Chapter 17
Arteriovenous Malformations: Surgical Indications and Technique

Omar Tanweer, Gillian Harrison, Peter Rozman, and Howard A. Riina

Arteriovenous malformations (AVMs) comprise one of four main subtypes of vascular malformations that are considered to be congenital rather than acquired. They are characterized by direct arterial-to-venous shunting, usually through a tangle of vessels called a *nidus*, without the normal intervening capillary beds, and are thus considered to be high-pressure, high-flow malformations. The other three subtypes, developmental venous anomalies, capillary telangiectasias, and cavernous malformations, which are beyond the scope of this chapter, are under much lower hemodynamic pressure and low flow. However, all are considered rare lesions and as such remain incompletely understood.

Attempts to define the exact prevalence of AVMs in the general population have been limited by methodology and sampling; the often cited prevalence of 0.14% is likely an underestimate, and more recent analyses have suggested a prevalence of 1–1.3/100,000 person-years [1, 2]. The rarity of these malformations would require an exceedingly large sample size to determine true prevalence in the general population.

While the underlying pathogenesis of AVMs remains a subject of active research, clinicians generally accept that AVMs, unlike many other vascular pathologies, are present from birth. This assumption finds support in the existence of genetic disorders with predispositions for the development of AVMs (hereditary hemorrhagic telangiectasia, or Sturge-Weber disease, for instance). Studies have implicated elevated levels of vascular endothelial growth factor (VEGF), angiopoietins, and fibroblast growth factors (FGFs) in the ultimate instability of the embryological vascular-capillary plexus that gives rise to the early AVM [3]. Over time, AVMs do remodel and can grow, and it is likely that environmental factors also contribute to the ultimate architecture of the mature AVM.

O. Tanweer (✉) · G. Harrison · P. Rozman · H. A. Riina
Department of Neurosurgery, New York University Medical Center, New York, NY, USA
e-mail: omar.tanweer@nyumc.org; Gillian.Harrison@nyumc.org; Peter.Rozman@nyumc.org; howard.riina@nyumc.org

A. M. Spiotta et al. (eds.), *Management of Cerebrovascular Disorders*,
https://doi.org/10.1007/978-3-319-99016-3_17

The danger of these rare, congenital malformations is, of course, hemorrhage. Other symptoms such as headaches, seizures, and deficits from steal phenomenon are encountered as well. Over the past century, efforts directed at treating these lesions to prevent this consequence have led to four main treatment modalities that clinicians use today: medical management, endovascular embolization, microsurgical resection, radiosurgery, or some combination of the above. The focus of this chapter is mainly on the indications and techniques for surgical resection, but discussion is afforded to the use of other modalities to render previously high-risk or difficult-to-resect AVMs resectable.

Following a brief discussion of the clinical traits of AVMs and AVM ruptures, we will address the surgical classification, patient stratification, and preoperative planning that lead up to the day of surgery. An overview of surgical technique and intraoperative management follows, as well as a description of common complications and expected surgical outcomes.

Natural History and Clinical Presentations

As with most cerebrovascular lesions, screening for AVMs is not routinely performed, and these lesions are most commonly discovered in the setting of hemorrhage. However, the increasing ease and rapidity, as well as decreasing cost, of imaging studies, have led to more and more incidentally discovered AVMs. This shift has led to increasing interest in, and understanding of, the natural history of the unruptured AVM.

The annual risk of hemorrhage for an AVM is approximately 2.8% per year [4–7]. This figure does not stratify by AVM size or location and fails to take into account history of previous hemorrhage or symptomatic presentation. AVM size particularly has been associated with rupture risk, with smaller AVMs found to be at higher risk of rupture. The risk of hemorrhage is of special importance because approximately half of all AVMs will initially present in this way. Over 80% [8] of these hemorrhages are intraparenchymal. The remainder are intraventricular, usually by direct extension, subarachnoid, or even subdural hemorrhages. Spontaneous intracranial hemorrhage in an otherwise healthy or young individual should always raise the concern for an underlying malformation and prompt appropriate follow-up studies. Estimates of rebleeding rates vary greatly, and such analyses are limited by small study populations.

Cumulative (lifetime) risk of AVM rupture may be calculated as $[1 - (\text{risk of no hemorrhage})^n]$, where n is the remaining life expectancy. For an accepted annual risk of 3%, this is estimated as [105 – age]/100.

Of those AVMs that do not present as hemorrhage, approximately half present as seizures [9]. The exact pathophysiology that underlies AVM-associated seizures is not understood, but certain characteristics of the AVM, such as cortical – particularly temporal or parietal – location or large varices, do seem to predispose to this presentation. There is some suggestion that hemorrhagic presentation is more common in younger (less than 20 years old) or older (greater than 60 years old) populations, while seizures may predominate in the intervening years.

Beyond hemorrhage and seizure, less common presentations of AVMs include headache without rupture (~15% of total) and neurological deficit either as a result of direct parenchymal compression or steal syndrome. Steal syndrome describes a phenomenon in which the arteriovenous shunt provides a lower resistance than the surrounding capillary beds feeding brain parenchyma and thus results in tissue ischemia.

Surgical Grading Systems

As we consider the lifetime risk of AVM rupture as an impetus to treat the disease process, it becomes apparent that this lifetime risk must be weighed against the risks inherent in surgical resection. Yet not all AVMs portend identical surgical risk. Since 1977, surgeons have developed grading systems to stratify AVMs into surgically favorable and unfavorable strata. The most widely utilized and well known of these systems is the Spetzler-Martin grading system, published in 1986 [10]. The system assigns points to the AVM based on three primary characteristics (size, location, and drainage), and these ultimately summate to grades I–V, with grade I being the lowest risk to resect and grade V carrying the highest risk (Table 17.1). Grade VI also exists and is used to denote AVMs deemed too complex to even consider resection.

In terms of size, AVMs are divided into those with a nidus less than 3 cm in diameter, 3–6 cm in diameter, or greater than 6 cm in diameter. In terms of location, a point is assigned those AVMs that occur in eloquent areas. Eloquent areas are defined as areas responsible for sensorimotor, visual, or language processing, as well as the hypothalamus, internal capsule, brainstem, cerebellar peduncles, and deep nuclei. Finally, drainage addresses whether *any* deep venous structures contribute to the AVM's drainage. Supratentorially, these are considered to be internal cerebral veins, basal vein of Rosenthal, and vein of Galen. Infratentorially, any drainage not to the straight or transverse sinus is considered deep.

This system is elegant in its simplicity and ease of use with available vascular imaging and has been validated in several cohorts by analyzing patient outcomes following surgical resection [11]. Spetzler and Ponce [12] even narrowed the final grades down into only three classes: A, comprising grades I/II; B, comprising grade

Table 17.1 The Spetzler-Martin grading system

Size	<3 cm	1 point
	3–6 cm	2 points
	>6 cm	3 points
Location	Eloquent	0 point
	Non-eloquent	1 point
Drainage	Superficial only	0 point
	Deep	1 point

III; and C, comprising grades IV/V. Class A AVMs are generally considered resectable, and class C AVMs are generally considered unresectable without compelling reason (recurrent hemorrhage, severe neurologic deficit, or associated aneurysms, for instance).

The Spetzler-Martin grading system improved upon earlier classification systems that recognized similar traits as important to surgical outcomes. Luessenhop and Gennarelli (1977) developed the first grading system in which they assigned a grade solely based on number of arterial feeders from a single vascular distribution (i.e., MCA, ACA, etc.) [13]. Luessenhop and Rosa (1984) developed a grading system based on size, which carried over into the Spetzler-Martin system [14].

Shi and Chen (1986) developed a complex system taking into account not only size, eloquence/depth, and venous drainage but also arterial supply [15]. While more granular and subtle than the Spetzler-Martin system, it was quickly abandoned, likely as a result of its complexity.

Lawton and his group at UCSF suggest that further considerations are warranted beyond those that comprise the Spetzler-Martin system. In particular, grade III AVMs span a wide range of pathologies. These include small, eloquent, deep-draining AVMs, medium/deep-draining AVMs (III), and medium/eloquent AVMs alike ("III+"). Surely outcomes and surgical risk must differ between these types. They suggest the use of a supplementary scale taking into account age (<20 years, 20–40 years, >40 years), presence of hemorrhage, and diffuseness or to what extent the brain parenchyma intervenes in the tangled vessels of the AVM. They reported an initial 300-patient analysis, and later 1000-patient analysis, that validates the improved outcome prediction with the addition of this system [16, 17].

All of the grading systems currently in use are now dated in their consideration of surgical resection as the sole treatment modality. As radiosurgery and interventional techniques become more available, curative treatment is becoming a possibility for previously unresectable malformations. Patient stratification is not as simple as a five-point, or even ten-point, grading scale, and a host of patient and anatomical considerations must factor into the ultimate treatment plan.

Risk Factors and Patient Selection

Management of patients with cerebral AVMs can be challenging, and recommendations for treatment require careful consideration of individual risk-benefit profiles. A surgeon's and an institution's experience with AVM management is important, particularly as multimodality management becomes more common; experts in each of the modalities should be available to contribute to a discussion of feasibility and associated risk for each patient.

A widely accepted indication for surgical intervention is prior hemorrhage; after an initial hemorrhage, annual rupture rates ranging from 6–15% in the first year [18, 19] to 2–18% in subsequent years [5, 7, 18, 20–24] have been observed, and prior hemorrhage has been a nearly universal predictor of subsequent hemorrhage across most large series [5, 22, 23, 25–27]. Even for patients with high-grade AVMs, rebleeding rates of 6% per year have been reported with 65% combined risk of permanent disability or death [28], suggesting that intervention may even be indicated for patients with AVMs classically considered high risk.

For management of unruptured AVMs, decision-making is more complex; surgical intervention must present a lower-risk profile than the natural history. In general, surgery is often considered for young patients with Spetzler-Martin grade I–II AVMs; furthermore, an additional supplementary scale incorporating age, prior hemorrhage, and nidus compactness suggests that surgery may carry acceptably low morbidity for a score ≤ 6 [16, 17]. In addition to surgical morbidity, patient and angioarchitectural factors that alter the natural history and are associated with increased risk of hemorrhage must be incorporated into the preoperative patient selection process.

Patient Factors

Patient age is one of the most important factors to consider in patient selection for surgical intervention. As suggested by the modified Spetzler-Martin scale, age is a critical component for assessing surgical morbidity. In addition to having fewer comorbidities and greater ability to tolerate and recover from neurologic injury, younger patients have higher lifetime risk of hemorrhage, justifying more aggressive treatment modalities. Some studies have identified increasing age as an independent risk factor for hemorrhage – either initial hemorrhagic presentation or re-hemorrhage – with one meta-analysis projecting a 30% increase in hemorrhage risk per decade [22, 26]; however, this has not been consistently supported across comparable large reviews [23, 25], and several cohort studies have in fact identified younger age as a risk factor for hemorrhage [5, 19]. Similarly, some cohort studies have identified gender [19, 29], race [30, 31], or history of hypertension [32, 33] as risk factors for hemorrhagic presentation; however, these results have not been widely studied. More recently, investigators have sought to identify genetic polymorphisms, primarily those involved with inflammatory and angiogenic pathways, associated with cerebral AVM diagnosis, hemorrhagic presentation, and outcome after treatment [34]. Finally, patient preference and lifestyle should be taken into account. Given the heterogeneity of data and spectrum of management options, thorough patient counseling is imperative. In addition, the psychosocial impact of the diagnosis should weigh into the patient's decision-making process.

Angioarchitectural Factors

Angiographic features associated with rupture of cerebral AVMs have been widely studied and have important implications for natural history risk. Table 17.2 summarizes the angioarchitectural characteristics found to be independent risk factors for AVM hemorrhage at time of diagnosis or in follow-up in multivariate analyses.

Table 17.2 Angioarchitectural characteristics associated with hemorrhagic presentation or re-hemorrhage of cerebral AVMs in multivariate analyses

Risk factor for hemorrhagic presentation	Risk factor for subsequent hemorrhage
Small size [22, 32, 38, 44, 45, 47]	Large size [5, 36]
Deep location [22, 37]	Deep location [5, 19, 22, 49]
Infratentorial location [22, 37]	Infratentorial location [5]
Non-borderzone location [22]	Diffuse morphology [24]
Perforating feeders [42]	Arterial aneurysms [25, 26]
Arterial aneurysms [22, 37, 44, 45]	Deep venous drainage [20, 22, 27]
Deep venous drainage [22, 32, 38, 42, 44, 45, 47, 48]	Single draining vein [24, 49]
Single draining vein [37, 47]	Presence of venous varices/ectasias [49]
Presence of venous varices/ectasias [37]	

General characteristics include size and location. Small size, typically defined as <3 cm, has been identified as a risk for hemorrhagic presentation [22, 23]; however, this may reflect a tendency for smaller lesions to escape diagnosis until they hemorrhage, compared to larger lesions which may present with other symptoms [35]. In contrast, multiple studies have either failed to find an association between AVM size and hemorrhage [25] or identified larger size [5, 23, 36] or diffuse morphology [24] as risk factors for subsequent hemorrhage. Deep, infratentorial, or "non-borderzone" (single major arterial feeder) locations have all been associated with higher risk of bleeding at presentation or afterward [5, 19, 22, 25, 36, 37].

Hemodynamic factors and specific vascular features of both the arterial and venous macrocirculation may correlate with hemorrhage risk. Several studies have reported higher feeding artery pressures, typically associated with small AVMs, longer feeding artery length [38–41], perforating arterial feeders [42], or intranidal fistulae [43] as potential risk factors for hemorrhage. Arterial aneurysms, either feeding artery, intranidal, or remote, are not uncommon in AVM patients and have all been studied as potential risk factors. In a recent meta-analysis by Gross et al., 18% of patients had an associated arterial aneurysm, half occurring in feeding arteries, and presence of an aneurysm was a risk factor for hemorrhage, with a hazard ratio of 1.8 (95% CI 1.6–2.0) [25]. Other groups have stratified risk by aneurysm type and reported increased risk of hemorrhagic presentation with feeding artery aneurysms [44] and intranidal aneurysms [45]. Deep venous drainage has been consistently implicated as an important angiographic feature of AVMs; however, studies have variably reported exclusively deep drainage versus a component of deep drainage as a risk factor for initial or subsequent hemorrhage [22, 23, 25, 26, 32, 42, 45–48]. The number of draining veins has also been investigated, with authors reporting presence of a single draining vein as associated with rupture [24, 37, 46, 47, 49], as have venous anomalies such as ectasias, stenosis, or occlusion [25, 33, 37, 46, 49]. In an effort to clarify the significance of angioarchitectural characteristics associated with hemorrhage and thus assist with clinical decision-making, Sahlein et al. proposed outflow impedance as a physiologic mechanism for increased risk of rupture. In addition to identifying a single draining vein as predictive of rupture, they showed that patients with multiple draining veins and outflow stenosis had increased risk of rupture, comparable to those with single veins. Furthermore, an agreement analysis looking at other factors that have an unclear physiologic rationale for increasing risk (small size, deep drainage, deep location, absence of pial-to-pial collaterals) supported the hypothesis that the significance of these factors can be explained by association with more physiologically plausible factors that cause outflow impedance [33]. Importantly, such studies emphasize the need to consider how clinical and angioarchitectural characteristics of AVMs may alter a patient's rupture risk.

Preoperative Planning

Once the decision has been made to treat an AVM, comprehensive preoperative planning is critical to ensure safe, successful intervention. In general, surgical resection is an elective procedure. For life-threatening hemorrhage requiring emergency surgery, clot evacuation without attempting AVM resection is typically performed. For ruptured AVMs that are not immediately life-threatening, delayed resection (at least 1–2 weeks) is commonly advocated, as this allows time for the hematoma to liquefy, surrounding inflammatory changes to resolve, and recovery from temporary neurologic deficit, all of which are important for appropriate decision-making. Though acute intervention has been advocated by some [50], this does not allow time for the patient to recover from temporary deficit or to reassess the AVM architecture after hemorrhage, both of which have implications for choice of treatment modality.

In the setting of hemorrhage, especially if urgent surgery is necessary, head CT and CT angiogram may be sufficient preoperative imaging, as they allow for rapid diagnosis and assessment of angioarchitecture; however, elective preoperative planning should also include MRI and digital subtraction angiography (DSA). MRI and MR angiography (MRA) can provide significant insight into the surrounding brain tissue. Particularly for lesions located in the eloquent cortex, evolving techniques using fiber tractography and functional mapping may prove extremely useful for surgical planning [51]. Future innovations in MRI technique, such as radial phase-contrast MRA, may improve noninvasive evaluation of AVM hemodynamics [52].

DSA remains the gold standard for evaluating AVMs and should be performed early after presentation with hemorrhage and again just prior to surgery. In addition to fully defining the feeding arteries and draining veins, it provides information about hemodynamics; furthermore, superselective microcatheterization of individual feeding pedicles can elucidate angioarchitectural characteristics associated with hemorrhage, such as nidal aneurysms or venous stenosis, that may otherwise be undetected [33, 53]. Preoperative embolization has emerged as an important step in the multidisciplinary management of AVMs. In the acute phase after hemorrhage, identification and embolization of the likely source of hemorrhage, such as intra- or perinidal aneurysms, may help reduce risk of early re-hemorrhage [54, 55]. Preoperative embolization has been shown to enhance the safety and efficacy of surgery by reducing operative time and blood loss, with no significant difference in postoperative complications or long-term neurologic outcome [56]. Some series have additionally shown improved rates of major neurologic deficit, seizure, and death with embolization prior to surgical resection [57]. Embolization can be used to significantly shrink the nidus size and secure deep arterial feeders or associated aneurysms that may be difficult to access surgically, thus facilitating complete resection [58–62]; moreover, this may effectively decrease the Spetzler-Martin grade of the lesion, thus making previously inoperable lesions operable [63]. Though morbidity and mortality secondary to embolization remain low, particularly with modern techniques and materials, the addition of superselective amytal testing can be utilized during the procedure to predict morbidity from vessel occlusion and thus lower complication rate [64–68].

SRS prior to surgical resection has also been described. Steinberg et al. first described a series of patients who underwent surgical resection of incompletely obliterated AVMs after SRS; they found the AVM to be less vascular, partially thrombosed, and more easily resected than patients who had not undergone SRS [69]. This was echoed in a later case report of a large AVM treated with staged SRS followed by resection, with authors describing gliotic brain tissue with an easily developed plane around the lesion [70]. More recent series have described favorable outcomes for surgery following SRS – radiosurgery significantly decreased lesion size and downgraded the Spetzler-Martin grade – thus facilitating resection with lower rates of preoperative embolization, shorter operative time, decreased blood loss and length of stay, and better functional outcome postoperatively [71–74]. Such results suggest that in carefully selected patients, namely, young patients with high-grade AVMs initially considered inoperable, SRS may play a role in a multimodality treatment plan. See Fig. 17.1 for a case presentation of a ruptured AVM with an associated aneurysm.

Surgical Techniques and Considerations

Surgical resection of AVMs remains among the most challenging lesions in the neurosurgical arena. These cases often involve complex anatomy, long spans of extreme attention to detail, meticulous hemostasis, and extreme psychological stress. These factors can be combated with careful study of preoperative films, operative planning, and honest patient counseling.

Techniques

Positioning will vary based on location of lesion. Attention to positioning to allow for good venous return is important. In addition, if the femoral artery is accessible, an intraoperative angiogram should be planned for. In certain cases an immediate postoperative angiogram would be necessary.

Good communication with the anesthesia team, neuro-monitoring, and the scrub technicians is paramount. Neuro-navigation has started to play a bigger role and should also be coordinated beforehand. A large craniotomy is necessary with ade-

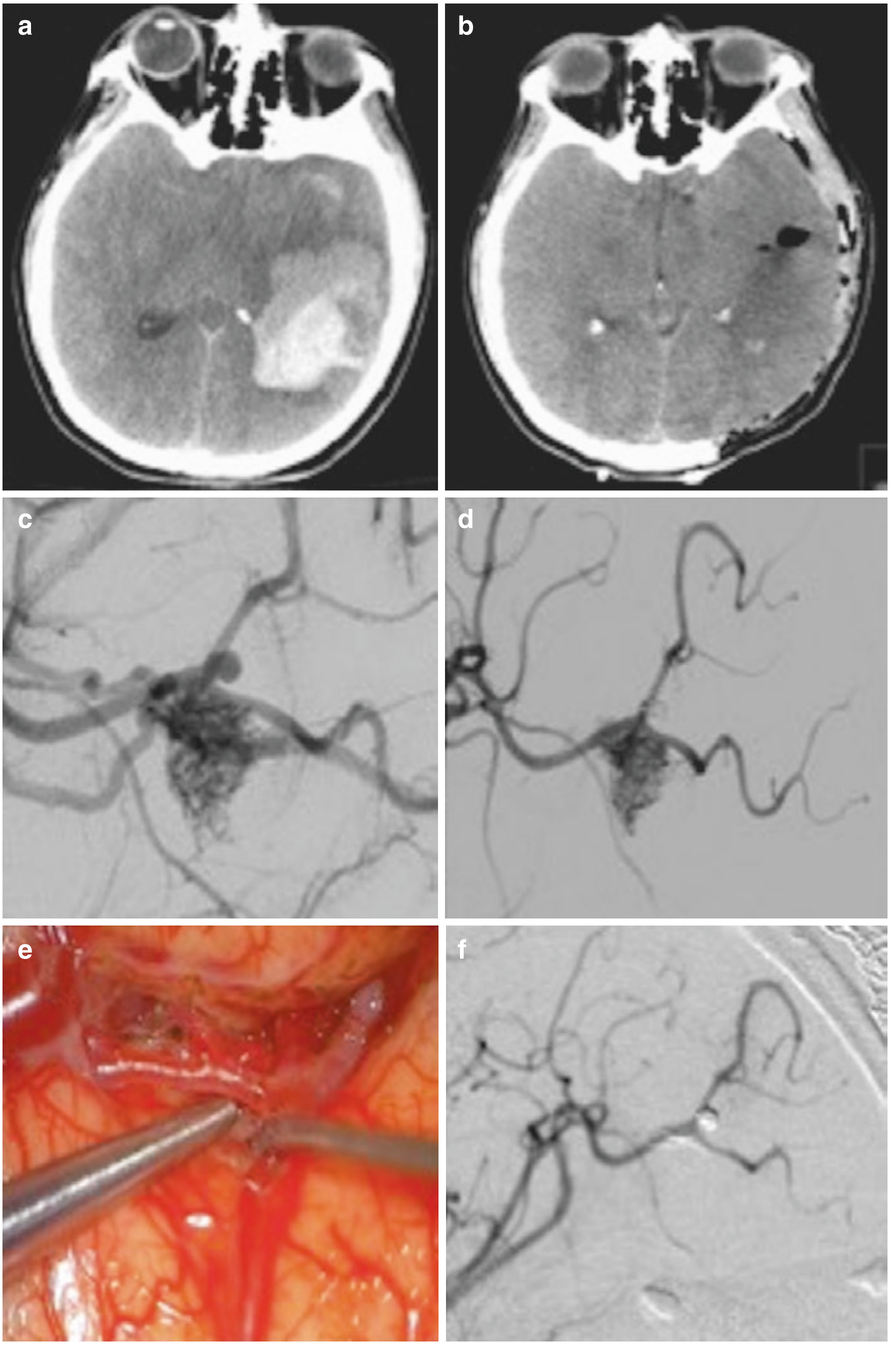

Fig. 17.1 Management of a ruptured left parietal AVM in a 25-year-old male. (**a**) Presentation CT with radiographic and clinical evidence of herniation. (**b**) s/p hemicraniectomy with evacuation of hematoma and no resection of AVM. (**c**) Angiogram showing an aneurysm on the peri-arterial bifurcation. (**d**) Coiling of aneurysm on POD 1. (**e**) Following 10 days of observant management, resection of AVM. (**f**) Intraoperative angiogram showing complete resection of AVM

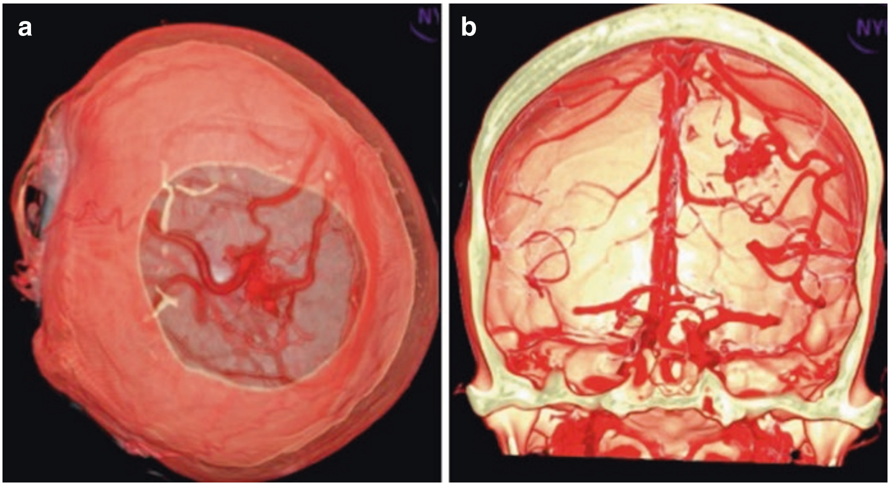

Fig. 17.2 (**a**, **b**) Use of a surgical planning system for visualization of surface vessels, allowing for identification of surface arterial feeders and draining veins

quate exposure of superficial arterial feeders or draining veins that are a distance from the nidus.

Vein preservation is crucial. Often, deciding which vessels are draining veins is among the first decisions to be made, especially in superficially draining AVMs. These draining vessels, due to arterialization, can be confused with arterial pedicles as well as passerby arteries. Careful preoperative examination of films will help prepare you for this decision. In addition, 3-D surgical planning platforms can assist (Fig. 17.2).

Resection of the AVM is usually carried out in a circumferential dissection and in a spiral fashion toward its depth. In cases where there are multiple draining veins, a decision to take a secondary draining vein for the purposes of exposure can be made. AVMs that track down to the ventricle usually have ependymal feeders, and these must be also coagulated, although it is usually the more difficult aspect of the case. As the resection nears completion, the draining vein can be noted to return to a darker color signifying a reduction in arterial shunting. If doubt remains, temporary clipping of the draining vein can be done to see if it is safe to disconnect.

Bipolar electrocautery forceps is one of the most important instruments in this surgery. Minimizing the adherence of the coagulated vessels to the bipolar tips is important for an efficient resection. Irrigating bipolar forceps or bipolars under constant irrigation will reduce that adherence. In addition, newer bipolars with different metallic surfaces allow for a better heat sink capacity and less thermal spread. Constant cleaning of the tips and keeping them in ice water will also allow for efficacious use.

Hemostatic materials are helpful in managing small venous bleeding in the cavity however should not be used for small arterial bleeding. Commonly, these arterial feeders will retract out of sight and can cause adjacent hematomas. These retracted vessels must be followed, even if further white matter dissection has to take place and be coagulated.

Surgical Outcomes and Complications

Surgical outcomes have improved over time with better patient selection and risk stratification, clarification of angioarchitectural risk factors, and refinement of surgical approaches; however, it is essential to critically evaluate treatment outcomes in comparison to the natural history risk. The goal of AVM resection is complete obliteration to mitigate the morbidity and mortality associated with the natural history. To this end, Laakso et al. studied the excess mortality experienced by patients diagnosed with an AVM and found that treatment reduced the excess mortality conferred by an AVM diagnosis [6]. Obliteration rates after surgical resection are extremely high, with reported angiographic cure rates of 94–100% [34, 75, 76].

Outcomes by Spetzler-Martin Grade

Classification of functional outcomes varies by author; however, a common stratification defines outcomes using modified Rankin scale (mRs), with a good outcome defined as ≤1 or ≤ 2. Postoperative complications may include hemorrhage, infarct, seizure, infection, need for CSF diversion, or, in extremely rare circumstances, retrograde arterial or venous thrombosis or vasospasm. In their series of 232 patients with Spetzler-Martin grade I or II AVMs who underwent surgical resection, Potts et al. demonstrated a 94% complete obliteration rate with 93% of patients mRS ≤ 2 and 97% of patients unchanged or improved postoperatively; furthermore, surgical mortality rate was only 0.4%, and only 3% of patients were neurologically worse postoperatively. These results were comparable to the summary of surgical series for grades I and II AVMs the authors reported, with mortality rates ranging from 0% to 2.2% (mean 0.3%) and morbidity rates ranging from 0% to 6.6% (mean 2.2%) [76]. Grade III AVMs represent a heterogeneous population, with four combinations of size, venous drainage, and eloquence, and reported surgical outcomes reflect this heterogeneity. Lawton et al. addressed this by analyzing a series of only grade III AVMs and proposing a modification of the Spetzler-Martin scale [75]. They achieved a 97.4% obliteration rate; notably, 25% of patients had undergone some prior treatment, and 75 of 76 patients were embolized preoperatively, with 2 hemorrhages attributed to the endovascular procedure. Postoperatively they reported three hemorrhages and a surgical mortality rate of 3.9%, for an overall surgical risk of 8.0%. Good outcomes (mRS ≤ 2) were achieved in 78.7% of patients, and 3.9% of patients experienced permanent treatment-associated neurological morbidity. The authors further stratified patients by type of grade III AVM, reporting that patients with small AVMs (S1V1E1) did the best, with 97.1% unchanged or improved postoperatively, compared to those with medium/deep AVMs (S2V1E0) or medium/eloquent (S2V0E1), with 92.9% and 85.2% of patients unchanged or improved postoperatively, respectively. Surgical morbidity and mortality for grades IV and V AVMs are high, with rates of up to 26% morbidity and 3.2% mortality described in early series [77–80], prompting many to defer surgical resection for these lesions. More recent series have tended to utilize a multimodality approach more frequently and have reported complete obliteration rates of 70–97.6%, with morbidity/mortality rates ranging from 10% to 23% [73, 80, 81]. When comparing outcomes after 2000 with the historical cohort prior to 2000, some authors noted a nearly 50% reduction in poor outcomes [82].

Outcomes for Seizures

Persistent seizures or drug-resistant epilepsy are important indications for surgical resection of AVMs, as complete obliteration leads to the best outcomes for seizure control. Some modern series report seizure control rates (Engel class I or II) of 93–100% [83, 84], though outcomes were not analyzed by type of preoperative seizure. In a series of 293 patients with sporadic seizures (41%), chronic seizures (35.9%), or drug-resistant epilepsy (23.3%) who underwent complete surgical resection, seizure control rates were favorable – 85.7% of patients with sporadic seizures, 80.5% with chronic seizures, and 58.3% with drug-resistant epilepsy were seizure-free [85]. Control rates in the drug-resistant subset improved to 80% for patients who underwent extended lesionectomy for seizure control.

Outcomes for ARUBA-Eligible Patients

"A Randomized Trial of Unruptured Brain AVMs" (ARUBA) was a prospective, multicenter, parallel design, nonblinded, randomized controlled trial designed to compare medical management alone to medical management with interventional therapy for prevention of death or stroke in patients with unruptured brain AVMs [86]. The study, which was halted early after interim analysis, concluded that medical management was superior to intervention for prevention of death or stroke in patients with unruptured AVMs followed for 33 months. This surprising result, which is at odds with much of the prior literature, was widely critiqued. Among comments on design, conduct, and result analysis, factors such as selection criteria, lack of standardization of the treatment arm, low enrollment rate, recruitment bias, short follow-up, and inappropriate conclusions were all frequently cited as problematic [87]. Specifically, the low number of randomized patients compared to those who refused or were treated elsewhere, low number of surgically treated patients (18%), and high number of patients treated with radiosurgery (33%) or embolization (32%) followed for a relatively short time period may have contributed to the study's conclusion. In the wake of this study, the importance of solidifying the safety and efficacy of AVM resection was emphasized, and many groups published their experience with surgical intervention for patients who could have been eligible for the ARUBA trial. Authors primarily focused on Spetzler-Martin grades I and II AVMs, as these are the most favorable for surgery and the ones most likely to have been selected for treatment outside the randomization process of ARUBA, and reinforced the low morbidity and mortality associated with intervention [76, 88–92]. A systematic review of this literature included 6 studies with 956 patients; of studies that included both surgery and radiosurgery with or without embolization, 50–58% of patients underwent surgical resection [93]. Compared to ARUBA, in which 30.7% of patients in the treatment arm reached the primary endpoint of symptomatic stroke or death, these studies reported a mean rate of 8.0% stroke or death, which was similar to the rate for the medical arm (10.1%) of ARUBA. Similarly, the percentage of patients with poor functional outcomes (mRS ≥ 2) in the reviewed studies (mean 9.9%) was more comparable to that reported in the medical arm of ARUBA (14%) than the intervention arm (38.6%) [93]. The review summarized that in contrast to the ARUBA results, surgical intervention can effectively treat appropriately selected unruptured AVMs with a safety margin similar to that of medical management [93].

References

1. Berman MF, Sciacca RR, Pile-Spellman J, Stapf C, Connolly ES Jr, Mohr JP, et al. The epidemiology of brain arteriovenous malformations. Neurosurgery. 2000;47(2):389–96; discussion 97.
2. Al-Shahi R, Warlow C. A systematic review of the frequency and prognosis of arteriovenous malformations of the brain in adults. Brain J Neurol. 2001;124(Pt 10):1900–26.
3. Moftakhar P, Hauptman JS, Malkasian D, Martin NA. Cerebral arteriovenous malformations. Part 1: cellular and molecular biology. Neurosurg Focus. 2009;26(5):E10.
4. Kondziolka D, McLaughlin MR, Kestle JR. Simple risk predictions for arteriovenous malformation hemorrhage. Neurosurgery. 1995;37(5):851–5.
5. Hernesniemi JA, Dashti R, Juvela S, Vaart K, Niemela M, Laakso A. Natural history of brain arteriovenous malformations: a long-term follow-up study of risk of hemorrhage in 238 patients. Neurosurgery. 2008;63(5):823–9. discussion 9–31.
6. Laakso A, Dashti R, Seppanen J, Juvela S, Vaart K, Niemela M, et al. Long-term excess mortality in 623 patients with brain arteriovenous malformations. Neurosurgery. 2008;63(2):244–53; discussion 53–5.
7. Ondra SL, Troupp H, George ED, Schwab K. The natural history of symptomatic arteriovenous malformations of the brain: a 24-year follow-up assessment. J Neurosurg. 1990;73(3):387–91.
8. Morgan M, Sekhon L, Rahman Z, Dandie G. Morbidity of intracranial hemorrhage in patients with cerebral arteriovenous malformation. Stroke. 1998;29(9):2001–2.
9. Brown RD Jr, Wiebers DO, Torner JC, O'Fallon WM. Frequency of intracranial hemorrhage as a presenting symptom and subtype analysis: a population-based study of intracranial vascular malformations in Olmsted country Minnesota. J Neurosurg. 1996;85(1):29–32.
10. Spetzler RF, Martin NA. A proposed grading system for arteriovenous malformations. J Neurosurg. 1986;65(4):476–83.
11. Hamilton MG, Spetzler RF. The prospective application of a grading system for arteriovenous malformations. Neurosurgery. 1994;34(1):2–6; discussion−7.
12. Han PP, Ponce FA, Spetzler RF. Intention-to-treat analysis of Spetzler-Martin grades IV and V arteriovenous malformations: natural history and treatment paradigm. J Neurosurg. 2003;98(1):3–7.
13. Luessenhop AJ, Gennarelli TA. Anatomical grading of supratentorial arteriovenous malformations for determining operability. Neurosurgery. 1977;1(1):30–5.
14. Luessenhop AJ, Rosa L. Cerebral arteriovenous malformations. Indications for and results of surgery, and the role of intravascular techniques. J Neurosurg. 1984;60(1):14–22.
15. Shi YQ, Chen XC. A proposed scheme for grading intracranial arteriovenous malformations. J Neurosurg. 1986;65(4):484–9.

16. Kim H, Abla AA, Nelson J, McCulloch CE, Bervini D, Morgan MK, et al. Validation of the supplemented Spetzler-Martin grading system for brain arteriovenous malformations in a multicenter cohort of 1009 surgical patients. Neurosurgery. 2015;76(1):25–31; discussion−2; quiz 2–3.
17. Lawton MT, Kim H, McCulloch CE, Mikhak B, Young WL. A supplementary grading scale for selecting patients with brain arteriovenous malformations for surgery. Neurosurgery. 2010;66(4):702–13; discussion 13.
18. Graf CJ, Perret GE, Torner JC. Bleeding from cerebral arteriovenous malformations as part of their natural history. J Neurosurg. 1983;58(3):331–7.
19. Yamada S, Takagi Y, Nozaki K, Kikuta K, Hashimoto N. Risk factors for subsequent hemorrhage in patients with cerebral arteriovenous malformations. J Neurosurg. 2007;107(5):965–72.
20. Mast H, Young WL, Koennecke HC, Sciacca RR, Osipov A, Pile-Spellman J, et al. Risk of spontaneous haemorrhage after diagnosis of cerebral arteriovenous malformation. Lancet. 1997;350(9084):1065–8.
21. Halim AX, Johnston SC, Singh V, McCulloch CE, Bennett JP, Achrol AS, et al. Longitudinal risk of intracranial hemorrhage in patients with arteriovenous malformation of the brain within a defined population. Stroke. 2004;35(7):1697–702.
22. Stapf C, Mast H, Sciacca RR, Choi JH, Khaw AV, Connolly ES, et al. Predictors of hemorrhage in patients with untreated brain arteriovenous malformation. Neurology. 2006;66(9):1350–5.
23. Abecassis IJ, Xu DS, Batjer HH, Bendok BR. Natural history of brain arteriovenous malformations: a systematic review. Neurosurg Focus. 2014;37:E7.
24. Pollock B, Flickinger J, Lunsford L, Bissonette D, Kondziolka D. Factors that predict the bleeding risk of cerebral arteriovenous malformations. Stroke. 1996;27:1–6.
25. Gross BA, Du R. Natural history of cerebral arteriovenous malformations: a meta-analysis. J Neurosurg. 2013;118:437–43.
26. Kim H, Al-Shahi Salman R, McCulloch CE, Stapf C, Young WL. Untreated brain arteriovenous malformation: patient-level meta-analysis of hemorrhage predictors. Neurology. 2014;83:590–7.
27. da Costa L, Wallace MC, Ter Brugge KG, O'Kelly C, Willinsky RA, Tymianski M. The natural history and predictive features of hemorrhage from brain arteriovenous malformations. Stroke. 2009;40(1):100–5.
28. Laakso A, Dashti R, Juvela S, Isarakul P, Niemela M, Hernesniemi J. Risk of hemorrhage in patients with untreated Spetzler-Martin grade IV and V arteriovenous malformations: a long-term follow-up study in 63 patients. Neurosurgery. 2011;68(2):372–7; discussion 8.
29. Tong X, Wu J, Lin F, Cao Y, Zhao Y, Ning B, et al. The effect of age, sex, and lesion location on initial presentation in patients with brain arteriovenous malformations. World Neurosurg. 2016;87:598–606.
30. Yang W, Caplan JM, Ye X, Wang JY, Braileanu M, Rigamonti D, et al. Racial associations with hemorrhagic presentation in cerebral arteriovenous malformations. World Neurosurg. 2015;84(2):461–9.
31. Kim H, Sidney S, McCulloch CE, Poon KY, Singh V, Johnston SC, et al. Racial/Ethnic differences in longitudinal risk of intracranial hemorrhage in brain arteriovenous malformation patients. Stroke. 2007;38(9):2430–7.
32. Langer DJ, Lasner TM, Hurst RW, Flamm ES, Zager EL, King JT. Hypertension, small size, and deep venous drainage are associated with risk of hemorrhagic presentation of cerebral arteriovenous malformations. Neurosurgery. 1998;42:481–9.
33. Sahlein DH, Mora P, Becske T, Huang P, Jafar JJ, Connolly ES, et al. Features predictive of brain arteriovenous malformation hemorrhage: extrapolation to a physiologic model. Stroke. 2014;45:1964–70.
34. Spetzler RF, Kondziolka DS, Higashida RT, Kalani MYS. Comprehensive management of arteriovenous malformations of the brain and spine. Cambridge: Cambridge University Press; 2015.
35. Laakso A, Hernesniemi J, Yonekawa Y, Tsukahara T. Surgical management of cerebrovascular disease. Vienna: Springer; 2009.

36. Stefani MA, Porter PJ, terBrugge KG, Montanera W, Willinsky RA, Wallace MC. Large and deep brain arteriovenous malformations are associated with risk of future hemorrhage. Stroke. 2002;33(5):1220–4.
37. Lv X, Wu Z, Jiang C, Yang X, Li Y, Sun Y, et al. Angioarchitectural characteristics of brain arteriovenous malformations with and without hemorrhage. World Neurosurg. 2011;76(1–2):95–9.
38. Kader A, Young WL, Pile-Spellman J, Mast H, Sciacca RR, Mohr JP, et al. The influence of hemodynamic and anatomic factors on hemorrhage from cerebral arteriovenous malformations. Neurosurgery. 1994;34(5):801–7; discussion 7–8.
39. Miyasaka Y, Yada K, Kurata A, Tokiwa K, Irikura K, Tanaka R, et al. Correlation between intravascular pressure and risk of hemorrhage due to arteriovenous malformations. Surg Neurol. 1993;39(5):370–3.
40. Nornes H, Grip A. Hemodynamic aspects of cerebral arteriovenous malformations. J Neurosurg. 1980;53(4):456–64.
41. Spetzler RF, Hargraves RW, McCormick PW, Zabramski JM, Flom RA, Zimmerman RS. Relationship of perfusion pressure and size to risk of hemorrhage from arteriovenous malformations. J Neurosurg. 1992;76(6):918–23.
42. Pan J, Feng L, Vinuela F, He H, Wu Z, Zhan R. Angioarchitectural characteristics associated with initial hemorrhagic presentation in supratentorial brain arteriovenous malformations. Eur J Radiol. 2013;82:1959–63.
43. Soderman M, Andersson T, Karlsson B, Wallace MC, Edner G. Management of patients with brain arteriovenous malformations. Eur J Radiol. 2003;46(3):195–205.
44. Stapf C, Mohr JP, Pile-Spellman J, Sciacca RR, Hartmann A, Schumacher HC, et al. Concurrent arterial aneurysms in brain arteriovenous malformations with haemorrhagic presentation. J Neurol Neurosurg Psychiatry. 2002;73(3):294–8.
45. Kim EJ, Halim AX, Dowd CF, Lawton MT, Singh V, Bennett J, et al. The relationship of coexisting extranidal aneurysms to intracranial hemorrhage in patients harboring brain arteriovenous malformations. Neurosurgery. 2004;54(6):1349–57; discussion 57–8.
46. Miyasaka Y, Yada K, Ohwada T, Kitahara T, Kurata A, Irikura K. An analysis of the venous drainage system as a factor in hemorrhage from arteriovenous malformations. J Neurosurg. 1992;76(2):239–43.
47. Alexander MD, Cooke DL, Nelson J, Guo DE, Dowd CF, Higashida RT, et al. Association between venous angioarchitectural features of sporadic brain arteriovenous malformations and intracranial hemorrhage. AJNR Am J Neuroradiol. 2015;36:949–52.
48. Duong DH, Young WL, Vang MC, Sciacca RR, Mast H, Koennecke HC, et al. Feeding artery pressure and venous drainage pattern are primary determinants of hemorrhage from cerebral arteriovenous malformations. Stroke. 1998;29:1167–76.
49. Stefani MA, Porter PJ, TerBrugge KG, Montanera W, Willinsky RA, Wallace MC. Angioarchitectural factors present in brain arteriovenous malformations associated with hemorrhagic presentation. Stroke. 2002;33:920–4.
50. Kuhmonen J, Piippo A, Vaart K, Karatas A, Ishii K, Winkler P, et al. Early surgery for ruptured cerebral arteriovenous malformations. Acta Neurochir Suppl. 2005;94:111–4.
51. Bendok BR, El Tecle NE, El Ahmadieh TY, Koht A, Gallagher TA, Carroll TJ, et al. Advances and innovations in brain arteriovenous malformation surgery. Neurosurgery. 2014;74(Suppl 1):S60–73.
52. Chang W, Loecher MW, Wu Y, Niemann DB, Ciske B, Aagaard-Kienitz B, et al. Hemodynamic changes in patients with arteriovenous malformations assessed using high-resolution 3D radial phase-contrast MR angiography. AJNR Am J Neuroradiol. 2012;33:1565–72.
53. Turjman F, Massoud TF, Vinuela F, Sayre JW, Guglielmi G, Duckwiler G. Correlation of the angioarchitectural features of cerebral arteriovenous malformations with clinical presentation of hemorrhage. Neurosurgery. 1995;37(5):856–60. discussion 60–2.
54. Perata HJ, Tomsick TA, Tew JM Jr. Feeding artery pedicle aneurysms: association with parenchymal hemorrhage and arteriovenous malformation in the brain. J Neurosurg. 1994;80(4):631–4.

55. Mpotsaris A, Loehr C, Harati A, Lohmann F, Puchner M, Weber W. Interdisciplinary clinical management of high grade arteriovenous malformations and ruptured flow-related aneurysms in the posterior fossa. Interv Neuroradiol. 2010;16(4):400–8.
56. Jafar JJ, Davis AJ, Berenstein A, Choi IS, Kupersmith MJ. The effect of embolization with N-butyl cyanoacrylate prior to surgical resection of cerebral arteriovenous malformations. J Neurosurg. 1993;78(1):60–9.
57. Pasqualin A, Scienza R, Cioffi F, Barone G, Benati A, Beltramello A, et al. Treatment of cerebral arteriovenous malformations with a combination of preoperative embolization and surgery. Neurosurgery. 1991;29(3):358–68.
58. Nataraj A, Mohamed MB, Gholkar A, Vivar R, Watkins L, Aspoas R, et al. Multimodality treatment of cerebral arteriovenous malformations. World Neurosurg. 2014;82(1–2):149–59.
59. Natarajan SK, Ghodke B, Britz GW, Born DE, Sekhar LN. Multimodality treatment of brain arteriovenous malformations with microsurgery after embolization with onyx: single-center experience and technical nuances. Neurosurgery. 2008;62(6):1213–25. discussion 25–6.
60. Vinuela F, Dion JE, Duckwiler G, Martin NA, Lylyk P, Fox A, et al. Combined endovascular embolization and surgery in the management of cerebral arteriovenous malformations: experience with 101 cases. J Neurosurg. 1991;75(6):856–64.
61. Starke RM, Komotar RJ, Otten ML, Hahn DK, Fischer LE, Hwang BY, et al. Adjuvant embolization with N-butyl cyanoacrylate in the treatment of cerebral arteriovenous malformations: outcomes, complications, and predictors of neurologic deficits. Stroke. 2009;40(8):2783–90.
62. Weber W, Kis B, Siekmann R, Jans P, Laumer R, Kuhne D. Preoperative embolization of intracranial arteriovenous malformations with Onyx. Neurosurgery. 2007;61(2):244–52. discussion 52–4.
63. Spetzler RF, Martin NA, Carter LP, Flom RA, Raudzens PA, Wilkinson E. Surgical management of large AVM's by staged embolization and operative excision. J Neurosurg. 1987;67(1):17–28.
64. Ogilvy CS, Stieg PE, Awad I, Brown RD Jr, Kondziolka D, Rosenwasser R, et al. Recommendations for the management of intracranial arteriovenous malformations: a statement for healthcare professionals from a special writing group of the stroke council, American Stroke Association. Circulation. 2001;103(21):2644–57.
65. Purdy PD, Batjer HH, Samson D, Risser RC, Bowman GW. Intraarterial sodium amytal administration to guide preoperative embolization of cerebral arteriovenous malformations. J Neurosurg Anesthesiol. 1991;3(2):103–6.
66. Rauch RA, Vinuela F, Dion J, Duckwiler G, Amos EC, Jordan SE, et al. Preembolization functional evaluation in brain arteriovenous malformations: the ability of superselective amytal test to predict neurologic dysfunction before embolization. AJNR Am J Neuroradiol. 1992;13(1):309–14.
67. Moo LR, Murphy KJ, Gailloud P, Tesoro M, Hart J. Tailored cognitive testing with provocative amobarbital injection preceding AVM embolization. AJNR Am J Neuroradiol. 2002;23(3):416–21.
68. Tawk RG, Tummala RP, Memon MZ, Siddiqui AH, Hopkins LN, Levy EI. Utility of pharmacologic provocative neurological testing before embolization of occipital lobe arteriovenous malformations. World Neurosurg. 2011;76(3–4):276–81.
69. Steinberg GK, Chang SD, Levy RP, Marks MP, Frankel K, Marcellus M. Surgical resection of large incompletely treated intracranial arteriovenous malformations following stereotactic radiosurgery. J Neurosurg. 1996;84(6):920–8.
70. Firlik AD, Levy EI, Kondziolka D, Yonas H. Staged volume radiosurgery followed by microsurgical resection: a novel treatment for giant cerebral arteriovenous malformations: technical case report. Neurosurgery. 1998;43(5):1223–8.
71. Sanchez-Mejia RO, McDermott MW, Tan J, Kim H, Young WL, Lawton MT. Radiosurgery facilitates resection of brain arteriovenous malformations and reduces surgical morbidity. Neurosurgery. 2009;64(2):231–8; discussion 8–40.

72. Zaidi HA, Abla AA, Nakaji P, Spetzler RF. Prospective evaluation of preoperative stereotactic radiosurgery followed by delayed resection of a high grade arteriovenous malformation. J Clin Neurosci. 2014;21(6):1077–80.
73. Abla AA, Rutledge WC, Seymour ZA, Guo D, Kim H, Gupta N, et al. A treatment paradigm for high-grade brain arteriovenous malformations: volume-staged radiosurgical downgrading followed by microsurgical resection. J Neurosurg. 2014;122:1–14.
74. Tong X, Wu J, Pan J, Lin F, Cao Y, Zhao Y, et al. Microsurgical resection for persistent arteriovenous malformations following gamma knife radiosurgery: a case-control study. World Neurosurg. 2016;88:277–88.
75. Lawton MT, Project UBAMS. Spetzler-Martin grade III arteriovenous malformations: surgical results and a modification of the grading scale. Neurosurgery. 2003;52(4):740–8; discussion 8–9.
76. Potts MB, Lau D, Abla AA, Kim H, Young WL, Lawton MT, et al. Current surgical results with low-grade brain arteriovenous malformations. J Neurosurg. 2015;122:912–20.
77. Heros RC, Korosue K, Diebold PM. Surgical excision of cerebral arteriovenous malformations: late results. Neurosurgery. 1990;26(4):570–7. discussion 7–8.
78. Hartmann A, Stapf C, Hofmeister C, Mohr JP, Sciacca RR, Stein BM, et al. Determinants of neurological outcome after surgery for brain arteriovenous malformation. Stroke. 2000;31(10):2361–4.
79. Nozaki K, Hashimoto N, Miyamoto S, Kikuchi H. Resectability of Spetzler-Martin grade IV and V cerebral arteriovenous malformations. J Clin Neurosci. 2000;7(Suppl 1):78–81.
80. Jizong Z, Shuo W, Jingsheng L, Dali S, Yuanli Z, Yan Z. Combination of intraoperative embolisation with surgical resection for treatment of giant cerebral arteriovenous malformations. J Clin Neurosci. 2000;7(Suppl 1):54–9.
81. Zhao J, Yu T, Wang S, Zhao Y, Yang WY. Surgical treatment of giant intracranial arteriovenous malformations. Neurosurgery. 2010;67(5):1359–70; discussion 70.
82. Reinard KA, Pabaney AH, Basheer A, Phillips SB, Kole MK, Malik GM. Surgical management of giant intracranial arteriovenous malformations: a single center experience over 32 years. World Neurosurg. 2015;84:1765–78.
83. Englot DJ, Young WL, Han SJ, McCulloch CE, Chang EF, Lawton MT. Seizure predictors and control after microsurgical resection of supratentorial arteriovenous malformations in 440 patients. Neurosurgery. 2012;71:572–9.
84. Nagata S, Morioka T, Matsukado K, Natori Y, Sasaki T. Retrospective analysis of the surgically treated temporal lobe arteriovenous malformations with focus on the visual field defects and epilepsy. Surg Neurol. 2006;66:50–5.
85. Von Der Brelie C, Simon M, Esche J, Schramm J, Boström A. Seizure outcomes in patients with surgically treated cerebral arteriovenous malformations. Neurosurgery. 2015;77: 762–8.
86. Mohr JP, Parides MK, Stapf C, Moquete E, Moy CS, Overbey JR, et al. Medical management with or without interventional therapy for unruptured brain arteriovenous malformations (ARUBA): a multicentre, non-blinded, randomised trial. Lancet. 2014;383:614–21.
87. Magro E, Gentric J-c, Darsaut TE, Ziegler D, Bojanowski MW, Raymond J. Responses to ARUBA: a systematic review and critical analysis for the design of future arteriovenous malformation trials. J Neurosurg. 2016:1–9.
88. Javadpour M, Al-Mahfoudh R, Mitchell PS, Kirollos R. Outcome of microsurgical excision of unruptured brain arteriovenous malformations in ARUBA-eligible patients. Br J Neurosurg. 2016;30:1–4.
89. Moon K, Levitt MR, Almefty RO, Nakaji P, Albuquerque FC, Zabramski JM, et al. Safety and efficacy of surgical resection of unruptured low-grade arteriovenous malformations from the modern decade. Neurosurgery. 2015;77:948–52; discussion 52–3.
90. Lawton MT. The role of AVM microsurgery in the aftermath of a randomized trial of unruptured brain arteriovenous malformations. AJNR Am J Neuroradiol. 2015;36:617–9.

91. Rutledge WC, Abla AA, Nelson J, Halbach VV, Kim H, Lawton MT. Treatment and outcomes of ARUBA-eligible patients with unruptured brain arteriovenous malformations at a single institution. Neurosurg Focus. 2014;37:E8.
92. Schramm J, Schaller K, Esche J, Boström A. Microsurgery for cerebral arteriovenous malformations: subgroup outcomes in a consecutive series of 288 cases. J Neurosurg. 2016:1–8.
93. Hong CS, Peterson EC, Ding D, Sur S, Hasan D, Dumont AS, et al. Intervention for a randomized trial of unruptured brain arteriovenous malformations (ARUBA) – eligible patients: an evidence-based review. Clin Neurol Neurosurg. 2016;150:133–8.