Results of ARUBA Are Applicable to Most Patients With Nonruptured Arteriovenous Malformations

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2006 (Kissimmee, FL) was the last such controversy session on brain arteriovenous malformations (AVMs) at an International Stroke Conference. The patient then was somewhat older but raised similar management issues. Intervention had produced a major stroke. A dissatisfied interventionist in the audience was overheard to murmur, “I want some answers.” A Randomized Trial of Unruptured Brain Arteriovenous Malformations (ARUBA) trial had just been funded by National Institutes of Neurological Diseases and Stroke (NINDS) but had not begun.

Some additional information would help hemorrhage risk assessment for the current case. Evidence of previous hemorrhage, symptomatic or not, raises the risk of further hemorrhage; based on current practice, it would argue for intervention with a goal of lesion eradication. Recent onset headaches could mean she is developing venous stenosis or dilatation, thought by some a risk factor for hemorrhage, albeit not easily treated. If the AVM site straddles the arterial border—zones, risk of first hemorrhage would be lower than for sites elsewhere. To be characterized as Spetzler–Martin Grading System (SMGS) 3 presumably means the 3 points are the sum of 2 points for the 4 cm (medium) size, the third point from eloquent site (superficial parietal location), not deep venous drainage. The score could be improved using the expanded scale proposed by the Center for Cerebrovascular Research, University of California, San Francisco.

The questions posed might make some readers assume the patient is expected to be referred for interventional therapy (a radiosurgery option not cited). We suggest she might be as well or better managed by medical therapy alone, treating the headache. Often-quoted annual hemorrhage risks of 4% and death of 1% have seemed to justify intervention. But modern reports for those not having bled have values as low as 1% to 2% for hemorrhage, and less for death.1 By contrast, adverse events for interventions have proved far higher than formerly assumed; for those both bled and no-bled, a recent meta-analysis2 cited point estimates for surgery 29% (range 1.5–54%), embolization 25% (range 7.6–55), and radiotherapy 13% (range 0–63).3

And no surprise: AVMs being embedded in brain, eradication efforts risk disturbing healthy tissue (adjacent to, possibly within the AVM), generating syndromes of varying degrees of severity. Intervention efforts have been sustained by hopes that some compensatory mechanisms may shorten the course or eventually yield an acceptable residual syndrome. Those favoring conservative management separately hope that hemorrhage will be long delayed, confined mainly to the nidus with minor syndrome effects, thereafter justifying subsequent eradication efforts for the expected. The dilemma has been posed as sleeping dogs or unexploded bombs?

The recently published data from the ARUBA trial,3 applicable for those never having bled, corroborates outcomes from both the recent meta-analysis2 and population-based reports.4 (Considering that the ARUBA cohort comes from 39 centers worldwide, the results serve to confirm both external and internal validity of the trial.) The majority (62%) of those randomized to ARUBA were of the smaller size and more superficial locations thought most favorable for attempted eradication: SMGS I 30%, II 32%, III 28%, and IV 10%. Begun in 2007, the randomization phase of the trial was ended in April 2013 by a NINDS-appointed data and safety monitoring board. Although strongly recommending long-term follow-up, their action was based on a >3-fold incidence of stroke (confirmed by imaging) and death in the interventional arm compared with the medical. There was a clear increase in stroke/death outcomes with intervention those whose with SMGS II–III (too few cases were in SMGS IV for suitable statistical analysis), but no similar indication of increased stroke events by SMGS in the medical arm. Follow-up for the 223 participants was at a mean of 3.3 years. The distribution of disability scores (≥2 as rated by the modified Rankin Scale) was also persistently and significantly worse for those having events in the interventional arm compared with the medical. These results disappointed hopes for substantial early syndrome improvement. (Longer-term follow-up can assess whether these disparities in event rates and functional status will persist.)

Available data justify a recommendation that she defer intervention: the frequency of headaches or seizures documented in ARUBA is the same whether or not patients undergo intervention to eradicate the AVM. However, if treated now, her likelihood of having symptomatic stroke or death is >3 times
higher as compared with being simply managed medically for headaches. There is reasonable hope that she may be spared hemorrhage in her lifetime, which any such event would prove clinically mild, and that improved methods of management will have evolved. We recommend she live a normal life and proceed with her eventual career and family plans.

Disclosures
None.

References

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