Cerebral arteriovenous malformation rupture risk

- Histological Analysis of Intracranial Cerebral Arteries for Elastin Thickness, Wall Thickness, and Vessel Diameters: An Atlas for Computational Modeling and a Proposed Predictive Multivariable Model of Elastin Thickness
- Feeder Artery Aneurysms in Cerebral Arteriovenous Malformations: Demographic, Clinical, and Morphological Associations
- Intra-operative neurophysiological monitoring as an adjunct to resection of eloquent cerebral arteriovenous malformations: a retrospective cohort study
- Varix Rupture Due to High-Flow Parasagittal Sinus Dural Arteriovenous Fistula: A Case Report and Literature Review
- Profiling Tight Junction Protein Expression in Brain Vascular Malformations
- Is Supplemented Spetzler-Martin grading Superior? A comparative study in AVM microsurgery risk stratification
- Robotic radiosurgery for the treatment of pediatric arteriovenous malformations
- Relationship of blood flow, angioarchitecture, and rupture in cerebral arteriovenous malformations

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For patients with unruptured intracranial arteriovenous malformations (AVMs), the risk of a hemorrhagic event is approximately 2% to 4% annually. These events have an associated 20-50% morbidity and 10% mortality rate. An understanding of risk factors that predispose these lesions to rupture is important for optimal management. We aimed to pool a large cohort of both ruptured and unruptured AVMs from the literature to identify angiographic risk factors that contribute to rupture. A systematic review of the literature was conducted in accordance with the PRISMA guidelines using Pubmed, Embase, Scopus, and Web of Science databases. Studies that presented patient-level data from ruptured AVMs from January 1990 to January 2022 were considered for inclusion. The initial screening of 8,304 papers resulted in a quantitative analysis of 25 papers, which identified six angiographic risk factors for AVM rupture. Characteristics that significantly increase the odds of rupture include the presence of aneurysm (OR = 1.45 [1.19, 1.77], $p < 0.001$, deep location (OR = 3.08 [2.56, 3.70], $p < 0.001$), infratentorial location (OR = 2.79 [2.08, 3.75], $p < 0.001$), exclusive deep venous drainage (OR = 2.50 [1.73, 3.61], $p < 0.001$), single venous drainage (OR = 2.97 [1.93, 4.56], $p < 0.001$), and nidus size less than 3 cm (OR = 2.54 [1.41, 4.57], $p = 0.002$). Although previous literature has provided insight into AVM rupture risk factors, obscurity still exists regarding which risk factors pose the greatest risk. We have identified six major angiographic risk factors (presence of an aneurysm, deep location, infratentorial location, exclusive deep venous drainage, single venous drainage, and nidus size less than 3 cm) that, when identified by a clinician, may help to tailor patient-specific approaches and guide clinical decisions [1)].

Genes

see Genes involved in Cerebral arteriovenous malformation rupture risk.

A review by Rutledge et al. focuses on the cerebral arteriovenous malformation epidemiology, Cerebral arteriovenous malformation rupture risk, and factors influencing risk of hemorrhage in the untreated natural course associated with sporadic cerebral arteriovenous malformation [2].

Previously ruptured cerebral arteriovenous malformation have a higher annual hemorrhage rate than unruptured cerebral arteriovenous malformation. Deep cerebral arteriovenous malformation location and prior hemorrhage may increase the risk for subsequent hemorrhage [3].

For patients with cerebral arteriovenous malformation, although the overall risk for hemorrhage seems to be 2.10%-4.12% per year, calculating an accurate risk profile for decision-making involves clinical attention and accounting for specific features of the malformation [4].

These hemorrhage rates are can change over time, particularly for hemorrhagic lesions, with the rebleed rate ranging from 6% to 15.8% in the first year after rupturing across several studies. Besides hemorrhage, other significant risk factors for AVM hemorrhage include deep location, deep venous drainage, associated aneurysms, and pregnancy. Other factors include patient age, sex, and small AVM size, which are not currently considered significant risk factors for AVM hemorrhage. In addition to hemorrhage risk and seizure risk, the natural history of an AVM also encompasses the daily psychologic burden that a patient must endure knowing that he or she possesses an untreated AVM [5].

Brown et al. conducted a long-term follow-up study of 168 patients to define the natural history of clinically unruptured intracranial arteriovenous malformations (AVM's). Charts of patients seen at the Mayo Clinic between 1974 and 1985 were reviewed. Follow-up information was obtained on 166 patients until death, surgery, or other intervention, or for at least 4 years after diagnosis (mean follow-up time 8.2 years). All available cerebral arteriograms and computerized tomography scans of the head were reviewed. Intracranial hemorrhage occurred in 31 patients (18%), due to AVM rupture in 29 and secondary to AVM or aneurysm rupture in two. The mean risk of hemorrhage was 2.2% per year, and the observed annual rates of hemorrhage increased over time. The risk of death from rupture was 29%, and 23% of survivors had significant long-term morbidity. The size of the AVM and the presence of treated or untreated hypertension were of no value in predicting rupture [6].

The majority of clinical studies determining hemorrhage rates in cerebral arteriovenous malformation patients come from single referral centers, although there have been a few defined population-based studies [7] [8] [9].

Estimates range from 2% to 4% per year for all AVMs, with generally higher rates in the first year after the presentation and in those who initially present with a hemorrhage [10].

Data suggest that the risk of cerebral arteriovenous malformation rupture is not increased during pregnancy and the puerperium. Therefore, Liu et al. would not advise against pregnancy in patients with intracranial AVM. However, they found that AVM rupture usually occurred in late gestational age; therefore, more attention should be provided to maintain relative hemodynamic stability in these patients during mid to late pregnancy. The issues facing patients with ruptured AVM in pregnancy remained challenging and required multidisciplinary management including neurosurgeons, obstetricians, pediatricians, and intensivists [11)].

Predictive models

In many cases, both the rupture rate of cerebral arteriovenous malformation (bAVM) in patients and the risk of endovascular or surgical treatment (when radiosurgery is not appropriate) are not low, it is important to assess the risk of rupture more cautiously before treatment. Based on the current high-risk predictors and clinical data, different sample sizes, sampling times, and algorithms were used to build prediction models for the risk of hemorrhage in bAVM, and the accuracy and stability of the models were investigated.

The purpose of Tao et al. was to remind researchers that there may be some pitfalls in developing similar prediction models.

The clinical data of 353 patients with bAVMs were collected. During the creation of prediction models for bAVM rupture, Tao et al. changed the ratio of the training dataset to the test dataset, increased the number of sampling times, and built models for predicting bAVM rupture by the logistic regression (LR) algorithm and random forest (RF) algorithm. The area under the curve (AUC) was used to evaluate the predictive performances of those models.

The performances of the prediction models built by both algorithms were not ideal (AUCs: 0.7 or less). The AUCs from the models built by the LR algorithm with different sample sizes were better than those built by the RF algorithm (0.70 vs 0.68, $p < 0.001$). The standard deviations (SDs) of the AUCs from both prediction models with different sample sizes displayed wide ranges (max range > 0.1).

Based on the current risk predictors, it may be difficult to build a stable and accurate prediction model for the hemorrhagic risk of bAVMs. Compared with sample size and algorithms, meaningful predictors are more important in establishing an accurate and stable prediction model [12)].

References

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