Considerations in the Management of Cerebral Arterio-Venous Malformations

A brain arteriovenous malformation is characterised by rapid blood flow from arteries to veins due to the absence of an intervening capillary bed. The venous components develop arterialisated walls and often become distorted. "Nidus" is the term used to describe the tangled mass of abnormal arteriovenous connections. The nidus should be distinguished from the feeding vessels and draining veins. AVMs occur anywhere in the neuraxis but are much more frequent in the brain. Whilst AVMs can be discovered incidentally (15%) they most commonly present with a spontaneous intracranial haemorrhage (85%) or seizures (20%). Occasionally other presenting symptoms occur (e.g. ischaemic deficits, headaches).

The incidence of brain AVMs is around 0.82 to 1.12/100 000 per annum,1,2 with a point prevalence of around 18/100 000.3 The incidence of around 18/100 000.3 with no randomised controlled trials to support the decision making process. The clinician therefore needs to consider several factors:

1. What is the risk of further haemorrhage?
2. Are there any risk factors predictive of haemorrhage?
3. What are the morbidity and mortality data associated with an AVM bleed?
4. What is the obliteration rate associated with AVM treatments?
5. What are the risks associated with AVM treatment?

Management considerations

The management of a patient with an AVM is influenced by many factors. These relate to the mode of presentation, the clinical status of the patient, the anatomy of the AVM and the predicted outcome of any treatment undertaken. Studies influencing AVM management are all observational and with no randomised controlled trials to support the decision making process. The clinician therefore needs to consider several factors:

1. Natural History of AVMs

Early studies suggested that the risk of an AVM bleeding over a 20 year period of follow-up was in the region of 28-40%.4 More recent studies have evaluated the natural history of AVMs in more detail (Table 1).5,6 Many factors including the location, size, pattern of venous drainage, mode of presentation and angioarchitecture may influence the risk of haemorrhage. It is now clear that the natural history of an AVM can be stratified by the presence or absence of risk factors (see below). In population based studies the mortality from an initial AVM bleed was 12-18%,7,8,9 The risk of permanent or disabling neurological deficits after an AVM haemorrhage is substantial. The Scottish Intracranial Vascular Malformation study reported a modified Rankin score of 2 or less (slight disability or better) in nearly 40% of cases aged <60 years. Around 25% of this age group sustained moderate disability and around 25% had severe deficits with a 12 month mortality of 12%.10 Data on the outcome of subsequent bleeds is not clearly enunciated in large numbers.

Are there any risk factors predictive of haemorrhage?

A previous history of haemorrhage, exclusive deep venous drainage and deep location consistently increase the risk of a bleed (see Table 1).11 Other factors for haemorrhage that have been reported include a single draining vein, venous stenosis, and high feeding artery pressure.12,13,14 Many studies have indicated that small AVMs carry a higher risk of bleeding compared with larger AVMs. Indeed, the feeding artery pressures have been reported to be greater in smaller AVMs.15 However, the risk of subsequent haemorrhage was not greater for small AVMs compared with large AVMs in several studies.16,17 It has been postulated that small AVMs are more likely to present with a haemorrhage due to small size being associated with a lower risk of other symptoms, rather than an increased risk of bleeding per se.18 Aneurysms are associated with AVMs in around 10% of cases, although superselective angiography appears to show that the incidence...
may be as high as 50%. Other authors dispute the interpretation of the radiological findings and caution against over interpretation of angiographic signs. Aneurysms have been classified as dysplastic, flow-related on proximal feeders, flow related on distal feeders, and intranidal in patients presenting with a haemorrhage the possibility of a bleed from an associated aneurysm should be considered. Such a diagnosis is based upon correlating CT scan findings with angiographic information. If an aneurysmal bleed has been identified initial treatment should target occlusion of the aneurysm.

### Classification of AVMs

Spetzler and Martin developed a grading scale that has been widely used in describing the characteristics of an AVM. This is based upon scoring 3 parameters that influence the outcome of AVM surgery (see Table 1). Size, location and pattern of venous drainage. Size was based upon angiographic measurements. Eloquent regions were described as sensorimotor, motor, and visual cortex; the hypothalamus and thalamus; the internal capsule; the brainstem; the cerebellar peduncles; and the deep cerebellar nuclei. Deep venous drainage included any lesion with a deep venous drainage component, even if most of the drainage was superficial. Summation of the scores leads to grading of the lesion on a Grade I to V range. Using this scale, Spetzler and Martin showed that the morbidity associated with surgery was very low for grade I and II AVMs, but increased progressively for grade III, IV and V lesions. Indeed, due to the high risks associated with surgery and the diminishing success with other treatment modalities, Spetzler's group advocate that the majority of patients with Grade IV and V AVMs are managed conservatively. Surprisingly this group reported an annual risk of haemorrhage of only 1.5% per annum in their series of 73 cases. Overall, 25% of the 73 patients sustained a haemorrhage during follow-up. Pollock and Flickinger analysed 220 AVM patients treated with stereotactic radiosurgery and reported that the Spetzler-Martin grade did not correlate with patient outcome. They identified several factors that were predictive of complete obliteration and excellent clinical outcome for SRS treated AVM patients and modeled these into a grading system. Many institutions have validated this grading system. In 2008 the scale was simplified to facilitate clinical application and utility. The factors predicting treatment success comprised AVM volume, age, and location (deep location - basal ganglia / thalamus / brainstem, versus other location - hemispheric / corpus callosum / cerebellar).

### Table 1: Spetzler-Martin AVM grading system

<table>
<thead>
<tr>
<th>Size</th>
<th>Eloquent (location)</th>
<th>Venous drainage</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1cm</td>
<td>Non-eloquent = 0</td>
<td>Superficial = 0</td>
</tr>
<tr>
<td>1-3cm</td>
<td>Eloquent = 1</td>
<td>Deep = 1</td>
</tr>
<tr>
<td>&gt;3cm</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Minimum score = 1; Maximum score = 5.

The AVM score is calculated as follows = (0.1) (volume, mL) + (0.02) (age, yr) + (0.5) (location; other = 0, deep = 1).

A strong correlation between the modified Pollock-Flickinger score (subdivided into 4 points - <1.00; 1.00-1.50; 1.51-2.00; >2.00) and outcome was reported. Patients with a score of <1.00 had a 90% chance of obliteration without new neurological deficit, whilst those with a score of ≥2.00 had less than a 50% chance of achieving complete obliteration without additional neurological deficit. Wider use of the scale in the radiosurgical literature is likely.

### What treatment options exist?

The treatment options available when managing patients with AVMs comprise:
- No intervention
- Surgical excision
- Endovascular treatment
- Stereotactic radiosurgery

The primary aim of any management strategy is to balance the risks associated with conservative treatment against those associated with intervention. If intervention is pursued, total obliteration of the AVM with as few deleterious effects as possible is the prime objective. For large AVMs, combinations of different treatment modalities are frequently utilised to maximise the chances of obliteration, although many Grade IV and V lesions are managed conservatively if total obliteration is considered improbable. The American Stroke Association has issued guidelines for the management of intracranial AVMs.

### Surgical Treatment

Surgical treatment is commonly employed for Spetzler-Martin grade 1 and II AVMs that have...
presented with a brain haemorrhage. The translation of imaging information into 3D visualisation is imperative. Studying the architecture of the nidus from angiography helps determine whether the nidus is compact or diffuse. Functioning neural tissue within a diffuse nidus may increase surgical morbidity. A wider resection should be undertaken if the nidus is diffuse to avoid incomplete resection. It is also important to understand that the nidus of an AVM fed by both the anterior and posterior circulation may be underestimated when it is not visualised simultaneously in the selective carotid and vertebral injections. The venous drainage of an AVM must also be studied to help plan surgery.

Operative technique
The craniotomy should be large enough to achieve adequate exposure of the AVM, the surrounding cortex and draining veins. Image-guidance can be useful when planning the flap. An associated liquefied haematoma cavity can provide a useful corridor of access. Meticulous microsurgical “skeletonisation” of the vascular mass from superficial to deep is performed. Reference to the pre-operative imaging is essential when conducting surgery. A trans-sulcal approach is used for sub-cortical AVMs if possible. Premature injury to the venous drainage should be avoided, as outflow occlusion results invariably in catastrophic intra-operative haemorrhage.

The appearance of the vascular nidus is usually unmistakable. Circumferential dissection with meticulous coagulation and division of all feeding arteries must be performed. If these vessels tear, they tend to retract into the surrounding white matter and may be responsible for deep parenchymal haematomas. In eloquent areas the dissection should not stray into the surrounding tissues. In periventricular locations control of the subependymal feeding vessels is important to avoid significant intraventricular haemorrhage. Some of the feeding arteries may supply the AVM en passant. Preservation of such blood supply is important to minimise morbidity. Once the anatomy is clearly established the main feeders can be occluded near the nidus with clips or coagulation and divided.

It is common towards the end of the AVM resection, even after division of the main feeders, that the nidus and draining veins appear increasingly tense. In these situations an arterial feeder is often encountered in close proximity to the vein’s adventitia, especially if it is a deep draining vein. Once this is occluded, the nidus and in particular the draining vein collapses completely and turns dark blue due to the loss of arterialised blood. This enables complete AVM removal.

Pitfalls, difficulties and their management
The most common mishap is the occurrence of haemorrhage resulting from intra-nidal dissection. If significant haemorrhage occurs, packing the area with haemostatic Surgicel™ and cottonoids plus applying gentle pressure by a fixed retractor on the nidus itself usually controls the situation. This region should be left undisturbed for some minutes whilst dissection proceeds in a different area. Frantic attempts at coagulation in these situations may aggravate the bleeding.

If significant haemorrhage is emanating from the peripheral feeders, attempts to control this by coagulation are usually futile due to retraction of the feeders into the parenchyma. It is advisable to undertake a wider resection margin to regain control of such a situation.

If there is continuous “ooze” from the resected AVM bed, controlled hypotension may be an option. The rationale being that the surrounding vascular bed lacks autoregulation and lowering the blood pressure therefore will decrease the bleeding.

Management of intracerebral haematomas secondary to AVMs
Most neurovascular surgeons favour an initial conservative approach when managing AVM patients presenting with an intracranial haematoma. This permits full angiographic characterisation of the AVM (including after haematoma resolution) and allows brain conditions to be optimised for any subsequent treatments. In addition, neurological deficits often improve significantly in the weeks and months after the initial presentation. Occasionally, an intracranial haematoma requires emergency evacuation due to the effects of raised ICP. In such cases, if the AVM is small and amenable to resection the haematoma is evacuated and the AVM removed. In cases with underlying complex AVMs, every attempt is made to evacuate the haematoma without disturbing the AVM. If bleeding occurs, suboptimal resection of the AVM may ensue. A decompressive craniectomy with a durotomy alone may be the most prudent option if the AVM is large and deep. Once recovery permits, an angiogram should be obtained and any residual AVM treated to avoid recurrent haemorrhage. Other modalities such as stereotactic radiosurgery may be used in these circumstances if an elective resection appears high risk. In AVM patients with an associated aneurysm that appears to be the culprit for the bleed, urgent aneurysm occlusion by endovascular techniques or surgical clipping is appropriate.

Endovascular Treatment
Endovascular AVM therapy is frequently used as an adjunct to surgical or radiosurgical treatment. Embolisation can achieve volume reduction making large AVMs suitable for surgical or radiosurgical treatments. Focal obliteration of part of the AVM is preferable to diffuse, patchy obliteration in achieving volume reduction. Endovascular treatments aid surgery if they occlude deep feeding vessels. Pre-operative embolisation may also decrease the risk of breakthrough phenomena resulting from disordered autoregulation in the parenchyma surrounding large high flow AVMs.
Endovascular therapy may be used as the sole treatment modality when treating small AVMs with few feeding arterial pedicles. Endovascular coiling may also be used in the treatment of flow aneurysms. Finally, embolisation can be used as a palliative modality in patients suffering from venous hypertension secondary to a large incurable AVM.

Endovascular therapy is usually performed using compounds (e.g., N-butyl cyanoacrylate, Onyx, polyvinyl alcohol) that are injected in a controlled fashion into feeding vessels. Technical complications may occur (up to 10% of procedures). AVM rupture is a rare but feared complication from inadvertent occlusion of significant venous drainage channels. The durability of endovascular treatment is not always robust due to re-canalisation of occluded vessels in some cases.

**Stereotactic Radiosurgery (SRS)**

SRS was developed by Lars Leksell and has been used as a primary modality for the treatment of AVMs for several decades. SRS causes endothelial cell proliferation and progressive vessel wall thickening leading to AVM obliteration. The timing of obliteration is usually two years or more after the treatment. This delay in effect is influential in determining the optimal treatment modality for any given patient. Pre-treatment MRI and CT images (including CT angiography) can be fused with day-of-treatment stereotactic angiographic imaging to maximise the definition of the radiosurgical target (see Figure 1). Radiation is then delivered by a gamma knife source (e.g., Perfexion Gamma Knife, Elekta) or by a LINAC generated conformal beam (e.g., Novalis, BrainLab, Cyberknife, Accuray). The prime objective of SRS is to irradiate the AVM with high dose radiation effecting obliteration and causing minimal collateral damage to surrounding structures. There are many studies in the literature testifying to the efficacy of SRS treatments. A large pooled series reported complications in 8% of cases, including a death rate of 0.16%. Complications included neurological deficits, seizures and radiocoeuriac cyst formation. Many of the patients improved with steroid therapy. The Pittsburgh group has published dose-response curves showing obliteration rates and tissue tolerance according to AVM location. They advise a maximum marginal dose of 25 Gy (with an obliteration rate of 86%) and a minimal marginal dose of 15 Gy.

For patients with very large AVMs, volume staged SRS may be employed. Treatments are delivered to different parts of the nidus several months apart. An alternative approach using hypofractionated stereotactic radiotherapy to the entire AVM has also reported some success in managing these challenging lesions. Such a strategy involves low dose treatment in seven fractions.

**Summary**

The management of a patient with an AVM is an individualised pathway that requires the multidisciplinary input of a neurovascular surgeon, a radiation oncologist and a stereotactic radiosurgeon. A neurologist can be a useful addition to the team approach having strengths in dealing with epilepsy and neurorehabilitation. In guiding patients, an understanding of the natural history of an AVM is required by all team members who may be advising the patient on treatment options. However, data on the probability of a subsequent bleed, whatever the initial mode of presentation, is difficult to predict with any degree of accuracy. Treatment morbidity and success rates also require accurate prediction to fully inform patients during the pre-treatment assessment phase.

---

**REFERENCES**


