



## Obliterating the Seizure Focus in AVMs is Effective: More Clinical Data Confirming Common Sense

### **Radiosurgery for Unruptured Cerebral Arteriovenous Malformations: Long-Term Seizure Outcome.**

Yang SY, Kim DG, Chung HT, Paek SH. *Neurology* 2012;78:1292–1298.

**OBJECTIVE:** To date, seizures in relation to arteriovenous malformations (AVM) have been a secondary target of most studies. The insufficient evaluation, in conjunction with the lack of consistent seizure outcome assessment, has made it difficult to draw conclusions about seizure outcome after radiosurgery for AVM. This study aimed to determine the effect of radiosurgery on seizure outcome depending on AVM obliteration and on the development of new seizure in patients with AVM. **METHODS:** Between 1997 and 2006, 161 consecutive patients underwent radiosurgery for unruptured AVM and were retrospectively assessed with a mean follow-up of 89.8 months by their medical records, updated clinical information, and, when necessary, direct patient contact. Seizure outcome was assessed using the Engel seizure frequency scoring system. **RESULTS:** Of the 86 patients with a history of seizure before radiosurgery, 76.7% (66/86) were seizure-free and 58.1% (50/86) were medication-free at the last follow-up visit. Of the patients who achieved AVM obliteration, 96.7% (58/60) were seizure-free while 30.8% (8/26) of those patients who did not achieve AVM obliteration were seizure-free ( $p = 0.001$ ). The proportion of patients who were medication-free was 81.7% (49/60) of the patients with obliteration and 3.8% (1/26) of patients without obliteration ( $p < 0.001$ ). Of the 75 patients with no history of seizure before radiosurgery, 10 had provoked seizures due to the direct and indirect radiosurgical influences after radiosurgery. **CONCLUSIONS:** Although radiosurgery tends to cause seizures temporarily, the radiosurgery may improve seizure outcomes in patients with AVM-related seizures, especially in patients with AVM obliteration.

### **Epileptic Seizures at Initial Presentation in Patients with Brain Arteriovenous Malformation.**

Garcin B, Houdart E, Porcher R, Manchon E, Saint-Maurice JP, Bresson D, Stapf C. *Neurology* 2012;78:626–631

**OBJECTIVES:** Brain arteriovenous malformations (AVMs) often present with epileptic seizures, but prospective data on the risk of seizures with respect to morphologic AVM characteristics are scarce. **METHODS:** We studied 155 consecutive patients with AVMs from a prospective, single-center database using demographic and morphologic factors based on prospectively coded MRI and digital subtraction angiography (DSA) data. Univariate analysis and multivariate logistic regression models were used to test the effect of demographic (age and sex) and morphologic characteristics (AVM size, anatomic and arterial location, and venous drainage pattern) on seizures as initial presentation in patients with unruptured brain AVMs. **RESULTS:** Overall, 45 patients with AVMs initially presented with seizures (29%). By univariate comparison, male sex ( $p = 0.02$ ), increasing AVM size ( $p < 0.006$ ), frontal lobe localization ( $p < 0.0001$ ), arterial borderzone location ( $p < 0.0006$ ), superficial venous drainage ( $p = 0.0002$ ), and presence of venous ectasia ( $p = 0.003$ ) were statistically associated with seizures. The multivariate analysis confirmed an independent effect of male sex, frontal lobe AVMs, and arterial borderzone location on seizure occurrence. All patients with seizures showed the presence of a superficial venous drainage component. **CONCLUSIONS:** Our study suggests that seizures mainly occur in AVMs with superficial drainage. Other predisposing factors include male sex, increasing AVM size, and frontal lobe and arterial borderzone location. Whether or not interventional treatment has an effect on the long-term risk of epilepsy remains to be determined.

### **Commentary**

AVMs are important to neurologists who treat epilepsy because ruptured AVMs are easily recognized when they cause intractable epilepsy. However, Garcin et al. (1) report that in a recent retrospective case series, almost one-third of 155 patients with *unruptured* AVMs presented with seizures. Thus,



unruptured AVMs may be a more common cause of epilepsy than generally appreciated or, at least, the topic receives less attention than it might deserve perhaps because vascular neurologists tend to be preoccupied with more acute and catastrophic presentations of AVMs and tend to think of seizures as a minor or incidental presentation until the seizures become intractable.

Standard treatment of *ruptured* AVMs includes intravascular techniques, resective surgery, and radiosurgery. However, the appropriate treatment of *unruptured* AVMs is controversial. The fundamental risk/benefit conundrum is familiar to epilepsy specialists and general neurologists: Which is worse, the complications of the natural history of the disease or the complications of treatment? For unruptured AVM treatment, the problem is vexing because the natural history is not entirely known, and the rates of hemorrhage, epilepsy, and neurologic deficit are relatively low. Thus, any viable treatment to eliminate seizures requires an even lower rate of complications.

A Randomized Trial of Unruptured Brain AVMs study (ARUBA) is a trial designed to answer the question of whether intervention is better than conservative management for unruptured AVMs (2). Carefully selected, essentially asymptomatic patients are randomized either to watchful waiting or intervention. The intervention is not specific or randomized and can be any of the common interventions of endovascular surgery, microsurgery, or radiosurgery. This well-designed NIH-funded study seems surprisingly controversial in the neurovascular community. Some think the study is underpowered and includes too broad of a population (3). However, the study authors provide a counterbalancing argument that the population studied is similar to the population for which the controversy exists (4). Even if ARUBA is successful in determining that intervention reduces the risk of complications, it is unlikely to have sufficient power to determine whether radiosurgery—or any other specific intervention—is more efficacious than another, especially with regard to those with seizures.

Until the results of ARUBA are available, we will have to rely on retrospective studies for deciding what to do about epilepsy due to unruptured AVMs. Yang et al. (5) recently reported a good seizure outcome from radiosurgery for treatment of seizures due to unruptured AVMs. They rendered three-fourths of 86 patients seizure-free that had seizures before radiosurgery. The seizure-free rate was more than 96% when the AVM was obliterated compared to just 30.8% among those in whom it was not obliterated. At face value, this would seem to be an effective treatment for seizures due to unruptured AVMs. However, 14% of their patients who did not have seizures before radiosurgery developed seizures after treatment. Furthermore, radiosurgery has known long-term complications that require years to appear. Nevertheless, radiosurgery will certainly have a place for patients who decline standard open resective surgery for intractable epilepsy due to unruptured AVMs.

Why are the articles under consideration important to the practice of epilepsy? It is generally accepted that AVMs cause seizures through hemosiderin-mediated irritation of the cortex, which is reasonable and is generally supported by the associations demonstrated by Garcin et al. (1). All of their cases

with seizures had a superficial draining vein that would be anatomically appropriate to provide a seizure focus in the cortex since, in most cases, the main body of the AVM has a subcortical rather than cortical location. Therefore, it is not surprising that eliminating the entire abnormality is more effective than just reducing its size. This may seem like common sense, but in radiosurgical planning, the surgeon must know how big to make the field of irradiation and what dose of radiation to use—which might be different if obliteration, rather than reduction in size, is an important goal. Analogously, it appears that a larger necrotic dose is probably more effective than a lower dose in radiosurgical treatment of mesial temporal lobe epilepsy, although the actual efficacy of radiosurgery for mesial temporal lobe epilepsy awaits the results of a randomized controlled trial (6).

If you decide to refer a patient for treatment of an unruptured AVM, should you refer the patient for radiosurgery, open resection, or endovascular therapy? Since there are no data to know whether one treatment is more effective or morbid than the others, it will depend on the options and level of expertise available and the disposition of the patient. Many patients find the noninvasive nature of radiosurgery so appealing that it seems to trump all other factors for them.

Epilepsy specialists must be aware of the controversy in treating unruptured AVMs as well as the treatment options available. The studies reviewed here may change practice to ablate the seizure focus for patients with unruptured AVMs, but the findings also have a wider implication by contributing to the growing literature that ablation of brain tissue is often needed in radiosurgery to treat seizures effectively.

by Nathan B. Fountain, MD

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