation of the carotid arteries is done only when surgical treatment is being considered and knowledge of a patient's vessel anatomy is necessary." We disagree strongly with this view. Angiography is a diagnostic test, and, like all diagnostic tests, it is used to help determine what is wrong with the patient. Rational treatment depends on accurate diagnosis. When the diagnosis is uncertain, physicians must guess at the best choice of therapy; they might err by omitting a treatment that may be helpful or give therapies that are not indicated and could be harmful.

There are a number of nonsurgical treatments of ischemic stroke including anticoagulation with heparin or warfarin, aspirin or other antiplatelet antagonists, hemodilution, specific treatments for embolisms of cardiac origin, and vigorous control of blood pressure. We have always advocated choosing treatment on the basis of the nature of the vascular lesion [22, 23]. Warfarin is chosen for situations in which so-called red fibrin-dependent clots form. These include dilated, fibrillating cardiac atria; severe stenosis of extra- and intracranial arteries; and acute occlusion of large arteries. Duration of treatment varies. Patients with complete occlusions are treated with Coumadin for only 3–6 weeks, during which time the thrombus organizes and adheres to the vessel wall. After this period, clot propagation and embolism are rare. In contrast, patients with emboli of cardiac origin and tight arterial stenoses are treated as long as the condition persists. Anticoagulants can be dangerous, especially if prescribed for long periods. We do not prescribe Coumadin without clear indications and knowledge of the vascular process. Aspirin or other antiplatelet aggregation drugs are used for patients with so-called white clots, platelet-fibrin aggregates that form in fast-moving streams such as nonstenosing plaques in extracranial and intracranial arteries [23].

Angiography is performed when the diagnosis is *unclear* and the degree of brain damage is not so severe that any treatment would be futile. If the diagnosis can be established with less invasive technology—for example, CT, MR imaging, sonography, or hematologic and cardiac tests—then angiography is unnecessary. When preliminary tests do not allow sufficient diagnostic certainty to make logical treatment decisions, then angiography is warranted.

The idea that angiography is used only as a prelude to surgery is sheer propaganda promulgated by surgeons and unwisely accepted by others. There is a general tendency in medicine today to second-guess with too many "what if's" before firm data are available: "Although I don't know the diagnosis, if angiography were performed, the most likely diagnosis statistically would be A, in which case there would be no treatment. Since this is the most likely outcome, I won't request angiography." When angiography is performed, the diagnosis often proves to be one unsuspected clinically and responsive to treatment. Take first steps first. Find out what is wrong with the patient before selecting or excluding treatment.

Myth 2

The cerebral circulation is an open net. All the large extracranial arteries must be visualized in patients with ischemia, since disease at any one locus can lead to ischemia at any other.—This ischemia-at-a-distance theory probably became popular after the publication in the 1950s of reports of patients with subclavian steal syndrome [24]. According to this theory, blood courses from one intracranial basilar artery in a retrograde direction down the other vertebral artery to supply the arm on the side of a proximal subclavian artery occlusion. Since the intracranial vessels form a circle of Willis in which there are interconnections between the two sides and between the anterior and posterior circulations, basilar artery flow may derive from the opposite vertebral artery or either carotid artery through the posterior communicating–PCA connections. Blockage at an extracranial site or intracranially may lead to decreased flow at distant sites depending on hydrodynamic and hemodynamic principles. The logical extension of this theory holds that physicians cannot predict from the brain symptoms where the vascular lesions are: "A brain full of dye is worth a room full of neurologists." By surgically repairing any stenosed artery or bypassing occluded ones, the brain circulation could be shored up and blood flow improved. Radiologists were urged to show all arteries, primarily through arch injections, and surgeons then fixed what they saw irrespective of brain symptoms or signs.

We now know that brain ischemia in the subclavian steal syndrome is related to decreased antegrade flow, not re-

versed flow. Patients with vertebral artery occlusions have the same symptoms as those with subclavian artery disease with reversed flow [25]. A recent study with TCD and continuous-wave Doppler techniques showed no correlation between retrograde flow and symptoms in patients with occlusive lesions of the subclavian artery [26]. In general, the hemodynamic theory of brain ischemia has been deemphasized by an accumulation of data that shows that the vast majority of brain infarcts are due to thromboembolism. Proximal occlusions cause temporarily decreased flow, which is usually soon compensated for by collateral circulation, or else minor so-called border-zone infarcts develop. However, more importantly, when an artery becomes critically stenosed or occluded, fresh thrombi are formed and initially are poorly organized and nonadherent. As a result, these thrombi and platelet-fibrin aggregates embolize intracranially, block distal vessels, and cause brain infarcts. Ringelstein et al. [27] were able to show that most patients with ICA occlusions in the neck had infarcts due to emboli. Angiography often showed "occlusio supra occlusionem," that is, distal artery-to-artery emboli. In Rome, Fieschi et al. [28] showed that early angiography (within 6 hr of symptom onset) in patients with acute ischemic strokes showed complete arterial occlusions in 76% of patients, and the majority of the lesions (66%) were intracranial. Unpublished data from a study investigating the use of tissue plasminogen activator in patients with acute brain ischemia demonstrated arterial occlusions thought to be due to atherosclerotic disease in 106 (76%) of 140 patients studied within 8 hr of symptom onset. The vast majority of ischemic strokes are due to artery-to-artery or cardiac-origin embolism, a conclusion evident from prospective series of cases collected in the Harvard Stroke Registry [4] and the Stroke Data Bank [29].

After 20 years of clinical stroke experience and registry work [4, 29], we cannot give readers a single example of a patient with an occlusive lesion at one site whose sole clinical or neuroimaging findings related to a distant site supplied by another arterial system. Invariably, when patients are carefully studied, another explanation is found for the localized brain ischemia. Left ICA disease is not seen with right cerebral or brainstem ischemia. When either or both carotid arteries are occluded, vertebrobasilar symptoms are not the sole finding. Occasionally a patient with prior occlusion(s) will have transient ischemia in the distribution of that occlusion in addition to ischemia in the territory of a newly obstructed artery. Several patients previously known to have right ICA occlusion and recent tight stenosis or occlusion of the left ICA had transient left limb numbness and weakness as well as right limb symptoms. In that situation, we have never seen only a left hemiparesis. Several patients cared for by one of us and by C. Miller Fisher (personal communication) have had symptomatic basilar artery occlusion that was documented angiographically. After anticoagulants and time, the clinical situation stabilized with no or little deficit. Later, when unilateral ICA stenosis developed, the only symptoms were in the ICA territory. No posterior circulation symptoms developed. Once collateral circulation develops and stabilizes, it is usually resistant to changes in distant hemodynamics. Symptoms, however, can occur with hypotension or hypovolemia.

With neuroimaging tests now able to show the ischemic region, clinical and imaging information usually is sufficient to locate the arterial system involved. Clinicians need detailed information about the arteries supplying this ischemic region in order to make therapeutic decisions. Occlusive lesions at other sites are nearly always incidental. In selected cases, it may be useful to opacify other arteries, but routine opacification of all the large arteries is not warranted. Sonographic data can help supply information about other sites and, ordinarily, should be performed before angiography. When water flows sluggishly to the bathroom sink on the second floor of the house, the plumber needs to investigate the state of the pipe supplying that sink or bathroom. A look at pipes supplying the kitchen or the other second-floor bathroom might reveal a general shocking state of home plumbing (and would lead to an increased risk of injury to the other pipes and a higher plumbing bill) but would not help deliver water under higher pressure to the malfunctioning bathroom sink. A look at the pump system and water tank, however, may be important. The open net idea is strictly a theoretical concept imaginable in a physics or biology laboratory but not practically applicable to human stroke disease. Investigate the heart and blood pressure and the arteries clinically involved. Routine four-vessel angiography is seldom needed.

Myth 3

The aortic arch must be opacified in all patients with ischemia in order to see all arteries and ensure that proximal occlusive lesions near the arch are not missed.—This myth is an extension of myth 2. We have already dealt with the theoretical issues related to multiple-vessel opacification. Herein, we will touch on the practical issues. The two main reasons not to routinely study the arch are that the yield of important lesions is extremely low and there is an added systemic risk with arch opacification, which uses large volumes of contrast media.

When Akers et al. [30] studied the results in 1000 consecutive patients studied with arch angiography and four-vessel studies, only six (0.6%) had hemodynamically significant intrathoracic vascular disease. Four had obstructive lesions at the common carotid artery (CCA) origin and two at the innominate artery origin. None were judged to require surgical intervention at the time of the study and none needed surgery for these lesions during 2 years of follow-up. Three of the lesions (two CCA and one innominate) likely would have been discovered had selective angiography alone been performed. The absence of a significant lesion in the neck or head should have alerted the angiographer to opacify the origin of the artery. Also, the inability to catheterize the artery selectively and fluoroscopy usually will lead to arch studies in these patients. Omission of an arch study leads to a missed important lesion in maybe one in 1000 cases.

The risk involved in arch injections is not negligible. An arch injection is usually performed with 40–50 ml of contrast material. Cardiac overload and renal toxicity can result. Studies on the risks yield conflicting results. One study reported that 8.2% of patients with previously normal renal function

developed acute renal dysfunction after an average injection of 215 ml of the contrast agent (type and iodine concentration not specified); dialysis was required in three patients [31]. In another study, 14.8% of patients previously known to have impaired renal function in whom an average of 258 ml of Conray-60, Renografin-76, Vascoray, or Isopaque alone or in combination was administered had worsening of function and 3.7% required dialysis [32]. However, in a third study of adequately hydrated low-risk patients with normal renal function in whom an average of 237 ml of both ionic and nonionic contrast media was administered, no impairment of renal function occurred [33]. A review of three IV DSA studies (656 patients) showed a systemic complication rate of 18.9% [34]. Three reviews of the complications of cerebral angiography in patients with brain ischemia contained almost no data about arch injections [32, 34–36]. Review of other studies indicate that arch injections are most likely to cause complications in poorly hydrated, diabetic patients or patients with impaired renal function, particularly when high doses of the contrast medium are administered. A difficult angiographic procedure may use over 100 ml of contrast medium for catheter placement and filming, particularly when three or more arteries need to be injected. It is particularly important in these patients that the benefits of the arch study be weighed against the risks.

Myth 4

Angiography is not indicated for patients with vertebrobasilar disease. There are no surgical or treatment implications and the study is dangerous.—We have already discussed under myth 1 arguments against limiting angiography to so-called surgical candidates. Actually, a wide variety of surgical procedures have been performed on the posterior circulation arteries in patients with ischemic disease of the posterior circulation [37]. These include bypass procedures at the origin of the vertebral artery and endarterectomy and bypass procedures for lesions in the distal extracranial vertebral artery and in the proximal intracranial vertebral artery. Bypass techniques are performed for severe intracranial occlusive disease. Anticoagulation is also frequently prescribed, and we have already stated that anticoagulation can be dangerous and should be used only for certain vascular lesions such as severe stenosis of the main vertebral or basilar arteries [38, 39]. For some lesions, only short-term treatment is used. Analysis of clinical signs, MR imaging, and continuous-wave Doppler and TCD sonography can yield considerable useful data about occlusive lesions of the posterior circulation, but all have limitations [40]. Angiography by selective catheterization of the subclavian or vertebral arteries with imaging of the intracranial vertebral and basilar arteries often is needed to make important therapeutic decisions.

There are differences between vertebral and carotid catheterizations. If 5-French catheters are used for both studies, more of the lumen of the vertebral artery will be compromised by catheterization than will that of the carotid artery, because the cross-sectional area of the vertebral artery is smaller than that of the carotid artery. In atherosclerotic patients particularly, we advocate withdrawal of the catheter from the vertebral artery immediately after the injection of contrast material. Also, we are not reluctant to carry out subclavian injections if vertebral artery catheterization is difficult. There are no data to support the inference that vertebral angiography is more risky than carotid angiography. Faught et al. [35] found a lower rate of complications in patients with isolated vertebrobasilar symptoms (3% [1/21] vs 16% [15/91] for carotid disease). Transient global amnesia was reported as a complication of vertebral angiography in 12 (0.9%) of 1321 patients [41]. Patients with atherosclerotic arteriomegaly of the vertebrobasilar system, however, are at a particularly high risk for complications following vertebral angiography, as reported by Smoker et al. [42].

Angiographers are reluctant to study patients with vertebrobasilar disease because some develop coma, quadriparesis, or even a locked-in state within days or hours after angiography. As early as 1966, Baum et al. [43] published a report documenting the risk of "no arteriography." The subsequent risk of clinical complications in those patients scheduled for peripheral artery angiography but who were canceled and had no angiography was about the same as for those who had angiography. Neurologists, especially those who care for many patients with vertebrobasilar occlusive disease, know that many patients do poorly whether or not they have angiography. The group of posterior circulation cases for which we advise angiography, in general, comprises those patients who we fear have severe disease and might do poorly without aggressive treatment. In milder cases, and those easily diagnosed clinically, angiography is not performed. Angiographers see patients who do poorly after studies; they do not see those who do poorly that are not studied. There are no data that indicate that patients do worse because of angiography. We believe that, over the years, accumulated knowledge of the abnormalities within the posterior circulation arteries has allowed us to take better care of these patients [24, 37, 38, 44]. Perhaps MRA will be a major advance for patients with occlusive disease of the posterior circulation and will convince others of the value of the approach we have pursued for more than a decade.

Myth 5

Patients should not be studied in the acute stage of ischemic stroke since the risk from angiography is higher at that time. Patients with deficits, especially if severe, have a higher risk. Angiography should be delayed, especially in ill patients.—We know of no data to support the idea that arteriography performed during acute stages of stroke is more dangerous or that complications relate to the severity of neurologic deficit. Faught et al. [35] found that the "neurologic state at the time of the study did not seem to matter, and neither did the time of the study after the onset of the deficit." The Joint Study of Extracranial Arterial Occlusion also failed to corroborate an increased risk of more severe deficits with angiography [45]. Dion et al. [36] found that only the duration of angiography and systolic hypertension increased the risk with angiography in 1002 prospectively studied patients. An-

other study found a slightly increased risk in patients with severe deficits, but the difference was not statistically significant [46].

We have already cited the study of Fieschi et al. [28] that documented the high yield of angiography during the first 6 hr after the onset of symptoms. In the Harvard Stroke Registry, we also found that most emboli were no longer visualized 48 hr after the onset of stroke [4]. Treatment decisions often need to be made quickly. If thrombolytic agents are to be used, they will need to be given within 8 hr, and probably sooner. A common strategy that we have seen pursued is to delay angiography to see if the patient improves: "If the hemiplegia improves and aphasia clears, we might readmit the patient for angiography after 6 weeks to see if there is a surgical lesion." This makes no sense to the patient: "Where were you, doctor, when I was badly off and sick? Now that I am better, why should I undergo the test with its risks?" Risks seem warranted when we are ill. After the worst is over, it is hard to convince patients to have angiography and illogical to do so. The advent of MRA may solve this problem. There are no logical or practical reasons to withhold angiography during the acute stroke period. In fact, the trend and push are for earlier and more urgent studies [47].

Rules for Proper Angiographic Studies

After stating what we think should not be done and emphasizing misconceptions and myths of the past, we will now take a more positive approach and outline what we think are the rules for proper study. Some of this material has been published in a book chapter [48].

Rule 1

Angiography is indicated only when it is likely to answer clinically relevant questions that cannot be answered satisfactorily by less invasive means.—The clinician caring for the patient should have analyzed the clinical symptoms and signs and arrived at diagnostic hypotheses. Noninvasive techniques and imaging are used to test these hypotheses and answer queries. When clinically important questions remain, and treatment is feasible, angiography may be warranted. Angiography should not be done routinely in all patients with brain ischemia.

Rule 2

Neuroimaging (CT and/or MR) and noninvasive sonographic tests ordinarily should be performed first.—CT and MR imaging are extremely valuable in helping to localize the symptomatic ischemic zone and to detect regions of previous ischemia. The results help plan angiography, since the symptomatic zones should be the first ones studied angiographically. In many patients, CT and MR imaging allow accurate diagnosis and obviate angiography.

Similarly, preliminary sonography is very helpful. In the anterior circulation, Duplex scanning of the ICA in the neck and TCD sonography of the intracranial anterior cerebral artery, MCA, and PCA are very helpful. Abnormal findings localize areas of interest for angiography. Normal areas may allow these regions to be omitted or scanned quickly by angiography. The noninvasive findings may yield enough data to obviate angiography. Even when angiography is performed, sonography is helpful in follow-up. In some stroke centers, sonographic testing is done immediately after the physical and neurologic examinations. Sonography is a logical extension of the physical examination.

Rule 3

During angiography, first study the vessel supplying the ischemic zone.—First things first. Willie Sutton robbed banks because that was where the money was. In a patient with an infarct in the territory of the right MCA clinically and by CT, opacify the right ICA first. If the lesion is in the territory of the left PCA, opacify one vertebral artery first. If the left PCA does not opacify, then study the left ICA because of the possibility of a fetal pattern of the PCA. Too often, angiographers find a catheter in a nonsymptomatic vessel and reason "let's shoot while we are here," or "they are going to want to see it later anyway, so let's shoot while we are here." Then, if complications occur, the angiography is stopped before the clinically relevant and important question is answered. Even with MRA, it is best to image the symptomatic artery first and in the segment most likely to harbor the lesion. Demographic data including the patient's age, race, and sex [1]; clinical symptoms and signs; and neuroimaging [49] and sonographic results should help locate the most likely region of vascular disease.

Rule 4

Decisions on vessel imaging or opacification should be made sequentially.—The decision as to which artery to study or opacify next depends on the results of the first study. An angiographer is asked to study a 57-year-old white man with known coronary artery disease who 1 day earlier had an episode of right hemiparesis and altered speech. From the description, the neurologist could not decide for certain if the patient was dysphasic or simply dysarthric. CT findings were normal. Duplex showed an irregular lesion in the origin of the left ICA without critical stenosis.

The epidemiology (presence of coronary disease, white race, male sex) predicts an occlusive neck lesion and a Duplex study shows a lesion in this region. The left ICA should be opacified or (if MRA) imaged first. If only a moderate degree of stenosis is found, the next most likely sites of disease would be the left ICA siphon and the left MCA [1]. If these sites appear normal, the left vertebral artery should be studied, since a left medullary or higher brainstem lesion could have caused transient right hemiparesis and dysarthria.

If the lesion had been a critical left ICA stenosis, the distal ICA-MCA should then be opacified. The surgeon might also want to know the state of the opposite ICA, so it should be studied also.

Optimally, the second step should be decided after the results of the first are known, and the third should follow the

results of the second. At times, only one step is needed, since the information gained from knowledge of that vascular lesion (in addition to sonography and other imaging) allows a logical therapeutic decision. Since the decisions are clinical and the responsibility for making them and the choice of treatment rest with the clinicians involved, the clinicians responsible should participate in each step of the procedure (see rule 6).

Rule 5

Minimize the amount of contrast material injected during angiography and the length of the procedure.—We believe that complications increase with the amount of contrast material injected and the length of the procedure. By tailoring the procedure to the patient's problem, performing preliminary imaging and sonography before angiography, tailoring the first "shot" to the suspected vascular lesion, deciding on the need for and type and location of subsequent studies sequentially, and establishing close clinician-angiographer communication, the length of the procedure and amount of contrast material injected can be minimized and complications prevented.

Rule 6

Optimum studies yielding clinically useful data are gained only by very close cooperation between the clinicians and the angiographers.—We have already stated our conviction that angiography should be performed only by neuroradiologists (or neurologists or neurosurgeons who have had formal training in neuroradiology). Only neuroradiologists have the required training, technical knowledge, and experience to perform arterial opacification. Although they perform the procedures, they certainly do not customarily make clinical management decisions. The best patient care occurs when the clinicians and neuroradiologists work together.

The clinician knows the question he or she wants answered. The clinician should approach the neuroradiologist as a consultant to decide on the best way to obtain the data and to share the clinical reasoning involved. The first shot should be planned together. If the clinician or surrogate will not be available, even by phone, during the study, subsequent shots might be discussed by using *what if* thinking. At times, the relationship between clinician and angiographer is so refined by experience that the angiographer knows what the clinician would want in ordinary situations. Sometimes formal protocols are constructed. When possible, discussions on site or by telephone at critical periods during the procedure, or if unexpected findings are uncovered, ensure that the clinicians will get answers to the relevant questions. We also believe that when a patient is undergoing angiography, that patient is under the direct clinical care of the neuroradiologist who is primarily responsible for the patient's welfare. The angiographer also wants to provide the data desired as safely as possible and has the right to abort the study when considered necessary. Mutual respect, consideration, and cooperation are important if the team is to work efficiently and effectively.

Rule 7

Examine the patient frequently between injections to identify problems or complications as early as possible.—The examiner should know the usual complications that might follow opacification of each vessel. Blindness, agitation, and amnesia may follow vertebral injections, especially when the vessels are widely patent and a high volume of contrast material is used [25]. Aphasia might follow left ICA injection as would monocular left visual symptoms. After each injection, a brief examination should be performed as well as checking for systemic and local catheter and equipment problems. If on site, the clinician or surrogate can perform the screening, as can trained nurses. Vigilance is an important safeguard against complications.

Summary

This review represents our own opinions and biases. They have been developed with the help of our neurologic and neuroradiologic colleagues. Our methods are not written in stone, but will change with new techniques, more information, and more experience. We hope they will prove useful.

REFERENCES

1. Caplan LR, Gorelick PB, Hier DB. Race, sex, and occlusive vascular disease: a review. *Stroke* **1986**;17:648–655
2. Gorelick PB, Caplan LR, Hier D, et al. Racial differences in the distribution of anterior circulation occlusive cerebrovascular disease. *Neurology* **1984**;34:54–59
3. Gorelick PB, Caplan LR, Hier DB, et al. Racial differences in the distribution of posterior circulation occlusive disease. *Stroke* **1985**;16:785–790
4. Mohr JP, Caplan LR, Melski J, et al. The Harvard Cooperative Stroke Registry: a prospective registry. *Neurology* **1978**;28:754–762
5. Caplan LR, Zarins CK, Hemmati M. Spontaneous dissection of the extracranial vertebral arteries. *Stroke* **1985**;16:1030–1038
6. Chiras J, Marciano S, Vega Molina J, et al. Spontaneous dissecting aneurysm of the extracranial vertebral artery (20 cases). *Neuroradiology* **1985**;27:327–333
7. Von Reutern G-M, Budingen HJ. *Ultraschalldiagnostik der hirnversorgenden Arterien.* Stuttgart: Thieme, **1989**
8. Caplan LR, Babikian V, Helgason C, et al. Occlusive disease of the middle cerebral artery. *Neurology* **1985**;35:975–982
9. Caplan LR. Intracranial branch atheromatous disease. *Neurology* **1989**;39:1246–1250
10. Millikan C, Futrell N. The fallacy of the lacune hypothesis. *Stroke* **1990**;9:1251–1257
11. Houser OW, Sundt TMJ, Holman CB, et al. Atheromatous disease of the carotid artery. Correlation of angiographic, clinical, and surgical findings. *J Neurosurg* **1974**;41:321–331
12. Masaryk TJ, Modic MT, Ruggieri PM, et al. Three-dimensional (volume) gradient-echo imaging of the carotid bifurcation: preliminary clinical experience. *Radiology* **1989**;171:801–806
13. Litt AW, Eidelman EM, Pinto RS, et al. Diagnosis of carotid artery stenosis: comparison of 2DFT time-of-flight MR angiography with contrast angiography in 50 patients. *AJNR* **1991**;12:149–154
14. Edelman RR, Mattle HP, Atkinson DJ, et al. MR angiography. *AJR* **1990**;154:937–946
15. Masaryk TJ, Modic MT, Ross JS, et al. Intracranial circulation: preliminary clinical results with three-dimensional (volume) MR angiography. *Radiology* **1989**;171:793–799
16. Ross JS, Masaryk TJ, Modic MT, Ruggieri PM, Haacke EM, Selman WR. Intracranial aneurysms: evaluation by MR angiography. *AJNR* **1990**; 11:449–456
17. Schmalbrock P, Yuan C, Chakeres DW, et al. Volume MR angiography:

methods to achieve very short echo times. *Radiology* **1990**;175:861–865
18. Pernicone JR, Siebert JE, Potchen EJ, Pera A, Dumoulin CL, Souza SP. Three-dimensional phase-contrast MR angiography in the head and neck: preliminary report. *AJNR* **1990**;11:457–466
19. Haacke EM, Masaryk TJ. The salient features of MR angiography. *Radiology* **1981**;173:611–613
20. Feussner JR, Matchar DB. Diagnostic evaluation of the carotid arteries. *Ann Intern Med* **1988**;109:835–837
21. Feussner JR, Matchar DB. When and how to study the carotid arteries. *Ann Intern Med* **1988**;109:805–818
22. Caplan LR, Stein RW. *Stroke, a clinical approach.* Boston: Butterworth, **1986**
23. Deykin D. Thrombogenesis. *N Engl J Med* **1967**;276:622–628
24. Reivich M, Holling E, Roberts B, et al. Reversal of blood flow through the vertebral artery and its effects on the cerebral circulation. *N Engl J Med* **196**;265:878–885
25. Caplan LR. Vertebrobasilar occlusive disease. In: Barnett HJM, Mohr J, Stein B, Yatsu F, eds. *Stroke, pathophysiology, diagnosis and management.* New York: Churchill-Livingston, **1985**:549–620
26. Hennerici M, Klemm C, Rautenberg W. The subclavian steal phenomenon: a common vascular disorder with rare neurologic deficits. *Neurology* **198**;38:669–673
27. Ringelstein EB, Zeumer H, Angelou D. The pathogenesis of stroke from internal carotid artery occlusion: diagnostic and therapeutical implications. *Stroke* **1983**;14:867–875
28. Fieschi C, Argentino C, Lenzi GL, et al. Clinical and instrumental evaluation of patients with ischemic strokes within the first six hours. *J Neurol Sci* **1989**;91:311–322
29. Foulkes MA, Wolf PA, Price TR, et al. The Stroke Data Bank: design, methods, and baseline characteristics. *Stroke* **1988**;19:547–554
30. Akers DL, Markowitz IA, Kerstein MD. The value of aortic arch study in the evolution of cerebrovascular insufficiency. *Am J Surg* **1987**;154: 230–232
31. Martin-Paredero VM, Dixon SM, Baker JD, et al. Risk of renal failure after major angiography. *Arch Surg* **1983**;118:1417–1420
32. Games AS, Baker JD, Martin-Paredero VM, et al. Acute renal dysfunction after major angiography. *AJR* **1985**;145:1249–1253
33. Miller DL, Chang R, Wells WT, et al. Intravascular contrast media: effect of dose on renal function. *Radiology* **1988**;167:607–611
34. Hankey GJ, Warlow CP, Sellar RJ. Cerebral angiographic risk in mild cerebrovascular disease. *Stroke* **1990**;21:209–222
35. Faught E, Trader SD, Hanna GR. Cerebral complications of angiography for transient ischemia and stroke: prediction of risk. *Neurology* **1979**; 29:4–15
36. Dion JE, Gates PC, Fox AJ, et al. Clinical events following neuroangiography: a prospective study. *Stroke* **1987**;18:997–1004
37. Berguer R, Bauer RB. *Vertebrobasilar arterial occlusive disease: medical and surgical management.* New York: Raven, **1984**
38. Caplan LR. Vertebrobasilar disease: time for a new strategy. *Stroke* **1981**;12:111–114
39. Caplan LR. Anticoagulation for cerebral ischemia. *Clin Neuropharmacol* **1986**;9:399–414
40. Tettenborn B, Estol C, DeWitt LD, et al. Accuracy of transcranial Doppler in the vertebrobasilar circulation. *J Neurol* **1990**;237:159
41. Pexman JHW, Coates RK. Amnesia after femorocerebral angiography. *AJNR* **1983**;4:979–983
42. Smoker WRK, Corbett JJ, Gentry LR, Keyes WD, Price MJ, McKusker S. High-resolution computed tomography of the basilar artery: 2. Vertebrobasilar dolichoectasia: clinical-pathologic correlation and review. *AJNR* **1986**;7:61–72
43. Baum S, Stern GN, Kuroda KK. Complications of "no arteriography." *Radiology* **1966**;86:835–838
44. Caplan LR, Rosenbaum A. The role of cerebral angiography in vertebrobasilar occlusive disease. *J Neurol Neurosurg Psychiatry* **1975**;38: 601–612
45. Hass WK, Fields WS, North RR, et al. Joint study of extracranial arterial occlusion: II. Arteriography, techniques, sites, and complications. *JAMA* **1968**;203:961–968
46. Patterson RH, Goodell H, Dunning HS. Complications of carotid arteriography. *Arch Neurol* **1964**;10:513–520
47. Barsan WG, Brott TG, Olinger C, Marler J. Early treatment for acute ischemic stroke. *Ann Intern Med* **1989**;14:449–450
48. Caplan LR, Wolpert SM. Conventional cerebral angiography in occlusive cerebrovascular disease. In: Wood JH, ed. *Cerebral blood flow: physiological and clinical aspects.* New York: McGraw-Hill, **1987**:356–384
49. Caplan LR, Cerebrovascular disease: large artery occlusive disease. In: Appel S, ed. *Current neurology*, vol. 8. Chicago: Yearbook Medical, **1988:**179–226