Unruptured Brain Arteriovenous Malformations Should Be Treated Conservatively

No

Kevin M. Cockroft, MD, MSc, FACS

The case for treatment of asymptomatic cerebral arteriovenous malformations (AVM) is based on the premise that the morbidity and mortality of treatment should be less than the expected morbidity and mortality associated with the untreated AVM for the remainder of the patient’s expected lifetime—in other words the natural history of a treated AVM must be better than that of an untreated AVM. The literature contains a wide range of data on this subject, and by taking examples from across this spectrum one can easily support any viewpoint. Therefore, for the purposes of this discussion, published data from the Columbia AVM Databank will be used because this data are relatively “modern,” are prospectively acquired and are frequently used to support a position of nonintervention for asymptomatic AVM.

For many years, intracranial AVM were generally considered to carry a bleed risk of about 2% per year for symptomatic AVM and around 4% per year for symptomatic lesions, with each hemorrhage having an associated neurological morbidity of 20% to 30% and mortality of 10% to 30%. Based on a combination of retrospective and prospective studies, sometimes without a clear distinction between symptomatic and asymptomatic AVM, and with some studies performed in the pre-MRI or pre-CT era, these numbers deserve careful examination and confirmation. Yet, although some recent studies have reported a dramatically lower mortality rate with AVM hemorrhage, the yearly hemorrhage rate and rate of morbidity were not found to be dramatically different. Using prospective data from the Columbia AVM Databank, Stapf et al in 2006 reported a 1.3% yearly rate of hemorrhage in unruptured AVM (5.9% for those that presented with hemorrhage) and this was with a median follow-up of only 102 days. If one takes the average age of the AVM population from this study of 34 years of age and uses a life expectancy of 44 additional years (42.25 years male, 46.75 years female, Period Life Table, Actuarial Publications, http://www.ssa.gov/OACT/STATS/table4c6.html), the cumulative risk of hemorrhage from an asymptomatic AVM is 44%. In terms of outcome, again using the Columbia AVM Databank, the same group recently published clinical outcomes after first and recurrent AVM hemorrhages and reported a 30-day rate of moderate to severe disability (Rankin Score 3 to 5) of 33%. Clearly, even this “new” data does not suggest an insignificant risk to the young patient with an asymptomatic AVM.

If our data regarding the natural history of asymptomatic AVM continue to show significant risk, then what of our treatments? Have the risks of AVM treatment increased in the last 20 years? In viewing treatment related morbidity it is important to use the same criteria for evaluation that are used when considering morbidity after hemorrhage. The “independent neurological examination” is frequently touted as a requirement for evaluating the effects of intervention, but only rarely, if ever, is such a rigorous approach used in the examination of the consequences of natural history events. Typically, the Rankin Score is used for functional outcome after hemorrhage and therefore should also be used when assessing morbidity after intervention. By way of example, again from the Columbia AVM Databank, Hartman et al in 2005 published prospective outcome data from 119 consecutive patients with a mixture of symptomatic and asymptomatic AVM that had undergone staged endovascular and surgical treatment. There were no treatment-related deaths and overall significant morbidity was 9% (Rankin Score 3 to 5). Among the 78 patients who had not experienced a hemorrhage before treatment, the rate of significant morbidity was only 6%. Using our hypothetical 34-year-old mentioned earlier, the patient’s lifetime risk of significant morbidity is approximately 14%, meaning that even assuming a complicated multimodality intervention to treat the patient’s AVM, the overall result is a >50% reduction in the relative risk of significant morbidity.

Obviously, the above example does not account for the many variations in natural history and treatment risk known to exist related to both patient and AVM factors. The fact that such a plethora of potentially significant variables exists only serves to further complicate treatment decisions and makes the extrapolation of data from published trials to individual patients exceedingly difficult. Although the A Randomized Trial of Unruptured Brain AVMs (ARUBA) study will endeavor to offer definitive resolution to this debate, it is

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From the Department of Neurosurgery, Penn State MS Hershey Medical Center, Hershey, Pa.
Correspondence to Kevin M. Cockroft, Department of Neurosurgery, Penn State MS Hershey Medical Center, PO Box 850, Hershey, PA 17033. E-mail kcockrof@psu.edu
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unlikely that this goal will be attained. As designed, ARUBA is subject to many of the same methodological problems common to most prospective, randomized, controlled trials. Selection bias remains a major challenge and in a disease such as cerebral AVM with a long history of established treatment patterns, the randomization of an adequate representation of lesions with various risk profiles and multimodality treatment patterns will be difficult. Without such representation, the external validity of this trial is threatened. In addition, adequately controlling for all these covariates will likely render the study underpowered to detect a significant difference at only 5-years. Although the use of a 5-year end point is typical of prospective, randomized, controlled trials of this type, the relevance of such a short time period to clinical decision-making in a disease that may play out over 20-plus years is at best questionable. It is important to remember that 5 years of follow-up in 1000 patients is not the same as 20 years of follow-up in 250 patients, even though the number of patient-years is the same. Put another way, even the most aggressive neurosurgeon would be unlikely to treat a patient with an asymptomatic AVM, if the patient was known to have only a 5-year life expectancy. In the end, ARUBA will undoubtedly provide clinicians with new information, but the scope and applicability of this information will likely be much more limited than first anticipated.

Ultimately, as with any disease, and most certainly with one in which the patient is asymptomatic and future morbidity is uncertain, whenever intervention is contemplated the risks and benefits of treatment must be carefully weighed against those of observation alone. For cerebral AVM a considerable body of evidence continues to support treatment in many asymptomatic patients.

Disclosures
None.

References

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