Unruptured Arteriovenous Malformations of the Brain

Unruptured, asymptomatic arteriovenous malformations (AVMs) lurk in the brains of approximately one person in every thousand; their prevalence, based on four studies of magnetic resonance imaging (MRI) of 7,359 people without brain disorders,[1-4] was 0.1 % (95% confidence interval [CI] 0% to 0.2%). Some of these brain AVMs may be discovered if and when they cause intracranial haemorrhage, epileptic seizure(s), headache, or a focal neurological deficit, but many brain AVMs may potentially lie dormant from the cradle to the grave.

The detection of this reservoir of unruptured brain AVMs is likely to depend on the differences in availability, uptake, and indications for brain MRI between countries. Indirect evidence for this comes from the two ongoing population-based studies of the clinical epidemiology of brain AVMs:[5,6] in Scotland 54% of all brain AVMs detected in an incidence study were unruptured at presentation,[5] whereas this proportion was 62% in New York (difference -8%, 95% CI -19% to 4%).[6] The detection rate of unruptured brain AVMs seems set to rise with the increasing appropriate use of brain MRI for investigating epilepsy and stroke, as well as more indiscriminate uses such as 'health check-ups' purchased from private health screening companies.[7]

What's the prognosis for an adult with an unruptured brain AVM?

Only a few published studies are of sufficient quality to provide reliable estimates of the prognosis for unruptured brain AVMs.[8-10] Most cohorts have been small, retrospective, hospital-based, with short incomplete follow-up from an unclear inception point, using unblinded assessment according to bespoke rather than generic outcome measures, without stratification by differences in treatment. Even in high quality studies, the outcome described for unruptured brain AVMs that are not treated is inevitably biased, since a conservative strategy may be adopted either because of the 'untreatability' of the AVM, or due to the patient's burden of disability or co-morbidity.

Nevertheless, some generalisations can be made about the crude first bleed rate from an unruptured brain AVM after diagnosis (Table). The most important elements of brain AVM vascular anatomy ('angioarchitecture') for risk stratification are deep venous drainage (Figure) and location deep within the brain (Table).

An old population-based study found 30-day case fatality after a bleed to be ~18%,[12] which is likely to be less nowadays, and certainly less than the case fatality following non-traumatic intracerebral haemorrhage or aneurysmal subarachnoid haemorrhage.[13] Few have estimated the morbidity due to haemorrhage, but it does seem to vary between studies: by the time of hospital discharge after a haemorrhage, 33% of patients had a modified Rankin score ≥3,[10] and others found this proportion to decrease to ~5% after ~1 year.[14] However, the Toronto AVM study group found that only 45% of adults made a recovery from a haemorrhage without a permanent deficit.[15] Although re-bleed rates do not concern us in this article, it is worth mentioning that they are higher than first bleed rates, and they seem to be particularly high in the first 6-12 months after a first bleed,[9,10] although the magnitude of the re-bleed rate varies between studies.[10,11,16]

Table: First bleed rates from unruptured brain AVMs

Subgroup	*Annual bleed rate*
Crude (overall) first bleed rate[9,11]	*~1%*
Exclusive deep venous drainage[9]	*~2%*
Deep brain location[9]	*~3%*
Exclusive deep venous drainage and deep location[9]	*~8%*
Neither deep location nor deep venous drainage[9]	*~1%*

Should an adult with an unruptured brain AVM be treated?

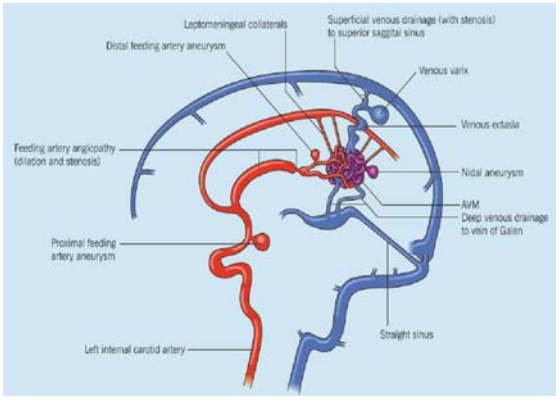
People with brain AVMs are likely to benefit from multidisciplinary management, although there is considerable value from a one-on-one meeting between doctor and patient. A neuroradiologist, neurosurgeon, radiotherapist, and clinical nurse specialist should ideally work with a neurologist with interest and expertise in the assessment and treatment of seizures, headaches and chronic disability. A neurologist also has an important independent role in counselling a patient about the risks and benefits of various management strategies.

In the absence of controlled studies, the decision to treat the brain AVM (with any combination of endovascular embolisation, microsurgical removal, and/or stereotactic radiation therapy) is based on the potential benefit of treatment reducing the future risk of haemorrhage, plus an indirect comparison of the possible risk of intervention against the presumed risk of future death/disability if the brain AVM is left untreated.[17] This decision involves the potentially flawed extrapolation of short-term outcome data to the rest of the patient's presumed life expectancy.[18,19] Recent research – albeit based on observational data at a single tertiary referral centre – leaves many physicians uncertain that treatment does more good than harm:[19,20] interventional treatment of unruptured brain AVMs was associated with a highly significant excess of subsequent haemorrhage and disability at five years in comparison to conservative management. If these findings and the paucity of controlled data aren't enough to support the case for randomisation, further justification is provided by the likely variation in treatment practice by personal conviction, local experience, centre, country, continent, available treatments, and health insurance policy.[13,18,19]

A Randomised trial of Unruptured Brain AVMs (ARUBA)

A potential solution to the clinical dilemma posed by an unruptured brain AVM is randomisation in ARUBA (www.arubastudy.org). ARUBA is investigating whether conservative management is superior to interventional

Figure: The vascular anatomy ('angioarchitecture') of brain AVMs



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treatment for consenting adults aged ≥18 years, with an unruptured brain AVM that is potentially treatable, over a minimum follow-up period of five years, based on outcome assessments by a neurologist. Although enrolment in this trial may prove challenging because of the instinctive difficulties some patients (and doctors) may face in allowing randomisation to decide whether their 'time bomb' is treated or not, fully informed consent – involving a sanguine discussion of the risks of intervention – is crucial.

ARUBA is funded by the National Institutes of Health (ISRCTN 44013133), with per-patient reimbursement. The trial has ethical approval in the UK, and a decision about trial adoption by the UK Stroke Research Network is pending. Interested investigators should contact any of the authors, and may also consider participating in a similar trial randomising people with an unruptured intracranial aneurysm to endovascular or conservative management (www.teamstudy.org, ISRCTN 62758344).

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