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Interventional Neuroradiology: An Overview of Intracranial Arteriovenous Malformations

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Abstract

Arteriovenous malformations (AVMs) are vascular deformities involving fistula formation of arterial to venous structures without an intervening capillary bed. Although uncommon in the general population, brain AVMs (bAVMs) have significant health risks if a rupture occurs. They are an important cause of intracerebral hemorrhage in young adults. This article aims to review the therapeutic options for bAVM, particularly the role of interventional neuroradiology. The Spetzler-Martin grading scale (SMG) is used to classify the bAVMs based on size, location, and type of venous drainage; in order to guide treatment. Available treatments include observation, microsurgical resection, endovascular embolization, stereotactic radiosurgery, or a combination of these treatments. Microsurgical resection is considered the first-line therapy for most low-grade bAVM since it has the highest rate of complete obliteration (over 90% according to multiple studies). However, it is the most invasive of the three interventions. Stereotactic radiosurgery (SRS), which uses radiation to induce occlusion of the affected vessels, is particularly useful for the treatment of deep AVMs in eloquent territories with associated high surgical risk. The rate of complete obliteration of AVMs by SRS is inversely proportional to AVM size, reaching up to 75% for low-grade AVMs (I, II) and 0 to 61% for grade V AVMs. Endovascular embolization is regarded as a coadjuvant treatment strategy rather than a standalone procedure. Even though it is capable of obliterating vessels immediately, its cure rate may be as low as 5%. Most SMG I or II bAVMs can benefit from a single therapeutic intervention, while grade III might need a multimodal treatment. Usually, grades IV and V are monitored closely without any intervention since the risks associated with the procedure outweigh the benefits.

Keywords: Arteriovenous Malformations; Brain; Interventional Radiology; Stereotactic Radiosurgery; Microsurgical Resection; Endovascular Embolization.

Abbreviations: AVMs: Arteriovenous Malformations, ICH: Intracranial Hemorrhage, bAVMs: Brain Arteriovenous Malformations, SMG: Spetzler-Martin Grade, CAE: Complete Angiographic Exclusion, SRS: Stereotactic Radiosurgery.

Introduction

Brain arteriovenous malformations (bAVMs) are anomalous vascular formations involving shunts between arteries and veins without an intervening capillary bed [1]. The arteriovenous shunt

results in multiple arterial pedicles convalescing into a vascular nidus or network in the cerebral parenchyma, creating early drainage into the venous system [2,3]. Direct arterial blood flows into venous structures and can disrupt the vessel walls causing life-threatening intracranial hemorrhage (ICH) or permanent neurological impairment [1,4]. Most bAVMs are sporadic and congenital, resulting from genetic mutations and aberrant vasculogenesis during embryological development [5]. However, recent findings suggest that Arteriovenous Malformations (AVMs) may also develop postnatally due to vascular regrowth or remodeling after cerebral vascular injury [5,6].

Currently, there are no clear estimates of the overall prevalence of bAVMs due to the condition's rarity and the existence of asymptomatic individuals [7]. Study data from population-based studies indicate that bAVM detection rates range from 0.89 to 1.34 cases per 100,000 person-years. Furthermore, prevalence estimates range from less than 0.02% to 0.2% [8]. According to some studies, at least 45% of patients with bAVMs are symptomatic, but asymptomatic cases may represent up to 88% of bAVM cases [4]. An estimated 25% of hemorrhagic strokes among adults under 50 are caused by bAVMs [4]. Bleeding rates for previously unruptured malformations are approximately 1% per year, and, once ruptured, the subsequent risk increases to 4.8% [5,9]. Ruptured AVMs have an average mortality rate of 10% and a morbidity rate of 20% to 30% [10]. The most significant risk factors for AVM hemorrhage include prior rupture, deep location, deep venous drainage, associated aneurysms, history of hypertension, older age, and pregnancy [1,5,9,11]. Studies have suggested that smaller AVMs may exhibit a greater risk of rupture than larger AVMs due to a higher artery pressure, while other studies indicate the opposite [9]. Additionally, 20- 29% of bAVMs are associated with aneurysms, increasing the overall bleeding risk [3,10].

AVMs are diagnosed most commonly in adults in their third decade of life, and the most common clinical manifestations include intracranial bleeding, headache, seizures, or progressive neurologic deficits [1,3]. However, many asymptomatic cases are detected incidentally during noninvasive brain imaging [2,3,12]. Despite the capability of CT, MRI, and angiography to identify these lesions, diagnosing cerebral AVMs could be challenging, as these anomalies represent a complex vascular pathology with different manifestations [1,5]. Current therapeutic modalities for bAVMs include microsurgical resection, stereotactic radiosurgery, endovascular embolization, and observation. Moreover, combinations of these treatments are sometimes required as AVMs are diverse lesions that may vary widely in location, size, and complexity [2,6,12]. Furthermore, uncertainty and controversy surround the management of unruptured bAVMs, since the risks of invasive therapies may outweigh the risk of spontaneous rupture [4,6]. The most commonly used classification method to select treatment is the Spitzer-Martin system. AVMs grades I/II usually respond well to surgical resection alone, grade III lesions are traditionally treated via a multimodal approach, and grades IV/V lesions are generally observed [13]. Therefore, selecting the most appropriate treatment will depend on the AVMs and the patient's characteristics [2]. In this review, we aim to provide a contemporary and comprehensive overview of the role of interventional neuroradiology as a therapeutic technique in the setting of bAVMs.

Microsurgical Resection

In treating AVMs with grades S-M I, II, and III, microsurgical resection is considered the most effective and safe treatment method, as it is associated with a low risk of complications and a low risk of mortality. To achieve favorable results, an individual choice must be made based on the patient's general health and the AVM's characteristics [14-19]. Surgery generally leads to complete obliteration in 94 to 95.9% of cases [16,18,20], making microsurgery a promising method for eliminating AVMs [14-17]. Conservative or interventional approaches are utilized for the treatment of AVMs. These managements were selected using the Spetzler-Martin scale, which consists of three classes of approaches. Class A comprises grades I and II, and microsurgical resection is advised. The multimodal approach is recommended for class B, consisting of bAVM grade III. The suggested approach for class C, which includes grades IV and V, is multimodal therapy or observation [14]. However, conservative treatment is associated with a higher risk of bleeding or rebleeding. Therefore, an interventional approach is preferred over observation for most class C AVMs [14,16,17].

When choosing a surgical approach, several characteristics must be considered, including whether the AVMs are located near the surface of the brain or easily accessible through open surgery. Other essential factors include the number and accessibility of arterial feeders, the number of drainage veins, their location (deep or shallow), and the density and compactness of the nest [4,14,19]. Essentially, microsurgery provides numerous advantages. First, this procedure results in high rates of complete angiographic exclusion (CAE), which could be as high as 90% for minor lesions. Second, as surgery has an immediate effect, its utility becomes evident when treating life-threatening hemorrhagic lesions. Finally, it allows tissue collection for subsequent genetic analysis. Some limitations of this therapeutic measure might include invasive procedures, operator-dependent, and higher mortality [4].

Stereotactic Radiosurgery

Stereotactic radiosurgery (SRS) is a form of radiation therapy consisting of multiple converging radiation beams, such as X-rays, gamma rays, or protons, delivered to a radiographically defined discrete treatment volume. As a result of the intersection of multiple radiation beams, the treatment volume receives a high therapeutic dose, while the surrounding normal brain tissue receives a relatively low dose [20]. SRS is employed to treat

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brain metastases and primary tumors, functional disorders, spinal and paraspinal injuries, and vascular pathologies, such as arteriovenous malformations AVMs [20,21]. The use of SRS is particularly beneficial in the treatment of deep AVMs within the eloquent territory. SRS shows a significant advantage over microsurgery and embolization since these malformations are generally associated with high surgical risk [18,22,23]. There is a very high risk of morbidity and mortality associated with arteriovenous malformations; however, with proper treatment, a good long-term prognosis can be achieved, resulting in low rates of morbidity and mortality as well as complete eradication [22,24].

Regarding the effects of SRS treatment on AVMs, it has been described that these are inversely proportional to the size and dose of the treatment, which suggests more significant benefits may be obtained for AVMs with a size ≤ 3-3.5 cm. Nevertheless, complete obliteration takes approximately one to three years after treatment, and healing is not always successful [18,25,26]. Furthermore, higher rates of complete obliteration can also be observed in patients with low-grade AVMs classified as Spetzler-Martin grade (SMG) I and II. At the same time, patients with AVMs classified as SMG grade III, IV, and V (high grades) have been associated with a lower percentage of complete obliteration [20,25]. Successful obliteration is determined by gender, size or morphology of the nidus, the pattern of venous drainage, AVM volume, marginal dose, AVM location, history of cardiovascular disease, and time since obliteration [4,22,23,25]. The treatment of SRS has also been described in conjunction with embolization therapy. However, there has been no significant difference between this and SRS treatment alone [26]. Finally, the use of magnetic resonance imaging (MRI) and arterial spin labeling (ASL) to follow up and determine the final diagnosis of complete obliteration after SRS is suggested [27].

Endovascular Embolization

Historically, endovascular embolization of brain AVMs has been primarily used as an adjuvant therapy before other interventions such as SRS or microsurgical resection to reduce the risks of complications [4,8,28]. However, there is evidence to support the use of embolization as an independent and definitive treatment for selected cases of bAVMs [8,28]. Currently, embolization is most commonly employed in the pre-surgical approach of AVMs [4,8]. In this context, embolization aims to reduce the size of medium-to-large AVMs, eliminate deep arterial pedicles, and target perforator supply and AVM-related aneurysms [1,4,8]. Furthermore, adjunctive embolization before SRS has been demonstrated to reduce the risk of obliteration and hemorrhage compared to non-embolized lesions undergoing radiosurgery. In addition, pre-radiological embolization is beneficial when applied to large AVMs [8,29].

As an independent therapy within an intent-to-cure setting, embolization may be considered in carefully selected patients [30,31]. There are several proposed indications for curative embolization of unruptured or ruptured AVMs, including small or medium-sized lesions, fewer feeding pedicles, compact nidus of the AVM, high-risk/surgically inaccessible lesions, and the incompatibility of other treatments [1,8,30,31]. Though AVM embolization is less invasive than other therapeutic techniques, it can cure only a minority of lesions on its own [4]. The cure rate for AVMs treated with embolization alone has been reported to be as low as 5%, which might be because many patients with angiographically cured AVMs remain at risk for ICH if undetected vessels continue to fill a partially embolized nidus [4,8]. Furthermore, AVM endovascular embolization has been associated with a complication rate of approximately 5% to 15% [8]. Most common complications include postprocedural hemorrhage, transient/persistent neurological deficits, and death [8,32,33]. There is little evidence supporting the use of endovascular embolization alone in the vast majority of AVMs, as it appears to be associated with a higher complication rate when compared to adjunctive embolization [8,13,33]. Nonetheless, with proper patient selection and a clear understanding of the purpose of embolization, the risks can be outweighed by the benefits. In order to establish the effectiveness of stand-alone endovascular treatment, more extensive randomized trials and prospective data are needed.

Conclusion

The treatment of brain arteriovenous malformations usually includes microsurgical resection, stereotactic radiosurgery, endovascular embolization, combination therapy, and/or observation. For AVMs grades SMG I-III, microsurgical resection is considered the most effective and safest treatment method and is associated with a low risk of complications and mortality. When choosing a surgical approach, several characteristics must be considered, including whether the AVMs are located near the surface of the brain or easily accessible through open surgery. Stereotactic radiosurgery (SRS) is particularly beneficial in the treatment of deep AVMs. SRS shows a significant advantage over microsurgery and embolization since these malformations are generally associated with high surgical risk. Conventionally, endovascular embolization of bAVMs has been established as an adjuvant therapy before other interventions. Currently, embolization is typically performed in the pre-surgical management of AVMs, mainly to reduce the size of medium-to-large AVMs. However, the cure rate for bAVMs treated with embolization alone has been reported to be as low as 5%. Furthermore, common complications include postprocedural hemorrhage, transient/persistent neurological deficits, and even death. Embolization alone appears to be associated with a higher complication rate when compared to adjunctive embolization. More extensive randomized trials and prospective data are needed to establish the effectiveness of stand-alone endovascular treatment.

Despite advancements in current treatments, there are still unmet needs for managing bAVMs. Most SMG I or II AVMs can benefit from a single therapeutic intervention, while grade III

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might require a multimodal approach. Grades IV and V are only monitored due to the high risks associated with the intervention compared to its benefits. Therefore, further research is necessary to refine these procedures to safely and effectively improve outcomes for patients with bAVMs. To improve outcomes for patients in the future, further studies are required to optimize the implementation of these procedures with the lowest rate of adverse effects, integrate them with medical and surgical treatment, and determine if these therapies are effective across various types of bAVMs to ensure that these procedures are effective.

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