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Microsurgical resection is the first-line therapy or criterion standard for many brain arteriovenous malformations because of its high cure rate, low complication rate, and immediacy. Surgical results have improved with time with the following: 1) the creation of grading systems to select patients likely to experience optimal outcomes; 2) the development of instruments like bipolar forceps and AVM microclips that coagulate or occlude feeding arteries effectively; 3) the recognition of AVM subtypes that help decipher AVM anatomy; and 4) the refinement of surgical approaches, strategies, and dissection techniques that facilitate safe AVM resection.[1-3] This impressive evolution of AVM surgery is at odds with the finding of A Randomized Trial of Unruptured Brain AVMs (ARUBA) that medical management alone was superior to interventional therapy for the prevention of death or stroke in patients with unruptured AVMs followed for 33 months.[4]

An important explanation for the ARUBA finding is the surprisingly nonsurgical management of patients in the interventional group in the trial. Overall, 81% of patients were treated with embolization alone (32%), radiosurgery alone (33%), or combined embolization and radiosurgery (16%), and only 17 patients (18%) were treated surgically, with or without embolization. Therefore, the 3-fold increase in death or stroke in the interventional arm reflects current nonsurgical therapies and should not be interpreted as an indictment of AVM surgery. In the aftermath of ARUBA, it is important to clarify the safety, efficacy, and outcomes associated with AVM resection.

Our experience in managing 232 Spetzler-Martin grade I and II AVMs, the most favorable AVMs for surgery and the ones most likely to have been selected for treatment outside the randomization process of ARUBA, exemplifies a surgical posture toward low-grade AVMs that regards curative resection as the first-line or criterion standard therapy for most lesions.[5] We used embolization as a preoperative adjunct and reserved radiosurgery for risky AVMs in deep, inaccessible locations; in eloquent areas that might be associated with postoperative neurologic deficits; and/or with diffuse nidus morphology that might complicate microdissection. Patients were carefully selected to optimize outcomes, with a mean age of 38 years, Lawton-Young grades of ≤III in 69% of patients, and few (<4%) AVMs in deep locations or the brain stem. Conservative embolization minimized additional treatment risk, with only 43% of patients undergoing embolization and no patients experiencing endovascular complications. Surgical cures were confirmed in all patients who underwent postoperative angiography. Overall, 6 patients (3%) were worse neurologically after surgery, with 161 patients (78%) in total and 91 patients (91%) with unruptured AVMs experiencing good outcomes (modified Rankin Scale scores, 0–1). These surgical results are consistent with other reports in the literature. In a review of 1235 patients with low-grade AVMs, the average surgical morbidity and mortality rates were 2.2% and 0.3%, respectively, with an average cure rate of 98.5% and a postoperative or delayed hemorrhage rate of 0.3%.[5]

The management of AVMs in other parts of the world is diverging from the surgical approach described above. In Europe, for example, treatment is often limited to only ruptured AVMs, beginning with aggressive embolization, frequently adding radiosurgery for incompletely embolized AVMs, and rarely resorting to surgical resection. Onyx (Covidien, Irvine, California) is an important endovascular advancement over N-butyl 2-cyanoacrylate glue and has improved the efficacy of endovascular therapy, but cure rates are still low and curative attempts are associated with increased complications, occlusion of critical draining veins, and adverse imaging findings in as many as 40% of patients. In a review of 1297 patients with mostly low-grade AVMs, the average endovascular morbidity and mortality rates were 6.2% and 1.6%, respectively, with an average cure rate of 29% and a postoperative or delayed hemorrhage rate of 8.0%.[5] Therefore, aggressive endovascular therapy has higher procedural risks, substantially lower cure rates, and increased hemorrhage risks compared with surgery.

A similar comparison can be made with radiosurgery for low-grade AVMs. Although these lesions are ideal for radiosurgery because of their lower target volumes and higher obliteration rates, the 2- to 3-year latency period between treatment and obliteration opens a time window for AVM hemorrhage and associated complications. Radiation-induced complications are low, but in a review of 1051 patients with low-grade AVMs, 7.2% of patients hemorrhaged after treatment, resulting in morbidity and mortality rates of 6.5% and 1.2%, respectively.[5] The 75.2% radiosurgical cure rate was substantially better than the endovascular cure rate, but still less than that of surgery. Therefore, despite the technologic advances in endovascular and radiosurgical therapy, surgery still offers the best cure rate, lowest risk profile, and greatest protection against hemorrhage for low-grade AVMs. Surgery cannot compete with the minimally invasive appeal of these other modalities, but this issue remains secondary to functional outcome.

How do we interpret the ARUBA findings in this context? First, on the basis of the surgical experience described above, a substantial number of neurosurgical investigators in ARUBA did not consider AVMs with low Spetzler-Martin grades (low treatment risk) to be in equipoise with medical management (high hemorrhage risk) and "selected treatment outside of the randomization process"[4] (177 patients, or close to the number of included

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patients). Conversely, intermediate (31.8%) and high-grade AVMs (10.3%) that are generally considered to have a more benign natural history and high risk for any treatment were included in the trial, diminishing the interventional results.

Second, with its unusual bias toward nonsurgical therapy and no data published on cure rates, the number of incompletely obliterated AVMs was likely high and resulted in ongoing ruptures. Therefore, the event rates observed in Kaplan-Meier estimates of "as-treated" patients reflected the procedural morbidity of interventional therapies plus the delayed morbidity of latency hemorrhages associated with radiosurgery and incomplete embolization. The outcome of such a group could never exceed that of an observational group whose only morbidity was the natural history risk.

Third, the shortage of surgical expertise in the ARUBA trial is apparent. Two-thirds of patients in the interventional group had low-grade, surgical AVMs; yet, only 18% underwent surgery, which is well below the expectation for the criterion standard therapy. The rates of stroke and death in this trial do not match the reported surgical outcomes. Therefore, the management of AVMs in ARUBA reflects a nonsurgical posture consistent with the fact that 38 of the 65 ARUBA sites were in Europe, Australia, and Brazil. Centers were required to manage 10 patients with AVMs per year, but there were no minimum requirements for neurosurgeons. AVM resection is among the most challenging neurosurgical cases, and the best AVM surgeons typically perform more than 25 resections annually. Had the ARUBA trial been embraced by the neurosurgical community, the application of surgical therapy would have been higher, the interventional outcomes would have been better, and the benefits of intervention would have been apparent. Had ARUBA been more surgical with complete resections and no delayed hemorrhages in incompletely treated patients, the event rates observed in Kaplan-Meier estimates of "as-treated" patients would have plateaued and the benefits of intervention would have been realized in much fewer than 10 years.

These critiques were validated in an analysis of our ARUBA-eligible patients managed outside the trial. As a participating ARUBA site, the University of California, San Francisco, screened 473 patients for eligibility, enrolled 4 patients, and had complete data on 74 eligible patients managed outside the trial, of whom half had low-grade AVMs. Forty-three patients (71% of treated patients) were treated surgically with or without preoperative embolization, 15 patients (25% of treated patients) were treated radiosurgically, and 13 patients (18% of the overall cohort) were observed. The risk of stroke and death and the degree of clinical impairment among treated patients were lower than those in ARUBA, with primary outcome rates of 11%, 27%, and 8% for surgery, radiosurgery, and observation, respectively. The 3-fold difference in primary outcome reported in ARUBA disappeared with a different management strategy and a different surgical expertise, leaving no significant difference in the rate of stroke or death between treated and observed patients (hazard ratio, 1.34; 95% CI, 0.12–14.53; $P = .807$).[6] Therefore, our results in ARUBA-eligible patients managed outside that trial led to an entirely different conclusion about AVM intervention, due to the primary role of surgery, judicious surgical selection with established outcome predictors, and technical expertise developed at a high-volume AVM center.

These critiques beg for another trial to re-establish the role of surgery in AVM management, this time conducted and embraced by the neurosurgical community: *B*eyond *A*RUBA: *R*andomized Low-Grade *B*rain *A*VM stu*D*y, *O*bservation versus *S*urgery (BARBADOS). Effort is ongoing to organize, fund, and initiate it. There is now urgency among neurosurgeons to respond to ARUBA, which we expect to increase acceptance of such a trial. In the meantime, the management of ruptured AVMs should remain unaffected by ARUBA and surgery should be regarded as the first-line or criterion standard therapy for most low-grade AVMs, with conservative embolization as a preoperative adjunct. High surgical cure rates and excellent functional outcomes in patients with both ruptured and unruptured AVMs support a dominant surgical posture, with radiosurgery reserved for risky AVMs in deep, inaccessible, and highly eloquent locations.

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