ELSEVIER
SAUNDERS

Neurosurg Clin N Am 16 (2005) 367–380

NEUROSURGERY
CLINICS
OF NORTH AMERICA

Endovascular Treatment of Cerebral Arteriovenous Malformations: Indications, Techniques, Outcome, and Complications

Kevin M. Cockroft, MD, MSc, FACS[a], Sung-Kyun Hwang, MD[b,c], Robert H. Rosenwasser, MD, FACS[c,*]

[a]*Department of Neurosurgery, MC H110, M.S. Hershey Medical Center, Pennsylvania State University, PO Box 850, Hershey, PA 17033, USA*
[b]*Department of Neurosurgery, Ewha Women's University School of Medicine, 70 Changro 6 KR, Changro-gu, Seoul 110-783, South Korea*
[c]*Division of Cerebrovascular Surgery and Interventional Neuroradiology, Department of Neurosurgery, Thomas Jefferson University Hospital, 909 Walnut Street, Third Floor, Philadelphia, PA 19107, USA*

In 1960, Luessenhop and Spence [1] reported the first case of the endovascular treatment of a cerebral arteriovenous malformation (AVM). In the early cases subsequently reported, plastic microspheres were often injected through direct access from the cervical carotid artery. Emboli were guided solely by flow and often ended up in the lungs. Over the years, endovascular therapy for cerebral AVMs has advanced greatly, although the basic principles and goals have remained similar. Microcatheters are now flow directed, and liquid embolic agents have replaced particles for the most part, but the eventual angiographic obliteration of the AVM remains the ultimate goal. In the following article, we review the basic indications, techniques, and complications associated with the current endovascular treatment of cerebral (pial) AVMs.

Cerebral arteriovenous malformations

Cerebral vascular malformations are commonly classified as belonging to one of four categories: (1) AVMs, (2) cavernous angiomas (ie, cavernomas, cavernous malformations), (3) capillary telangiectasias, and (4) venous angiomas (ie, developmental venous anomalies) [2]. Based on McCormick's autopsy series of 5743 consecutive patients [3], the incidence of venous angiomas seems to be the highest of the group at approximately 3%, followed by capillary telangiectasias at 0.9%, AVMs at 0.5%, and cavernous angiomas at 0.3%. Capillary telangiectasias and venous angiomas are almost always incidental or asymptomatic; as such, they rarely require treatment. In contrast, AVMs and cavernous angiomas commonly present with hemorrhage, seizures, or progressive neurologic deficit, and treatment is often required.

Like the other types of cerebral vascular malformations, high-flow pial AVMs are thought to be congenital lesions that arise during the first trimester of fetal development. Unlike cavernous angiomas, which are collections of low-flow venous sinusoids, AVMs are composed of multiple, primitive, high-flow arteries connected directly to the venous system without an intervening capillary network. Dysplastic brain tissue is present between the vessels of the AVM nidus. Because cavernous angiomas are, by definition, angiographically occult, no endovascular role is available for their management. AVMs, conversely, show a typical pattern of arteriovenous shunting on angiography, with venous outflow usually provided by one or two dilated and arterialized veins. This appearance makes cerebral AVMs quite amenable to all major forms of treatment,

* Corresponding author.
E-mail address: robert.rosenwasser@mail.tju.edu (R.H. Rosenwasser).

doi:10.1016/j.nec.2004.08.001

including endovascular embolization, microsurgical resection, and stereotactic radiosurgery.

Natural history

Approximately 50% to 60% of patients with AVMs come to medical attention after intracerebral hemorrhage (Fig. 1), making hemorrhage the most common—and, arguably, the most devastating—presenting symptom of cerebral AVMs [4–6]. Seizures, the next most common presenting symptom, have been reported to occur in approximately 30% of patients with supratentorial AVMs [6]. The hemorrhage rate for cerebral AVMs has been estimated at between 2% and 4% per year [7–13]. The most often quoted yearly hemorrhage rate for symptomatic lesions is probably that of 4% per year, based on the review by Ondra et al [12] of 166 symptomatic patients with AVMs who were followed prospectively for an average of 20 years without surgical treatment. Although the yearly rate of hemorrhage may be lower in asymptomatic patients, equal rates of hemorrhage have been reported [7]. In addition, although Ondra et al [58] did not find that the rehemorrhage risk was higher than that of the initial hemorrhage risk in patients harboring AVMs, other authors have noted higher rebleeding rates, especially in the first year [8–11,13]. The risks of morbidity and mortality associated with a particular hemorrhage are estimated at 10% and 30%, respectively [13,14].

Over the years, considerable effort has been spent in trying to stratify further the risk of hemorrhage according to various patient and AVM characteristics. The relation between AVM

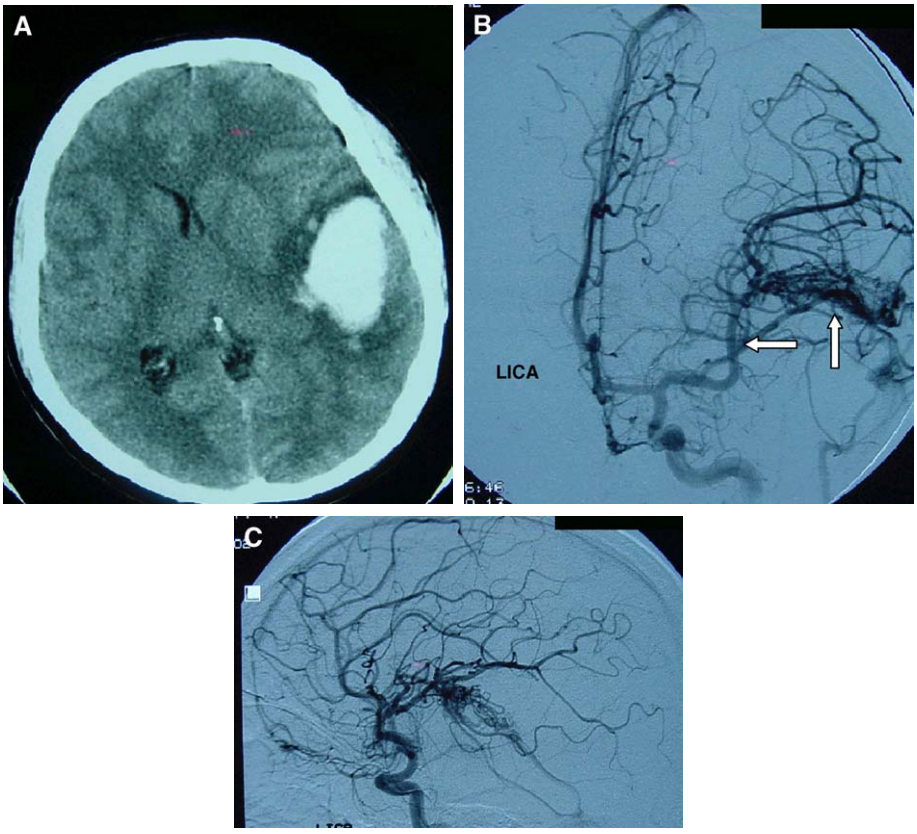

Fig. 1. (*A*) An axial noncontrast CT scan performed on a 27-year-old-man, who presented with the sudden onset of a severe headache and right hemiparesis, shows an acute left intracerebral hemorrhage with associated mass effect and shift. (*B, C*) A subsequent angiogram demonstrates an arteriovenous malformation located in the right posterior temporal lobe and fed by branches of the right middle cerebral artery (MCA). Note medial and upward displacement of the MCA (*arrows*) from the hematoma.

size and the risk of hemorrhage is controversial. A preponderance of evidence seems to suggest that small AVMs bleed more frequently than larger ones [11,15–21]. This may possibly result from increased feeding artery pressures in smaller AVMs [22,23]. Many studies have shown no association with size [18,24–27] or an increased risk of hemorrhage with increasing AVM size [28,29], however. On the venous side, deep venous drainage as well as venous outflow stenosis has been highlighted by several authors as a risk factor for hemorrhage [30–35]. The location of an AVM as it relates to the bleeding risk has also been controversial, but some reports suggest that infratentorial or deep (periventricular) lesions may be at increased risk for hemorrhage [6,32,36,37]. For infratentorial AVMs, this may be at least partially a result of the fact that posterior fossa lesions do not produce seizures, thereby leading to a selection bias in favor of hemorrhage for malformations in this location.

AVMs are known to be associated with aneurysms at a rate greater than that of chance alone, with various reports putting this association between 2.7% and 14% [18,38–42]. Furthermore, the presence of an associated aneurysm, particularly an intranidal aneurysm, seems to increase the risk of hemorrhage [32,34,37,38,42,43]. AVM-associated aneurysms may be located on feeding arteries, at remote sites, or within the AVM nidus itself; the wide-ranging estimate of prevalence is most likely a result of the inconsistent definitions of aneurysms used in the literature.

Management of AVM-associated aneurysms has been the subject of much discussion. Although the regression of some AVM-associated aneurysms after treatment of the AVM has been reported [41], other factors lend support to strategies of early intervention. In particular, it has been shown that in instances of intracranial hemorrhage in which an AVM and an aneurysm are present, the aneurysm is the lesion more likely to have bled [37]. Such evidence, combined with the higher morbidity and mortality associated with aneurysm hemorrhage, has led many to recommend that the aneurysm be treated first if at all possible.

Patient factors that influence hemorrhage are less well understood. Increasing age may contribute to an increased risk of hemorrhage [44]. Other characteristics, such as gender, hypertension, pregnancy, and tobacco use, may not be associated, however.

Various grading scales for cerebral AVMs have been proposed to aid in the prediction of patient morbidity or mortality with or without treatment. The most commonly applied grading scale is that proposed by Spetzler and Martin [45] in 1986 (Table 1). Based on a review of 100 consecutive surgically treated AVM patients, the grading system was designed to predict the risk of operative treatment. Three categories are described, and a "grade" is assigned based on point totals from each category. In the location category, a patient receives one point for an AVM located in eloquent brain and no points for a noneloquent location. Similarly, an AVM with deep venous drainage is assigned one point, whereas one with superficial venous drainage receives no points in this category. Size is broken down into three groups: less than 3 cm, 3 to 6 cm, and greater than 6 cm, with one to three points assigned as size increases. By categories, the maximum point total that can be assigned is five; however, an AVM may be given a grade of VI if it is deemed "unresectable." Because this grading scale is based on patients who were treated primarily with surgical resection, its applicability to endovascular therapy may be questionable. At present, however, there is no widely accepted grading scale for the endovascular treatment of cerebral AVMs.

Indications for treatment and treatment outcome

Given the natural history of these lesions, treatment is frequently recommended, particularly in those patients who are relatively young, demonstrate symptoms, or have angiographic or clinical risk factors that may predispose to hemorrhage. Treatment is undertaken to prevent future neurologic injury or to improve current

Table 1
Spetzler-Martin surgical grading scale for cerebral (pial) arteriovenous malformations

Category	Point value
Size (maximal dimension)	
<3 cm	1
3–6 cm	2
>6 cm	3
Location	
Noneloquent brain	0
Eloquent brain	1
Venous drainage	
Superficial only	0
Deep	1

From Spetzler RF, Martin NA. A proposed grading system for arteriovenous malformations. J Neurosurg 1986;65:476–83; with permission.

neurologic status. To this end, the goal of any single treatment modality or combination of modalities is the ultimate obliteration of the AVM. Each treatment modality may have its own specific role in the overall treatment plan, however. Endovascular embolization as a treatment modality usually assumes one of three roles: adjunctive, curative, or palliative.

Adjunct to microsurgery

The most commonly used role of endovascular embolization is that of an adjunct to microsurgical resection or stereotactic radiosurgery. For patients with surgically accessible lesions, microsurgical removal can provide an immediate cure. A large nidus, deep-feeding vessels, and high-flow shunts can make surgical resection more challenging, however. In such patients, the added risks of endovascular treatment may compare favorably with the risks of surgery alone (Fig. 2). In a comparison of patients undergoing embolization with N-butyl-cyanoacrylate (NBCA) before surgical resection versus patients undergoing surgery alone, Jafar et al [46] found that rates of complications and good or excellent outcomes were similar in both

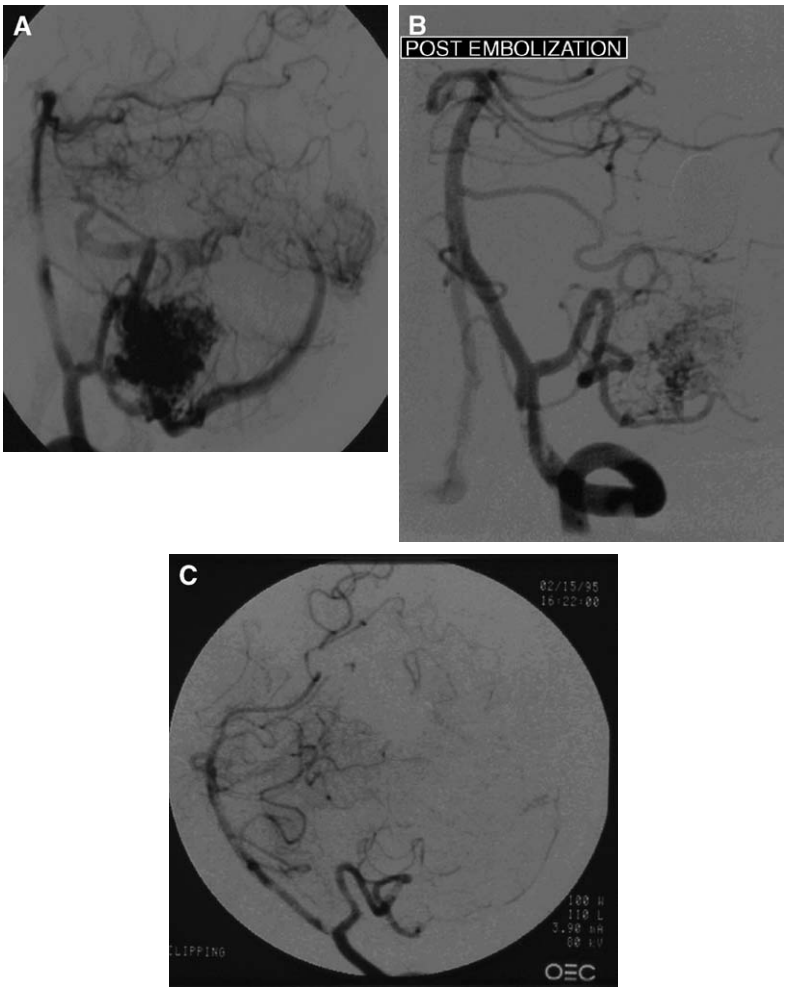

Fig. 2. (*A*) Initial cerebral angiogram from a 20-year-old woman, who presented with a small intraparenchymal hemorrhage, shows an arteriovenous malformation (AVM) located in the inferior portion of the left cerebellar hemisphere. (*B*) A control angiogram performed after a single session of N-butyl-cyanoacrylate embolization shows a considerable reduction in the nidus size. Given the patient's previous history of hemorrhage, the small size of the residual AVM, and the surgically accessible location, the patient underwent microsurgical excision of the lesion. (*C*) An intraoperative angiogram shows no residual nidus and no persistent early venous drainage.

groups despite the fact that the embolized patients had higher Spetzler-Martin grade lesions. Embolization shortened operative time and reduced blood loss. Similar findings have been reported by other practitioners [47–54].

The degree of volume reduction necessary before surgery to effect a difference in surgical resection is debatable. It has been suggested that although elimination of more than 75% of the AVM nidus facilitates surgical resection, occlusion of less than 50% does little to aid operative removal [55]. In cases in which less than 50% obliteration is likely with endovascular therapy and surgical resection is planned, benefit can still be achieved if deep-feeding arteries are occluded. It should be remembered that endovascular embolization is not without risk. Therefore, in general, the risks of embolization for surgically accessible small AVMs (<3 cm in diameter, Spetzler-Martin grade I or some grade II) probably outweigh the benefits.

Adjunct to radiosurgery

In patients with AVMs located in eloquent cortex or deep structures, stereotactic radiosurgery may be a preferable alternative to microsurgical resection when the risk of morbidity and mortality may be unacceptably high. In such patients, endovascular embolization may be used to reduce the size of the AVM before radiosurgery or to eliminate certain angiographic features, such as intranidal aneurysms, that may provide for elevated risk while the patient is awaiting AVM obliteration after radiosurgery (Fig. 3).

It is well known that the rate of AVM cure after stereotactic radiosurgery decreases as the volume of the AVM being treated increases [56–63]. Therefore, the role of endovascular embolization in this setting is to reduce the nidus size such that a cure after radiosurgery is more likely [58,60,64]. Case series have shown a greater percentage of radiosurgical cure for those patients with a reduction in AVM volume to below 10 cm^3 [65,66]. In preradiosurgery patients, it is helpful but not essential for the AVM nidus to be reduced to a smaller single focus. If this is not possible, a volume-staged approach may be used to treat two or more areas of residual AVM separately [67]. Alternatively, for those patients in whom the lesion does not proceed to obliteration after stereotactic radiosurgery, repeated embolization or surgical resection may still be used, often with greater success [68,69].

Curative treatment

The primary goal of AVM treatment is the eventual obliteration of the lesion. Only after the AVM has been obliterated can the treating physician have any confidence that the patient's future risk of hemorrhage has been eliminated. For endovascular embolization to be curative, there must be no residual filling of the nidus and the angiographic shunt or abnormal early venous drainage must be eliminated (Fig. 4). For most cerebral AVMs, however, endovascular embolization alone is unable to provide complete occlusion. The most common reason for this is probably the inability to catheterize and thereby embolize many of the small arterial feeders associated with most brain AVMs.

Published endovascular cure rates are difficult to interpret. Because embolization evolved primarily as a therapeutic adjunct, many published series suffer from considerable referral bias, whereby only "large" AVMs incapable of being treated with radiosurgery or open microsurgery alone are referred for embolization and smaller lesions with only one or two feeding pedicles are treated without endovascular intervention. In addition, the lack of a widely accepted endovascular grading scale makes comparison between various studies problematic. Nevertheless, in a series of 465 patients, Vinuela et al [70] reported a 9.7% rate of complete AVM occlusion with embolization alone. Gobin et al [65] reported a similar cure rate of 11.2% in a cohort of patients scheduled for radiosurgery who had undergone embolization initially as an "adjunctive" therapy. Both series found cure to be more likely in patients with small AVMs. Gobin et al [65] also found that the rate of cure was inversely related to the number of feeding pedicles. In contrast, other authors have reported much higher rates of cure with endovascular therapy when patients were selected specifically for embolization as a primary modality. After selecting a subgroup of patients on the basis of angiographic features they thought were likely to promote endovascular obliteration, Valavanis and Yasargil [71] noted a cure rate of 74% (or 35% of their overall series) with embolization alone. Factors that predisposed to complete occlusion included the presence of dominant feeders without perinidal angiogenesis, a single nidus, and a more fistulous than plexiform nidus.

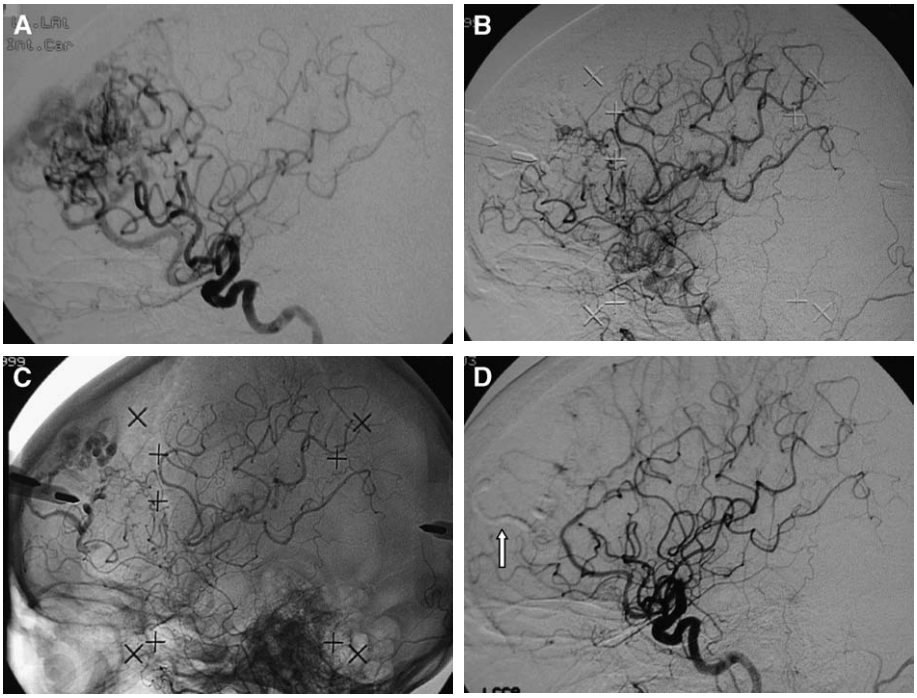

Fig. 3. (*A*) Pretreatment angiogram, performed on a 56-year-old woman with new-onset seizures, reveals a left frontal arteriovenous malformation (AVM) fed by branches of the left anterior cerebral artery and middle cerebral artery. After the nidus volume was reduced with multiple sessions of glue embolization, the patient was scheduled for gamma knife stereotactic radiosurgery. (*B*) An angiogram performed for gamma knife treatment planning shows a small area of residual AVM (*arrow*). (*C*) In an unsubtracted image from the same study, the glue cast is visible (*arrow*) as well as the skull pins and markers (+ marks) of the Leksell gamma knife head frame. (*D*) A follow-up angiogram performed approximately 3 years after radiosurgery shows no persistent filling of the AVM. A glue cast is still visible in the left frontal lobe (*arrow*).

Palliative treatment

Although only complete elimination of the AVM constitutes a true cure, palliative treatment may be used in selected cases. Specifically, patients who are symptomatic with large or deep-seated AVMs that are unlikely to be cured with any combination of modalities may benefit from subtotal endovascular embolization. Whether partial treatment of an AVM is at all beneficial, however, remains somewhat controversial, with some authors reporting a similar or worse natural history in incompletely treated patients [72,73].

In patients with repeated hemorrhages, embolization may be used to eliminate angiographic risk factors for hemorrhage, such as intranidal aneurysms. For those with intractable headaches or progressive neurologic deficits, the benefits of partial treatment are less certain. Nonetheless, embolization to reduce the arteriovenous shunt, and thereby decrease the amount of "steal" or venous hypertension associated with a lesion, has been reported to cause clinical improvement [74,75].

Surgical versus endovascular perspectives on treatment

Intellectual controversy exists between neurosurgeons and endovascular therapists in their approach to the indications for AVM treatment. As neurosurgeons who perform all three of the major modalities of AVM treatment, we prefer to view indications for treatment from a multidisciplinary perspective, with treatment tailored to the individual patient and AVM.

The first decision of the treating physician should be whether the AVM needs to be treated. Once that question has been answered in the affirmative, the process of tailoring a treatment plan may begin. For patients who have sustained a hemorrhage, every effort should be made to eliminate the risk of future bleeding as soon as

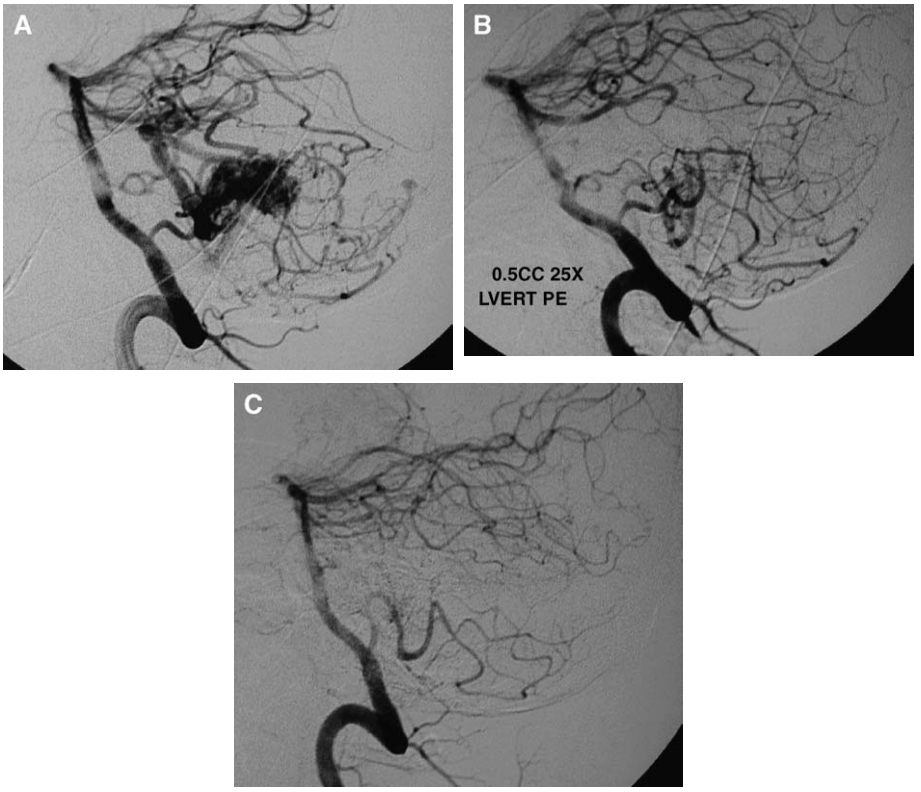

Fig. 4. Lateral projections of vertebral artery angiograms (*A,B,C*) from a 48-year-old woman with a cerebellar arteriovenous malformation (AVM) treated with N-butyl-cyanoacrylate embolization show progressive obliteration of the AVM after endovascular therapy alone.

possible. For such patients, this may mean a combination of surgical resection or endovascular embolization. If the morbidity or mortality associated with these treatments is likely to be greater than that of the natural history of the untreated AVM over the next few years, a combination of stereotactic radiosurgery or embolization may be desirable. Traditionally, surgical resection alone has been favored for patients with mass effect symptoms from a sizable acute intracerebral hemorrhage. Even in many of these patients, however, we have used emergent aggressive embolization before surgery to reduce intraoperative blood loss or simply evacuated the hematoma and left the AVM for later treatment with any combination of modalities. In general, however, most AVMs seen at our institution (a tertiary care referral center) are large and arise within or partially within eloquent brain. As a result, more than 50% of the patients with AVMs treated in the senior author's series were treated with stereotactic radiosurgery and embolization.

In the end, success is most likely to be achieved by a multidisciplinary approach tailored to the individual patient and the characteristics of the lesion itself. Such an approach may be best delivered at a tertiary care institution, where practitioners experienced in the latest microsurgical, radiosurgical, and endovascular techniques are readily available.

Endovascular techniques

The first reports of endovascular AVM treatment involved the nonselective use of particles; it was not until 1972 that Zanetti and Sherman [76] reported the first use of a liquid embolic acrylate polymer to treat cerebral AVMs. Today, liquid cyanoacrylate glue derivatives delivered through superselective microcatheterization are the most commonly used embolic agents for the treatment of cerebral AVMs.

At our institution, almost all AVM embolizations are performed under general endotracheal

anesthesia with pharmacologic paralysis. This essentially eliminates patient movement and facilitates road-mapping for intravascular navigation. Tight blood pressure control is maintained. To minimize the risk of a neurologic deficit in patients treated under general anesthesia, we routinely use intraoperative neurophysiologic monitoring in the form of somatosensory evoked potentials and electroencephalography. Brainstem auditory evoked responses are used for lesions requiring access through the posterior circulation.

Arterial access is generally achieved through a transfemoral route. In adults, a 5- to 8-French guide catheter is usually used. The use of a 7-French sheath with a 6-French guide catheter allows for continuous blood pressure monitoring through the sheath, eliminating the need for a separate arterial line. In addition, the 6-French guide catheter provides for easy contrast injection such that a selective angiogram may be performed even with a microcatheter in place. Flow-directed microcatheters (rather than braided wire-driven catheters) are optimal for accessing AVM pedicles and delivering liquid embolic agents. Commonly used brands approved for use in the United States include the Spinnaker Elite (1.5- or 1.8-French; Boston Scientific-Neurovascular, Fremont, California) and the Regatta (1.8-French; Cordis Neurovascular, Miami, Florida). Although these catheters are flow directed, a hydrophilic guidewire (usually 0.10 in) is still required to facilitate the flow-independent movements often required for selecting a specific arterial pedicle. Aggressive manipulation with the wire, however, should be avoided so as to minimize the risk of vascular perforation.

After the appropriate first- or second-order vessel is selected and catheterized, a pretreatment biplane angiogram, including capillary and venous phases, should be obtained to serve as a reference. We attempt to place our guide catheter as distal as safely possible so as to provide added support for the microcatheter. A digital roadmap can then be created and used to navigate the flow-directed microcatheter into an appropriate pedicle (Fig. 5A). Larger pedicles are usually selected during initial sessions, because smaller pedicles may subsequently dilate as the flow characteristics of the AVM change with treatment. Once a specific pedicle has been selected, contrast injection through the microcatheter can then be used to judge flow through the nidus, assess the proximity of the draining vein(s), and determine whether any normal arterial branches are being supplied. In some instances, particularly in awake patients, selective barbiturate injections through the microcatheter may be used to assess the eloquence of brain served by the vascular territory in question (“Amytal testing”) [44,77–79]. For patients under general anesthesia, superselective barbiturate injection may lead to changes in neurophysiologic parameters. The lack of certainty with regard to flow distribution of the barbiturate in the presence of an AVM may limit the usefulness of this method. As a result, a negative Amytal test result does not necessarily guarantee a good outcome.

Occlusion of the AVM is achieved with an embolic agent. Over the years, various types of embolic agents have been used to treat cerebral AVMs. Many earlier treatments were performed using particles, particularly polyvinyl alcohol (PVA). Today, liquid embolic derivatives of cyanoacrylate have largely supplanted PVA as the agent of choice for most practitioners. The results of a prospective randomized trial comparing NBCA with PVA for the preoperative embolization of cerebral AVMs were published in 2002 and demonstrated equivalence for both agents, at least in terms of the percentage of nidus reduction and number of pedicles embolized [80]. PVA particles are unlikely to provide permanent arterial occlusion, however; as such, they should only be used as an adjunct to timely surgical extirpation [81]. Occasionally, in lesions with fistulous components, the injection of glue may be facilitated by the use of pushable platinum coils to reduce flow [82].

Several liquid embolic agents have been used in the endovascular occlusion of cerebral AVMs, and these agents are discussed in an article elsewhere in this issue. The most popular liquid embolic agents are cyanoacrylate derivatives, including Trufill (Cordis Neurovascular) and Histocryl (Braun-Aesculap, Tuttlingen, Germany). Absolute ethyl alcohol has also been used as an embolic agent for vascular malformations, primarily those of the extracranial circulation. The treatment of cerebral AVMs with absolute alcohol has been reported [83], but its use remains controversial. Currently, the only “glue” approved by the US Food and Drug Administration for use in cerebral AVMs is Trufill (NBCA).

NBCA glue is a clear, colorless, and radiolucent liquid and comes packaged in single-concentration 1-mL vials. The glue begins to polymerize on contact with ionic material, such as blood, saline, and ionic contrast media. To alter the polymerization properties of the glue and make it visible during injection on angiography,

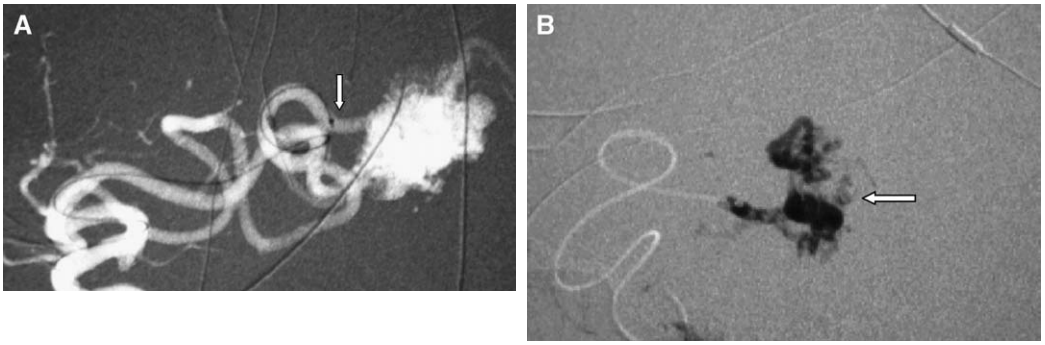

Fig. 5. (*A*) Lateral projection of a roadmap image obtained after internal carotid artery injection showing a microcatheter and microwire within a middle cerebral artery pedicle in close proximity to the arteriovenous malformation (AVM) nidus (*arrow*). (*B*) After N-butyl-cyanoacrylate embolization under roadmap (''mask'') conditions, a glue cast can be seen within the AVM nidus (*arrow*). The path of the microcatheter as it was rapidly withdrawn appears as a bright line against the background of the mask.

NBCA may be combined with Ethiodol (Cordis-Neurovascular) (oil-based nonionic contrast), nonionic water-soluble contrast, or tantalum powder. Trufill is packaged with Ethiodol for dilution, although many have found the behavior of various Ethiodol-NBCA concentrations to be inconsistent in terms of viscosity and polymerization. Nevertheless, NBCA concentrations between 20% and 70% are commonly used depending on the proximity of the microcatheter to the nidus and the rapidity of the arteriovenous shunt. Some authors have advocated the use of glacial acetic acid as the diluting agent for NBCA, believing that its effects are more reproducible [53]. Because acetic acid is also radiolucent, the glue must be combined with tantalum powder (also packaged with Trufill) to make it radiopaque. Tantalum, however, also adds viscosity to the mixture.

With the microcatheter in optimal position, the embolic agent may then be prepared. The appropriate glue concentration should be mixed on a separate table to avoid contamination with blood or other ionic substances that may cause premature polymerization. Unfortunately, determining the appropriate glue concentration is not an exact science. Observation of the AVM flow characteristics and angioarchitecture after contrast injection through the microcatheter is critical. In the end, however, there is no substitute for experience with a specific embolic agent.

At our institution, moderate hypotension (mean arterial pressure of approximately 50 mm Hg) is induced before embolization. The microcatheter is flushed with dextrose (5%) to prevent premature polymerization in the catheter. The glue is then injected under road-mapping to enhance visualization (see Fig. 5B). After glue administration, the microcatheter must be rapidly pulled from the site of injection to prevent the catheter from being glued in place. If necessary, in a patient under general anesthesia, a Valsalva maneuver may be performed by the anesthesiologist to increase venous pressure to help prevent the embolic agent from reaching the draining vein(s).

After glue injection and removal of the microcatheter, the microcatheter should be checked to ensure that the entire catheter has been removed. Because of the possibility of residual glue in the catheter, we prefer to discard the microcatheter after every glue injection. The guide catheter should be thoroughly flushed and then may be reused. A postembolization angiogram should be performed to assess the degree and location of AVM obliteration obtained during the embolization.

After surgery, our patients are observed in a monitored intensive care or intermediate care unit. Mild hypotension (mean arterial pressure $<$80 mm Hg) is maintained for approximately 24 hours to minimize the risk of breakthrough hemorrhage. Dexamethasone is used during surgery to control the inflammatory response that may occur secondary to the NBCA. We do not routinely use any anticoagulation during the procedure. Femoral sheaths are usually removed the evening after embolization, and most patients are discharged home the following day.

There are no specific guidelines as to the percentage volume or number of pedicles that should be embolized at any given sitting. It has

been suggested that major alterations in the hemodynamic characteristics of an AVM may occur after the rapid occlusion of a large percentage of its volume, thus increasing the risk of a hemorrhagic complication. This, however, continues to be controversial. In this regard, we prefer a conservative approach to endovascular AVM treatment, and we frequently embolize only one pedicle at any given session. Larger AVMs may thus require three or more sessions of embolization, usually spaced 4 to 5 weeks apart.

Complications and complication avoidance

The risks of endovascular AVM treatment are not insignificant. Because AVM embolization alone is not usually curative, it is important to weigh the risks of an adjunctive procedure against the potential benefits that such a procedure may have in improving cure with another modality.

Complications related to endovascular AVM treatment usually fall into one of two broad categories: ischemic or hemorrhagic. Ischemic complications may result from errant glue emboli in physiologic vessels or catheter/wire manipulation causing dissection and vascular occlusion. Careful review of the pre-embolization superselective angiogram is essential to prevent the inadvertent occlusion of normal distal branches or en passage vessels. Selecting the appropriate glue concentration to avoid early polymerization around the catheter tip and subsequent showering of emboli when the catheter is removed is likewise important. Some practitioners also administer anticoagulants to patients during embolization to reduce the risk of thromboembolic complications [84]. We have not found this to be necessary, however.

Hemorrhagic complications are perhaps more common and may be equally devastating. Too dilute a glue concentration can cause glue to travel through the nidus and occlude the draining vein(s); hemorrhage may then ensue as a result of venous outflow obstruction. Some believe that too rapid an alteration in the hemodynamics of an AVM, such as through the embolization of multiple pedicles at a single sitting, may also promote hemorrhage. Finally, catheter/wire manipulation may cause a vascular perforation, resulting in intracerebral or subarachnoid hemorrhage. Newer, softer, flexible-tipped microwires and more pliable flow-directed catheters have reduced the risk of this complication. Guidewire use should still be minimized, however. Whenever possible, the microwire should be used only for selecting the desired proximal pedicle while letting the natural flow characteristics of the AVM carry the microcatheter to the appropriate distal position for embolization.

Complication rates

The literature is replete with case series reporting rates of morbidity and mortality for endovascularly treated AVMs. Studies published in the 1980s, using mostly liquid embolic agents, documented rates of morbidity and mortality in the range of 10% to 22% and 2% to 6%, respectively [43,47,85,86]. In the late 1990s, Gobin et al [65] reported similar numbers, with a morbidity rate of 12.8% and a mortality rate of 1.6%. That there has been little change in the risk of embolization over the last several years was further confirmed by Frizzel and Fisher [87], who published a review of 32 case series that included 1246 patients treated over 35 years. The overall rates of permanent and temporary morbidity in their series were 8% and 10%, whereas the rate of mortality was 1%. When broken down into cohorts treated before and after 1990, the permanent morbidity rate went from 9% to 8%, respectively (not statistically significant), and the mortality rate changed from 2% to 1%, respectively (also not statistically significant).

Thomas Jefferson University Hospital experience

In the senior author's personal series covering a period from October 1995 to August 2003, a total of 448 AVMs were embolized, 225 underwent gamma knife radiosurgery, and 135 were surgically removed. An additional 164 patients have had no treatment and are being followed because of age or medical comorbidities. In a subset of 170 patients from this series, all treated with endovascular embolization and with complete follow-up at 36 months, permanent morbidity was noted in only 7 patients (4.1%). In this group, there were no cases of postembolization hemorrhage and no deaths after embolization. Most patients (125 [73%]) underwent one or two sessions of embolization. Twenty-six (15%) and 9 (5%) patients had three and four sessions, respectively, whereas 10 patients underwent five or more embolizations. The overall cure rate to date, including all modes of treatment, is 24.7%.

The cure rate for patients treated with endovascular embolization alone (49 of 170 patients or 28.8% of the total series) stands at 14.3% (7 patients). Those cured with embolization alone all harbored AVMs with a Spetzler-Martin grade of III or lower. None of these lesions had a maximal dimension over 6 cm.

Cure rates

As discussed previously, cure rates after endovascular embolization are difficult to interpret. This is at least partially a result of the lack of prospective, randomized, controlled studies comparing various treatment modalities. Given the current trend toward the multidisciplinary treatment of AVMs, it is doubtful that such studies will ever be performed. A multidisciplinary approach must thus be critically compared with the natural history of these lesions, and attention must be paid to clinical outcome in terms of functional status, quality of life, and patient satisfaction.

Summary

Untreated cerebral AVMs carry a significant risk of long-term morbidity and mortality. Endovascular embolization has evolved into an important treatment option for most AVMs, whether it is used as an adjunct or as the primary therapy. Although sometimes a challenge to use, liquid cyanoacrylate derivatives have become the material of choice for most practitioners performing endovascular AVM embolization. In addition, advances in flow-guided microcatheter technology have enabled safer access to ever more hard-to-reach areas of the cerebral vasculature. In the current era, the treatment of cerebral AVMs seems to be best approached from a multidisciplinary standpoint at facilities where the major treatment modalities of microsurgery, stereotactic radiosurgery, and endovascular embolization are all available.

References

[1] Luessenhop AJ, Spence WT. Artificial embolization of cerebral arteries: report of use in a case of arteriovenous malformation. JAMA 1960;172:1153–5.

[2] McCormick WF. The pathology of vascular (“arteriovenous”) malformations. J Neurosurg 1966;24: 807–16.

[3] McCormick WF. Pathology of vascular malformations of the brain. In: Wilson C, Stein B, editors. Intracranial vascular malformations. Baltimore: Williams & Wilkins; 1984. p. 44–63.

[4] Drake CG. Cerebral arteriovenous malformations: considerations for and experience with surgical treatment in 166 cases. Clin Neurosurg 1979;26: 145–208.

[5] Mast H, Mohr JP, Osipov A, et al. “Steal” is an unestablished mechanism for the clinical presentation of cerebral arteriovenous malformation. Stroke 1995;26:1215–20.

[6] Perret G, Nishioka H. Report on the cooperative study of intracranial aneurysms and subarachnoid hemorrhage: arteriovenous malformations. J Neurosurg 1966;25:467–90.

[7] Brown RD, Wiebers DO, Forbes GS, et al. The natural history of unruptured intracranial arteriovenous malformations. J Neurosurg 1988;68:352–7.

[8] Crawford PM, West CR, Chadwick DW, et al. Arteriovenous malformations of the brain: natural history in unoperated patients. J Neurol Neurosurg Psychiatry 1986;49:1–10.

[9] Forster DMC, Steiner L, Hakanson S. Arteriovenous malformations of the brain. A long-term clinical study. J Neurosurg 1972;37:562–70.

[10] Fults D, Kelly DL Jr. Natural history of arteriovenous malformations of the brain: a clinical study. Neurosurgery 1984;15:658–62.

[11] Graf CJ, Perret GE, Torner JC. Bleeding from cerebral arteriovenous malformations as part of their natural history. J Neurosurg 1983;58:331–7.

[12] Ondra S, Troupp H, George E, et al. The natural history of symptomatic arteriovenous malformations of the brain: a 24-year follow-up assessment. J Neurosurg 1990;73:387–91.

[13] Wilkins RH. Natural history of intracranial vascular malformations of the brain: a review. Neurosurgery 1985;16:421–30.

[14] Hartmann A, Mast H, Mohr JP, et al. Morbidity of intracranial hemorrhage in patients with cerebral arteriovenous malformation. Stroke 1998;29:931–4.

[15] Henderson WR, Gomez RD. Natural history of cerebral angiomas. BMJ 1967;4:571–4.

[16] Moody RA, Poppen JL. Arteriovenous malformations. J Neurosurg 1970;32:502–11.

[17] Parkinson D, Bachers G. Arteriovenous malformations. Summary of 100 consecutive supratentorial cases. J Neurosurg 1980;53:285–99.

[18] Paterson JH, McKissock W. A clinical survey of intracranial angiomas with special reference to their mode of progression and surgical treatment: a report of 110 cases. Brain 1956;79:233–66.

[19] Pelletieri L. Surgical versus conservative treatment of intracranial arterio-venous malformations. Acta Neurol Scand 1980;29:1–86.

[20] Pia HW. The acute treatment of cerebral arteriovenous angiomas associated with hematomas. In: Pia H, Gleave J, Grate E, editors. Cerebral angiomas. Advances in diagnosis and therapy. New York: Springer-Verlag; 1975. p. 155–71.

[21] Stehbens WE. Pathology of the cerebral blood vessels. St. Louis: CV Mosby; 1972.

[22] Miyasaka Y, Kurata A, Irikura K, et al. The influence of vascular pressure and angiographic characteristics on haemorrhage from arteriovenous malformations. Acta Neurochir (Wien) 2000;142: 39–43.
[23] Spetzler RF, Hargraves RW, McCormick PW, et al. Relationship of perfusion pressure and size to risk of hemorrhage from arteriovenous malformations. J Neurosurg 1992;76:918–23.
[24] Albert P, Salgado H, Polaina M, et al. A study on the venous drainage of 150 cerebral arteriovenous malformations as related to haemorrhagic risks and size of the lesion. Acta Neurochir (Wien) 1990;103: 30–4.
[25] Duong DH, Young WL, Vang MC, et al. Feeding artery pressure and venous drainage pattern are primary determinants of hemorrhage from cerebral arteriovenous malformations. Stroke 1998;29: 1167–76.
[26] Karlsson B, Lindquist C, Johansson A, et al. Annual risk for the first hemorrhage from untreated cerebral arteriovenous malformations. Minim Invasive Neurosurg 1997;40:40–6.
[27] Mast H, Young WL, Koennecke HC, et al. Risk of spontaneous haemorrhage after diagnosis of cerebral arteriovenous malformation. Lancet 1997;350: 1065–8.
[28] Hirai S, Mine S, Yamakami I, et al. Angioarchitecture related to hemorrhage in cerebral arteriovenous malformations. Neurol Med Chir (Tokyo) 1998;38:165–70.
[29] Jomin M, Lesoin F, Lozes G. Prognosis for arteriovenous malformations of the brain in adults bases on 150 cases. Surg Neurol 1985;23:362–6.
[30] Albert P. Personal experience in the treatment of 178 cases of arteriovenous malformations of the brain. Acta Neurochir (Wien) 1982;61: 207–26.
[31] Fry DL. Acute vascular endothelial changes associated with increased blood velocity gradients. Circ Res 1968;22:165–97.
[32] Marks MP, Lane B, Steinberg GK, et al. Hemorrhage in intracerebral arteriovenous malformations: angiographic determinants. Radiology 1990;176: 807–13.
[33] Miyasaka Y, Yada K, Ohwada T, et al. An analysis of the venous drainage system as a factor in hemorrhage from arteriovenous malformations. J Neurosurg 1992;76:239–43.
[34] Muller-Forell W, Valavanis A. Neuroradiologic exploration of cerebral arteriovenous malformations. Radiologe 1991;31:269–73.
[35] Nataf F, Meder JF, Roux FX, et al. Angioarchitecture associated with haemorrhage in cerebral arteriovenous malformations: a prognostic statistical model. Neuroradiology 1997;39:52–8.
[36] Andoh T, Sakai N, Yamada H, et al. Cerebellar AVM–clinical analysis of 14 cases. No To Shinkei 1990;42:913–21.
[37] Brown RD, Wiebers DO, Forbes GS. Unruptured intracranial aneurysms and arteriovenous malformations: frequency of intracranial hemorrhage and relationship of lesions. Neurosurgery 1990;73: 859–63.
[38] Batjer H, Suss RA, Samson D. Intracranial arteriovenous malformations associated with aneurysms. Neurosurgery 1986;18:29–35.
[39] Cockroft KM, Thompson RC, Steinberg GK. Aneurysms and arteriovenous malformations. Neurosurg Clin N Am 1998;9:565–76.
[40] Higashi K, Hatano M, Yamashita T, et al. Coexistence of posterior inferior cerebellar artery aneurysm and arteriovenous malformation fed by the same artery. Surg Neurol 1979;12:405–8.
[41] Suzuki J, Onuma T. Intracranial aneurysms associated with arteriovenous malformations. J Neurosurg 1979;50:742–6.
[42] Thompson RC, Steinberg GK, Levy RP, et al. The management of patients with arteriovenous malformations and associated intracranial aneurysms. Neurosurgery 1998;43:202–11.
[43] Lasjaunias P, Manelfe C, Terbrugge K, et al. Endovascular treatment of cerebral arteriovenous malformations. Neurosurg Rev 1986;9:265–75.
[44] Kondziolka D, McLaughlin MR, Kestle JR. Simple risk predictions for arteriovenous malformation hemorrhage. Neurosurgery 1995;37:851–5.
[45] Spetzler RF, Martin NA. A proposed grading system for arteriovenous malformations. J Neurosurg 1986;65:476–83.
[46] Jafar JJ, David AJ, Berenstein A, et al. The effect of embolization with N-butyl-cyanoacrylate prior to surgical resection of cerebral arteriovenous malformations. J Neurosurg 1993;78:60–9.
[47] Debrun GM, Aletich V, Ausman JI, et al. Embolization of the nidus of brain arteriovenous malformations with N-butyl cyanoacrylate. Neurosurgery 1997;40:112–21.
[48] DeMerritt JS, Pile-Spellman J, Mast H. Outcome analysis of preoperative embolizations with N-butyl cyanoacrylate in cerebral arteriovenous malformations. AJNR Am J Neuroradiol 1995;16:1801–7.
[49] Deruty R, Pelissou-Guyotat I, Mottolese C, et al. The combined management of cerebral arteriovenous malformations. Experience with 100 cases and review of the literature. Acta Neurochir (Wien) 1993;123:101–12.
[50] Fournier D, TerBrugge KG, Willinsky R, et al. Endovascular treatment of intracerebral arteriovenous malformations: experience in 49 cases. J Neurosurg 1995;75:228–33.
[51] Grzyska U, Westphal M, Zanella F. A joint protocol for the neurosurgical and neuroradiologic treatment of cerebral arteriovenous malformations: indications, technique and results in 76 cases. Surg Neurol 1993;40:476–84.
[52] Pasqualin A, Scienza R, Cioffi F, et al. Treatment of cerebral arteriovenous malformations with a combi-

nation of preoperative embolization and surgery. Neurosurgery 1991;3:358–68.
[53] Pelz DM, Fox AJ, Vinuela F, et al. Preoperative embolization of brain AVMs with isobutyl-2 cyanoacrylate. AJNR Am J Neuroradiol 1988;9:757–64.
[54] Spetzler RF, Martin NA, Carter LP, et al. Surgical management of large AVM's by staged embolization and operative excision. J Neurosurg 1987;67: 17–28.
[55] Vinuela F, Dion JE, Duckwiler G, et al. Combined endovascular embolization and surgery in the management of cerebral arteriovenous malformations: experience with 101 cases. J Neurosurg 1991;75: 856–64.
[56] Colombo F, Pozza F, Chierego G, et al. Linear accelerator radiosurgery of cerebral arteriovenous malformations: an update. Neurosurgery 1994;34: 14–21.
[57] Friedman WA, Bova FJ, Bollampally S, et al. Analysis of factors predictive of success or complications in arteriovenous malformation radiosurgery. Neurosurgery 2003;52:296–307.
[58] Friedman WA, Bova FJ, Mendenhall WM. Linear accelerator radiosurgery for arteriovenous malformations: the relationship of size to outcome. J Neurosurg 1995;82:180–9.
[59] Karlsson B, Lindquest C, Steiner L. Prediction of obliteration after gamma knife surgery for cerebral arteriovenous malformations. Neurosurgery 1997; 40:425–31.
[60] Lunsford LD, Kondziolka D, Flickinger JC, et al. Stereotactic radiosurgery for arteriovenous malformations of the brain. J Neurosurg 1991;75:512–24.
[61] Pollock BE, Flickinger JC, Lunsford LD, et al. Factors associated with successful arteriovenous malformation radiosurgery. Neurosurgery 1998;42: 1239–44.
[62] Schlienger M, Atlan D, Lefkopoulos D, et al. LINAC radiosurgery for cerebral arteriovenous malformations: results in 169 patients. Int J Radiat Oncol Biol Phys 2000;46:1135–42.
[63] Steinberg GK, Fabrikant JI, Marks MP, et al. Stereotactic heavy-charged-particle Bragg-peak radiation for intracranial arteriovenous malformations. N Engl J Med 1990;323:96–101.
[64] Steiner L, Lindquist C, Adler JP, et al. Clinical outcome of radiosurgery for cerebral arteriovenous malformations. J Neurosurg 1992;77:1–8.
[65] Gobin YP, Laurent A, Merienne L, et al. Treatment of brain arteriovenous malformations by embolization and radiosurgery. J Neurosurg 1996;85: 19–28.
[66] Mathis JA, Barr JD, Horton JA, et al. The efficacy of particulate embolization combined with stereotactic radiosurgery for treatment of large arteriovenous malformations of the brain. AJNR Am J Neuroradiol 1995;16:299–306.
[67] Firlik AD, Levy EI, Kondziolka D, et al. Staged volume radiosurgery followed by microsurgical resection: a novel treatment for giant cerebral arteriovenous malformations: technical case report. Neurosurgery 1998;43:1223–8.
[68] Marks MP, Lane B, Steinberg GK, et al. Endovascular treatment of cerebral arteriovenous malformations following radiosurgery. AJNR Am J Neuroradiol 1993;14:297–303.
[69] Steinberg GK, Chang SD, Levy RP, et al. Surgical resection of large incompletely treated intracranial arteriovenous malformations following stereotactic radiosurgery. J Neurosurg 1996;84:920–8.
[70] Vinuela F, Duckwiler G, Gobin YP, et al. Contribution of Guglielmi detachable coil technique in the treatment of intracranial aneurysms. J Stroke Cerebrovasc Dis 1997;6:268–71.
[71] Valavanis A, Yasargil MG. The endovascular treatment of brain arteriovenous malformations. Adv Tech Stand Neurosurg 1998;24:131–214.
[72] 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;98:3–7.
[73] Pollock BE, Flickinger JC, Lunsford LD, et al. Hemorrhage after stereotactic radiosurgery of cerebral arteriovenous malformations. Neurosurgery 1996;38:659–61.
[74] Fox AJ, Girvin JP, Vinuela F, et al. Rolandic arteriovenous malformations: improvement in limb function by IBC embolization. AJNR Am J Neuroradiol 1985;6:575–82.
[75] Kusske JA, Kelly WA. Embolization and reduction of the "steal" syndrome in cerebral arteriovenous malformations. J Neurosurg 1974;40:313–21.
[76] Zanetti PH, Sherman FE. Experimental evaluation of a tissue adhesive as an agent for the treatment of aneurysms and arteriovenous anomalies. J Neurosurg 1972;36:72–9.
[77] Moo LR, Murphy KJ, Gailloud P, et al. Tailored cognitive testing with provocative amobarbital injection preceding AVM embolization. AJNR Am J Neuroradiol 2002;23:416–21.
[78] Rauch RA, Vinuela F, Dion J, 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: 309–14.
[79] Rauch R, Vinuela F, Dion J, et al. Preembolization functional evaluation in brain arteriovenous malformations: the superselective Amytal test. AJNR Am J Neuroradiol 1992;13:303–8.
[80] Tomsick TA, Purdy P, Horowitz M, et al. Investigators N-BCA trial: N-butyl cyanoacrylate embolization of cerebral arteriovenous malformations: results of a prospective, randomized, multi-center trial. AJNR Am J Neuroradiol 2002;23:748–55.
[81] Sorimachi T, Koike T, Takeuchi S, et al. Embolization of cerebral arteriovenous malformations achieved with polyvinyl alcohol particles:

angiographic reappearance and complications. AJNR Am J Neuroradiol 1999;20:1323–8.

[82] Richling B, Killer M. Endovascular management of patients with cerebral arteriovenous malformations. Neurosurg Clin N Am 2000;11:123–45.

[83] Yakes WF, Krauth L, Ecklund J, et al. Ethanol endovascular management of brain arteriovenous malformations: initial results. Neurosurgery 1997;40: 1145–52.

[84] Marks MP. Endovascular therapy for arteriovenous malformations. In: Marks M, Do H, editors. Endovascular and percutaneous therapy of the brain and spine. Philadelphia: Lippincott Williams & Wilkins; 2002. p. 243–75.

[85] Deruty R, Lapras C, Pierluca P, et al. Perioperative embolization of cerebral arteriovenous malformations with butylcyanoacrylate (18 cases). Neurochirurgie 1985;31:21–9.

[86] Merland JJ, Rufenacht D, Laurent A, et al. Endovascular treatment with isobutyl cyanoacrylate in patients with arteriovenous malformation of the brain. Indications, results and complications. Acta Radiol Suppl 1986;369:621–2.

[87] Frizzel RT, Fisher WS. Cure, morbidity, and mortality associated with embolization of brain arteriovenous malformations: a review of 1246 patients in 32 series over a 35-year period. J Neurosurg 1995; 37:1031–40.