Unruptured Brain Arteriovenous Malformations Should Be Treated Conservatively

Yes

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In the past, most brain arteriovenous malformations (AVMs) announced their presence by hemorrhage (70% at diagnosis), sometimes devastating, with important long-term morbidity and elevated case-fatality (combined 10-year morbidity and mortality: 27%). Such figures seemed ample justification for any invasive treatment attempt, either partially or in toto. However, these assumptions are largely based on data from the pre-CT era and have now been challenged by the increasing availability of noninvasive brain imaging, especially MRI, which have yielded both a large percentage of unbled lesions in ongoing population-based studies, and low rates of hemorrhage in outcome data from systematic prospective follow-up series.

Brain AVMs are diagnosed more commonly than previously assumed. Current detection rates range from 1.1 to 1.3 per 100,000 patient-years depending on the availability of MR brain imaging. More important, the prospective New York Islands AVM study found unruptured AVMs exceeded those ruptured almost twice as often. Similar to intracranial aneurysms, the natural history of unruptured AVMs seems more favorable than for those discovered after initial hemorrhage. The average risk of bleeding from an unruptured AVM (1.2% per year) seems to be about 5 times lower as compared with already ruptured malformations (5.6% per year). The bleeding risk seems to be particularly low in the most frequent subgroup of patients harboring lobar AVMs with superficial venous drainage (0.9% per year). Finally, although some instances of AVM rupture may indeed be disastrous, there seems to be a far lower morbidity and mortality than after intracerebral bleeding from other causes.

AVM-specific treatment is necessarily invasive and comprises endovascular embolization, surgical excision, or stereotactic radiotherapy (either alone or in combination). None of these strategies have been studied in controlled clinical trials or population-based studies, and available outcome data mainly derive from preselected single-center cohorts. The 2005 overview on endovascular AVM therapy by the World Federation of Interventional and Therapeutic Neuroradiology showed frequencies of embolization-related complications in well-established international centers between 9.1% and 11.9%. A meta-analysis of 2425 patients from 25 single institutions suggests surgical mortality was 3.3% with a permanent postoperative morbidity of 8.6%. Another series suggests the neurological risk of surgery may be twice as high for unruptured AVMs as compared with AVM removal after prior hemorrhage. Finally, a multicenter analysis of 1255 patients receiving radiotherapy found 102 (8%) who developed a neurological deficit after the radiation. Another recent series suggests 10% radiation-induced deficits and an additional 9% new intracranial hemorrhages in 308 prospective AVM patients followed >2 years.

For outcome comparisons, we analyzed the 15-year spanning prospective follow-up data of 352 patients with initially unruptured AVM from the Columbia AVM database, and found that the initiation of any invasive treatment strategy was associated with a >3-fold increased risk of AVM hemorrhage (P < 0.0001; hazard ratio = 3.61, 95% CI: 2.00 to 6.50). Intervventional treatment was also associated with an increased risk of clinical impairment as assessed by a Rankin score ≥2 (hazard ratio = 8.17, 95% CI: 5.13 to 13.01, P < 0.0001). These observational data raise serious doubt about the assumed clinical benefit of invasive treatment strategies for patients diagnosed with an unruptured AVM.

Economic considerations also apply. Based on the recent population-based data cited above, roughly 2000 patients are expected to be diagnosed in the United States with an unbled AVM every year. If all received invasive therapy (at expected average costs between $50,000 and $100,000 per patient), the US healthcare system would have to invest between $100 million and $200 million per year for treatment interventions with as yet unproven benefit (leaving any additional costs for an expected 10% treatment-related complications unaccounted for).
In conclusion, the natural history risk of hemorrhage in unruptured brain AVMs from data currently available seems to be relatively low, especially when compared with an expected 10% morbidity risk of interventional therapy of any type. These findings are clinically important enough to provide ethical equipoise for a randomized controlled clinical trial comparing long-term outcome of invasive versus noninvasive patient management in affected cases.\textsuperscript{14} Until trial results will be available, however, we consider invasive treatment strategies for nonhemorrhagic AVMs experimental therapy with a questionable cost/benefit ratio and suggest that patients with unruptured AVMs be currently treated conservatively or within a controlled clinical trial.\textsuperscript{8,14}

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**Disclosures**
None.

**References**
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