Commentary

Aneurysms and MR Angiography

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The magnetic resonance angiography (MRA) study reported by Dr Curnes and his associates (1) is in some senses astonishing, given the skepticism with which MRA for intracranial aneurysms has been viewed by neurosurgeons in many institutions. When mentioning that "MRA may be useful as a *screening* test for aneurysms larger than 3 mm in size" based on work by Ross (2), even this more restrained use of MRA has met with considerable skepticism.

The problem of the intracranial aneurysm not seen on conventional angiography in a patient with subarachnoid hemorrhage (SAH) has been with us since Egas-Moniz. It may be useful to review the current clinical assessment of intracranial aneurysms. Approximately 75% of patients with spontaneous SAH will be determined to have an underlying intracranial aneurysm. Five percent will be found to have an intracranial arteriovenous malformation (3). SAH can be associated with deficiencies of each of the known coagulation factors and can also occur with therapeutic anticoagulation. Uncommon medical diseases such as fibromuscular dysplasia or moya moya can be the source of the bleeding. In sickle cell anemia with SAH, as many as 50% of the patients will have an associated aneurysm in addition to the sickle cell occlusive disease (3). Collagen vascular disease such as systemic lupus erythematosus or polyarteritis nodosa can cause intracranial bleeding. Drug abuse that produces hypertension such as of cocaine, amphetamine, and phencyclidine ("angel dust") can cause SAH.

There are a few sources of SAH that may not show up on angiograms. These are designated "cryptic malformations." Small arteriovenous malformations, thrombosed or partially thrombosed, can lead to significant SAH. Other cerebral malformations (cavernous hemangioma, venous angioma) almost never produce significant SAH (3, 4). Cavernous hemangiomas may bleed recurrently, but the hemorrhage is usually confined locally.

There is one type of SAH in which the source of bleeding is usually never found. This is peri-mesencephalic SAH (5). In these patients, the SAH is confined mainly to the perimesencephalic cisterns but may extend anteriorly in the suprasellar space and to the cerebellopontine cisterns. However, in these patients, the SAH does not extend to the sylvian cisterns or the interhemispheric fissures to a significant degree. Although the question of a nonvisualized aneurysm has been raised in these patients, autopsy studies with SAH in which no defined source was detected only occasionally revealed an aneurysm that was not appreciated at the time of angiography. Usually, the autopsy does not reveal the source of the hemorrhage (6). One explanation offered is that the hemorrhage results from "leakage" of the thalamoperforate or lenticulostriate arteries, but this has not been confirmed.

Need for Repeat Angiography?

In the 1960s, it was customary to request routinely a second angiographic study if the first did not show the aneurysm. This was particularly true in patients who had local spasm in the arteries making up the circle of Willis. Sometimes up to four angiograms were required to show the aneurysm. Repeat angiogram was justified by the cooperative study of patients with SAH. As a part of this study, 13 of 72 patients with SAH and normal three-vessel angiography were found to have an intracranial aneurysm documented on the second study (6). The fact that aneurysms could be missed on the initial study was confirmed in another part of the same study. In 23 of the 210 patients whose premortem angiograms did not demonstrate the ruptured aneurysm, an aneurysm was identified at the time of autopsy (7).

Although present-day angiographic techniques have improved, and a second study will have a lower yield, there are still individual patients with a negative initial angiogram who will show an aneurysm on the second study. Some aneurysms do not fill with contrast whether or not vasospasm

is present (8, 9). Sometimes we are unable to discern an aneurysm because of overlying vessels despite multiple projections, but it can be pointed out in retrospect given the insight of the second study. For this reason, many neuroradiologists prefer stereoscopic angiography despite the technical demands of these systems. Anterior communicating artery aneurysms or middle cerebral artery trifurcation aneurysms are usually the source of bleeding in these patients.

Despite these data, some have abandoned the second angiographic study. Forster et al documented that only one patient in 56 (1.8%) was found to have an aneurysm on the second angiogram not seen in the first study (8). As Friedman (3) has pointed out, their patients were not studied by computed tomography so the denominator in this series may have been inflated by including patients with small intraparenchymal hemorrhages or tumor-related hemorrhages. In addition, three of the 94 patients who did not undergo a second angiogram had documented aneurysms later that were discovered at the time of the second hemorrhage (9). In Friedman's review of papers reporting individuals with SAH and who had extensive angiography, the rate of the rebleed averaged 4% (3). In patients selected to undergo a second angiogram, at least 3.6% were found to have an aneurysm upon repeat study (8, 10, 11). Suzuki et al reported that the second angiogram will document an aneurysm not yet discovered in 22% of patients (12). In the cooperative study on aneurysms and SAH, 13 of 72 repeat studies revealed an unsuspected aneurysm.

Because angiography has a risk of a major complication in only 0.25% and the risk of death from a second hemorrhage in a patient who is not studied is relatively high, we should continue to employ it. Friedman points out that it is particularly important for patients in whom 1) vasospasm has comprised the original angiogram, 2) a portion of the cerebral vascular tree is not optimally seen, 3) there is a large amount of subarachnoid blood, particularly if it is in a focal clot on computed tomography scan, and 4) a second SAH has occurred (3). In reviewing a number of series describing patients who have SAH of undetermined origin, Friedman reports that 80% will have a good outcome and return to full-time employment, whereas only 50% of patients with ruptured intracranial aneurysms will be able to return to work (3).

Patients in whom a structural lesion is not found rebled at a rate of approximately 4% over the 3 months that follow the hemorrhage. This group then suffers rebleeding at a rate of 0.8% per year for at least the next 3 years (11, 13). This is in sharp contrast to the rates of rehemorrhage following a ruptured aneurysm: 50% rebleed in the first 6 months; 3% per year subsequently.

MRA Demonstration of an Aneurysm Not Seen on Angiography

How could MRA image the anterior communicating aneurysm when conventional angiography could not detect it? What are the possible mechanisms that would explain a negative conventional angiogram? We could ask the following questions:

• Could one have stationary protons in tissue with short T1 giving a high signal intensity in the area of the aneurysm which, when superimposed on the high signal intensity of moving protons (blood) in arteries seen on MRA, appears to be an aneurysm? (Methemoglobin within a clot in the aneurysm or in a perianeurysm hematoma or mucin in anterior ethmoid air cells?)

While a high-intensity signal might be seen on gradient-echo MRA images using 3-D time of flight where suppression of stationary protons having a short T1 could be incomplete, it should not be seen with phase contrast MRA. In the phase contrast MRA, you would see only the hyperintense signal of flowing intravascular protons. For the record, Dr Curnes states that a preliminary sagittal T1-weighted image showed no high signal focus.

• At the time of the conventional angiogram was there blood clot within the aneurysm that lysed just before the MRA?

Thrombus in an aneurysm is always a possibility. However, with clot in the aneurysm it is difficult to see how the phase contrast MRA would show moving protons in the aneurysm. Also, it would not explain why the frontal image 7 days after the hemorrhage failed to show the aneurysm on conventional angiography, whereas the base view showed contrast within the aneurysm. With regard to clot formation, raising the question of an earlier episode of bleeding and thrombosis, the clinician member of the team (Dr Elsner) stated that the patient had not had an earlier episode of bleeding, and the headache associated with the current bleed began only several hours before the angiogram was performed.

Could increased perfusion after the angiogram have "washed out the clot" before the MRA? This mechanism is unlikely because of the short time interval between the angiogram and the MRA (less than 1 hour). Even if the clot were "washed out," this does not detract from the fact that the aneurysm was seen on the MRA. Finally, it is important to note that the second frontal angiogram 7 days postbleed did not show the anterior communicating aneurysm.

• Did the aneurysm fail to show because of spasm?

There is no arterial spasm on any of the angiographic projections.

In summary, this observer has no good explanation why the conventional angiogram was negative but the MRA was positive.

Just how good is MRA in the detection of intracranial aneurysms?

In Ross's series 3-D time-of-flight MRA plus routine spin-echo brain imaging demonstrated a sensitivity of 95% and a specificity of 100% for detecting at least one intracranial aneurysm greater than 3 mm in diameter in a patient (2). They studied 37 patients by MRA and compared them with 19 patients with digital carotid angiography, who had saccular or giant intracranial aneurysms. They used a velocity-compensated gradient-echo sequence (TR = 40–50/TE = 7–15), a 15° flip angle, cine 3-D reconstructions, individual partitions, and spin-echo studies. The sensitivity was 86% for the cine MRA, partitions, and spin-echo sequences. In the 19 patients who had intraarterial digital studies, the sensitivity rose to 95% for the cine MRA, partitions, and spin-echo studies. The size of the aneurysm in this study was at least 3 to 4 mm in diameter. This is a significant sensitivity as Locksley (13) and McCormick and Acosta-Rua (14) found no hemorrhages from aneurysms less than 3 mm in size. In addition, Locksley found that 90% of the single aneurysms that cause SAH fell within the circle of Willis; only 10% of single aneurysms involving SAH were located in more peripheral branches or within the cerebellar vessels (13). The entire circle of Willis volume can be readily encompassed by a limited transverse volume on MRA. However, evidence now indicates that 3-D phase contrast MRA is the best technique for the detection of aneurysms of the circle of Willis. This was documented in a comparison study with time-of-flight MRA and phase contrast MRA by Huston et al (15).

The time required for 3-D phase contrast MRA is about twice that of 3-D time-of-flight MRA for the same volume. The significant time commitment for postprocessing can be carried out while clinical scanning continues. Time-of-flight MRA has artifacts related to tissues having short T1 and flow spins tending to lose signal as the flow-related enhancement decreases as saturation occurs toward the top of the volume; phase contrast MRA has problems with aliasing. If the velocity encoding selected is below the peak velocity of the vessel imaged, the faster flowing blood will have phase shifts. The collapsed projection images will show a mottled-appearing vessel. One can usually "read through" these artifacts. Advantages include variable velocity sensitivity, a superior ability to detect the patent lumen in blood vessels, less problem with saturation effects, and better background suppression (15). One must look at the individual partitions comprising the MRA, as aneurysms can be seen that would otherwise be missed. As Ross (2) pointed out, detection is increased significantly by using the spin-echo images, along with the partitions and the reformations. One can assume that there will always be difficulty in visualizing the *neck* of the aneurysm. This means that any MRA study for aneurysms must inevitably be followed by a conventional angiogram to visualize the neck. Most neuroradiologists look at MRA as primarily a screening tool. Regardless, neuroradiologists will continue to seek improved MRA images; optimal MRA studies will include 1) 3-D phase contrast MRA with appropriate velocity encoding (Dr Curnes used 30 cm/sec), 2) velocity coding in all three directions, 3) reviewing individual partitions, 4) cine mode display, and 5) high-resolution thin sections of the brain at the base (perhaps fast spin-echo trading time for higher resolution).

What are the indications for MRA screening of aneurysms using the most optimistic scenario?

Assuming a sensitivity of 95% and a specificity of 100% for detection of at least one 3-mm intracranial aneurysm, the following indications may be useful:

1. Screening of aneurysm-prone disease populations such as patients with polycystic kidney disease, coarctation, fibromuscular disease, collagen vascular disease, or sickle-cell anemia. Levy et al (16) have stated that if the sensitivity and specificity of a new test for aneurysm were 80% and 85%, respectively, in polycystic kidney disease, then the benefit of subsequent arteriography and surgery in a 20-year-old patient would

be significant. MRA appears to have met these criteria.

2. Screening of family members of patients with documented aneurysms. With a sensitivity of 95%, some justifiable reassurance can be given to these patients.

3. Screening patients like Dr Curnes's when conventional angiography has been negative in the face of significant SAH.

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