Hemodynamics Associated With Intracerebral Arteriovenous Malformations: The Effects of Treatment Modalities

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The understanding of the physiology of cerebral arteriovenous malformations (AVMs) continues to expand. Knowledge of the hemodynamics of blood flow associated with AVMs is also progressing as imaging and treatment modalities advance. The authors present a comprehensive literature review that reveals the physical hemodynamics of AVMs, and the effect that various treatment modalities have on AVM hemodynamics and the surrounding cortex and vasculature. The authors discuss feeding arteries, flow through the nidus, venous outflow, and the relative effects of radiosurgical monotherapy, endovascular embolization alone, and combined microsurgical treatments. The hemodynamics associated with intracranial AVMs is complex and likely changes over time with changes in the physical morphology and angioarchitecture of the lesions. Hemodynamic change may be even more of a factor as it pertains to the vast array of single and multimodal treatment options available. An understanding of AVM hemodynamics associated with differing treatment modalities can affect treatment strategies and should be considered for optimal clinical outcomes.

KEY WORDS: AVM, Hemodynamics, Treatment effects

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Arteriovenous malformations (AVMs) have been described as cerebrovascular abnormalities that have fistulous connections of arteries to veins with no normal intervening capillary beds.[1-62] Geometrically, AVMs tend to be triangular with the base at the meninges and the apex located toward the ventricles.[9,10,28,29,58] AVMs are the most frequently detected symptomatic vascular malformation. They represent the cause of 2% of all strokes and 38% of all intracerebral hemorrhage in patients between 15 and 45 yr of age.[13] For AVMs that hemorrhage, the re-hemorrhage rate in the first year can be as high as 16%, with an associated 45% morbidity and 9% mortality.[63] Features that cause AVMs to rupture may be related to physical forces, specifically mechanical stress. Other features that can contribute to rupture may include intranidal aneurysms, elevated pressure in feeding vessels, and obstruction of venous outflow.[7,8,31,32,34,35,55] The generalized pathological formation of AVMs may be linked not only to flow-related factors but also to humoral and hormonal factors.[11,64] The hemodynamics of AVMs can be quite complex and may change in various ways, depending on specific treatment modalities.[12,31,42,56,59-62,65]

ABBREVIATIONS: AVM, arteriovenous malformation; **ENG,** endoglin; **EVOH,** ethylene vinyl alcohol copolymer; **MR,** magnetic resonance; **NBCA,** N-butyl cyanoacrylate; **SNP,** single nucleotide polymorphism; **TGF-β,** tumor growth factor beta; **VEGF,** vascular endothelial growth factor

EMBRYOLOGIC AND MOLECULAR BASES OF AVM PATHOPHYSIOLOGY

AVMs may have specific embryologic and molecular bases that influence their pathogenesis, hemodynamics, and changing morphology over time, with or without the application of different treatment modalities. Although a detailed review of the molecular and embryologic aspects of AVMs is outside the scope of this paper, a brief review may

TABLE 1. Animal Models for AVM Study[a]

Type of AVM	Author, Year	Animal Model	Characteristics	Application
Carotid jugular fistula	Scott et al, 1978[66] Spetzler et al, 1978[56] Morgan et al, 1989[67] Bederson et al, 1991[68] Hai et al, 2002[69]	Monkey Cat Rat Rat Rat	Different types of carotid jugular fistulas used to initiate hypoperfusion with or without draining vein, hypertension, fistula opening and closing that simulates the presence of and resection of an AVM	To evaluate hemodynamic, physiological, and pathological changes of AVM adjacent cortex, but not the AVM specifically; and to help explain AVM symptomatology and postoperative complications
Intracranial arteriovenous fistula	Numazawa et al, 2005[70]	Dog	Venous graft shunting blood from middle cerebral artery branch to superior sagittal sinus, with evaluation of the parenchyma with reduced flow mimicking that of AVM steal	To evaluate local perilesional hemodynamics rather than global hemispheric changes
Rete mirabile as AVM nidus	Chaloupka et al, 1994[71] Massoud et al, 1994[72] Qian et al, 1999[73]	Pig Pig Sheep	Inserting a needle to communicate the rete mirabile with the cavernous sinus; and establishing a carotid jugular fistula to drain blood from the rete mirabile in a retrograde fashion	To test and evaluate embolization material and treatment and radiosurgical treatment
Venous plexus as AVM nidus	Yassari et al, 2004[74]	Rat	Creating a carotid jugular fistula where the arterialized veins mimic an extracranial AVM	To study the molecular mechanisms of AVM development and the effect of radiosurgical doses
AVM-like lesions from implants	Pietila et al, 2000[75]	Dog	Implanting a pedicled muscular free flap onto the cortex with an arteriovenous bypass	To demonstrate the angiogenic contributions to AVM formation and progression
Xenograft AV fistula	Lawton et al, 2004[76]	Rat	Inserting an arterial graft from transgenic mice between the common carotid artery and the external jugular vein of nude rats	To evaluate the radiosurgical mechanism with the aim of developing new therapies
AVM tissue (implanted model)	Konya et al, 2005[77]	Rat	Transplanting human AVM tissue to the rat cornea	To evaluate AVM angiogenic and mechanistic properties in human specimens

AV, arteriovenous; AVM, arteriovenous malformation.
[a]Adapted from Xu et al, 2015.[78] Made available under Creative Commons 3.0. (https://creativecommons.org/licenses/by/3.0/).

prove useful in understanding the potential molecular underpinnings of changing AVM hemodynamics.

AVMs are thought to be congenital in nature because they lack intervening capillary beds. Kaplan et al[25] described AVMs as lesions with a congenital persistence of very primitive arteriovenous shunts that should have been replaced by normal intervening capillaries during the first 3 mo of embryogenesis. Multiple models have been used to investigate the embryologic, hemodynamic, and molecular underpinnings of AVMs. Cat, rat, monkey, dog, pig, and sheep studies have aided invaluably in our understanding of the hemodynamics and physiology of AVMs (Table 1).[56,66-78] Mouse models have been the primary method for creating AVM lesions by gene manipulation to enhance our understanding of the molecular biology of AVMs.

Several factors contributing to AVM pathology have been isolated, yet the exact mechanisms still bewilder researchers and physicians. Repression of vascular endothelial growth factor (VEGF), angiopoietin 1 and 2, and their receptor Tie2 result in AVM pathology through downstream effects on tumor growth factor beta (TGF-β) and vascular instability.[79] Moreover, mutation or deletion of integrin-β8 has an effect on the proper signaling pathway of TGF-β, which may cause AVMs.[80] The downregulation of endothelin-1 mRNA is also involved in the pathophysiology of AVMs through anomalous vascular remodeling and dysautoregulation of vessel injury.[49,81-84] Another molecular factor involved in AVM formation is endoglin (*ENG*), which has several roles in vascular physiology, including remodeling of capillary plexuses and proliferation of endothelial cells. Patients with type 1 hereditary hemorrhagic telangiectasia who have an *ENG* mutation also subsequently develop AVM pathology, providing further evidence for the role of *ENG* in AVM formation.[85] Furthermore, stromal cell-derived factor 1, a chemokine, is found in the AVM-affected vessels and causes an increase in the migration and deposition of endothelial cell progenitors in the involved vessels.[65] Three structural markers—smooth muscle α-actin, SM1 and SM2—which are normally present in 30-μm arteries, are also found in AVM veins, illustrating the thickened and fibrotic nature of the now-arterialized veins.[86,87] Several single nucleotide polymorphisms (SNPs) have

also been linked to the development of AVMs. One such variation is found in angiopoietin-like 4, a glycoprotein, which is involved in angiogenesis and vessel partitioning.[88] Four SNPs within VEGF-A are also thought to alter its factor-binding properties, causing an increase in its expression in AVMs.[89] Lastly, polymorphisms in interleukin-1β and activin-like kinase are also incriminated in AVM formation.[90,91]

The aforementioned angiogenic, molecular, and humoral factors have compelling physiological evidence that they may contribute to AVM formation. They may also alter AVM hemodynamics over time, particularly in response to the spectrum of available treatment modalities. Furthermore, as research persists in this area, the additional development of medical adjuncts (eg, VEGFR2, MMP-9 [matrix metallopeptidase 9], TNFα, β inhibitors) might create future viable strategies for managing altered hemodynamics and positively affect outcomes.[92]

FEEDING ARTERIES

The size and number of feeding arteries can have a tremendous impact on the local hemodynamics associated with AVMs.[35,40,41,93] Alterations in feeding arteries before complete obliteration or resection affect hemodynamics, size of the nidus, and hemorrhagic and nonhemorrhagic outcomes.[3,11,93-96] In attempting to elucidate a relationship between the radiographic and clinical presentation of AVMs, Norris et al[41] conducted a prospective blinded analysis of 31 patients and found hemodynamic parameters in patients who may have an increased risk of hemorrhage. In the analysis of arterial-phase cerebral angiography, an increased time to reach peak contrast density was associated with an increased risk of hemorrhage. In their cohort, increased time to peak contrast density in the arterial phase correlated with a higher rate of hemorrhage as the initial presentation. Evidence also shows that larger high-flow AVMs, often in low-pressure arteries, feed more. Spetzler et al[93] measured the inflow perfusion pressure of 24 AVMs in 24 patients intraoperatively; of these patients, 10 presented with hemorrhage and 14 presented with nonhemorrhagic neurological sequelae. The patients who presented with hemorrhage exhibited mean arterial feeding pressures that were 90% of systolic blood pressure, compared to 47% in those patients who did not present with hemorrhage. The authors also noted increased mean arterial feeding pressures in smaller AVMs. They concluded that this increased pressure may be the reason for the increased rupture rate seen in smaller AVMs.[41,56]

The parenchyma surrounding AVMs can exhibit gliosis, which is believed to be secondary to hypoperfusion, as an ancillary effect of high-flow shunting away from normal brain.[97] Honeycombing is also noted on T1- and T2-weighted magnetic resonance (MR) imaging as a result of high-velocity signal loss.[97-99] Phase-contrast MR angiography can be useful to completely evaluate the complex arterial feeders and early draining veins, but most lesions, especially complex ones, require digital subtraction angiography, which remains the gold standard for diagnostic evaluation.[97-99] Radiographic clues of AVM hemodynamics, such as perinidal gliosis as an indicator of high flow, may also aid in interventional risk analysis.[97-99] Partial interruption of one, but not all, feeding arteries may alter nidal perfusion pressure, potentially increasing the risk of hemorrhage.[93]

HEMODYNAMICS

Nidus Flow

A hypothesis regarding normal perfusion pressure breakthrough observed in AVMs was described in 1978.[56] The hypothesis, based on the experimental findings, was that arterioles associated with AVMs may be unable to constrict after prolonged dilation; essentially, they lose their autoregulatory capacity. The investigators noted that, upon AVM resection, arterial pressures would then break through the capillary bed resulting in increased edema and likely hemorrhage. Nearly 10 yr later, Hassler and Steinmetz[18] noted their results and reported findings incongruous with respect to the normal perfusion pressure breakthrough theory of AVMs. Hassler and Steinmetz[18] investigated local hemodynamics in 33 patients and used microvascular Doppler to measure flow velocity and vasomotor reactivity to CO_2 changes. They documented low intravascular pressure, high flow velocity, low peripheral stream resistance, and very poor vasomotor reactivity within the AVM feeders.[18,19] In other studies of AVMs, changes in feeding arteries suggest a return to normal intravascular pressure after microvascular resection of the AVMs. For these cases, remote arteries and branches of the former AVM feeders supplying the brain did not show any signs of impaired vasomotor reactivity following resection.[3,15,18,19] These findings are somewhat different with respect to the normal pressure perfusion breakthrough hypothesis. The prevailing understanding is, in essence, a crystallization and an evolution of the original description in that the surrounding perinidal parenchyma fundamentally has a lower autoregulatory range as a result of long-term hypoperfusion. As a result, blood pressures that would typically be in a standard range may in fact be outside this augmented autoregulatory spectrum.

A new understanding of flow through the AVM nidus was advanced by al-Rodhan et al[100] in 1993 with their theory of occlusive hyperemia as a major factor in hemodynamic sequelae of edema and hemorrhage after AVM resection. In their series of 293 patients with 295 AVMs, the authors identified 34 with postoperative deterioration; of these, 15 had residual AVMs and 19 had complete resection. Of the 19 cases they examined, 6 had edema alone and 13 had hemorrhage with associated edema. Obstruction of the venous system was found in 74% (n = 14). The authors expounded a very compelling conclusion, with supportive hemodynamic evidence from the literature, that postoperative hemorrhage or edema is due either to venous outflow obstruction of the adjacent parenchyma with resultant

passive hyperemia or stagnant arterial flow in former AVM feeders and worsening of hypoperfusion to any parenchyma with which the feeders may have been associated.[100] The authors also cited numerous prior investigations that suggest that although preexcision CO_2 reactivity in feeding arteries is perturbed,[18,66,101] postresection CO_2 reactivity likely returns to normal (ie, local autoregulation).[18,101-104]

Flow through the nidus can also be affected by the compartmental nature of cerebral AVMs. As originally described by Yaşargil,[105,106] AVMs can be monocompartmental with a compact nidus, 1 feeder, and 1 or more draining veins, or multicompartmental with several feeders and draining veins that can be either confluent or separated by functional or nonfunctional cerebrum.[35] A finding of multicompartmental AVMs may alter and even complicate treatment strategies. Thus, it may be useful to focus on higher flow pedicles, either at microsurgical resection or during adjunct endovascular embolization.[14]

Venous Outflow

Because intracerebral AVMs are frequently high flow in nature, they often cause a relative increase in cerebral blood volume.[52] The true nature of flow can be difficult to quantify, and rupture may permanently alter the hemodynamics of AVMs.[23] In a review of the hemodynamic properties of AVMs in 72 patients, Illies et al[23] noted that previous intracranial hemorrhage increased transit time by 2.4 s in an analysis using time-resolved 3-dimensional MR angiography. The increased perfusion and transit time can also be noted radiographically. In an analysis of AVM hemodynamics using continuous arterial spin labeling MR imaging, venous perfusion was found to be 34.6% greater than the nidal perfusion rate (of 15.7%) and the surrounding cortex perfusion rate (of 15.8%).[107] The increased venous perfusion and relative increase in blood volume can have various effects. Effect on venous outflow may influence cerebrospinal fluid drainage and subsequently increase intracranial pressure as a result. Chimowitz et al[108] described this phenomenon in 6 patients with unruptured intracranial AVMs. Their cohort comprised patients who were all relatively young; had high-flow lesions; and presented with headache, visual symptoms, and papilledema. All the AVMs appeared radiographically to drain in some fashion to the superior sagittal sinus.

The theory of occlusive hyperemia set forth in 1993 by al-Rodhan et al[100] offers convincing evidence from the literature and from their analysis of their own series on the contribution of obstruction of venous drainage. In 1980 and 1987, respectively, Nornes and Grip[40] and Barnett et al[101] reported modifications of venous outflow after resection of AVMs that may have converted veins from high-flow to low-flow conduits. About the same time, Vinuela et al[109] in 1985 and Yaşargil[106] in 1987 reported on the pre-existing narrowing of the outflow AVM veins or even the frank occlusion of the veins in AVMs.[40,105,109] In his 1982 series of 178 AVMs, Albert[110] noted the correlation of a small number of draining veins and increasing hemorrhage. He proposed that the higher the number of draining veins in an AVM, the less likely it is to bleed. In 1990, Miyasaka et al[111] reported on their observations with long and tortuous feeders that may predispose those feeders to retrograde thrombosis. As early as 1968, Fry[112] evaluated flow-related changes in venous endothelium associated with higher-flow AVMs. He noted that pressure and shearing stress affect endothelial cytoplasmic swelling, cell deformation, cell disintegration, and subsequent erosion, all of which contribute to local thrombosis. Against this backdrop, al-Rodhan et al[100] postulated that such risk factors could contribute to the development of occlusive hyperemia and reinforced this theory with laboratory data. Later, laboratory data support hemodynamically associated endovascular changes in the endothelium associated with AVMs and specifically implicate the function of VEGF[113] and Notch4 receptors.[114]

Preservation of venous outflow, prior to complete resection, has been seen as a crucial component in microsurgical management strategy.[14] Loss of venous outflow capability can have detrimental hemodynamic effects on intranidal resistance and perfusion pressure, potentially resulting in hemorrhage.[14,34,35,56,59,93] It is important to take this into consideration, particularly with microsurgical and endovascular treatments. However, some clinical anomalies potentially challenge the notion of venous outflow sparing. Pereira et al[45] challenged this notion with endovascular transvenous approaches to AVMs. Kessler et al[115] also reported success with transvenous embolization of AVMs. They used this approach in select AVMs, particularly those with a small nidus and a single draining vein. Although their report is quite compelling with respect to the current treatment paradigm and understanding of hemodynamics, larger series and hemodynamic validation are needed to codify their position.

Physics of Flow

The fluid dynamics associated with intracerebral AVMs has not been as extensively studied as other areas of AVM care and management. Lv et al[116] recently proposed a theoretical construct of intracerebral AVM flow based on Darcy's law and Maag's formula using n-butyl cyanoacrylate (NBCA) and ethylene vinyl alcohol copolymer (EVOH). According to Darcy's law, the instantaneous blood flow rate through an AVM is directly proportional to the pressure drop between 2 places within the AVM and indirectly proportional to the distance between them. Lv et al[116] used Maag's formula to explain the nidal diffusion pattern, as it relates to embolic materials (EVOH, NBCA), noting the filling radius of the embolic material will be inversely proportional to the viscosity of the particular embolic material. Intuitively and mathematically, the greater the pressure gradient through the AVM, the greater the discharge rate. The discharge rate of blood can vary in different AVMs or even within the same AVM for different directions of flow.[116] The physical and mathematical parameters related to hemodynamics can play a prominent role in disease presentation and treatment, eventually affecting clinical outcomes.[35,116,117] Higher-flow lesions are likely to be larger and

have perinidal gliosis.[97-99] Smaller lesions may exhibit greater perfusion pressure to the nidus, potentially increasing the risk for hemorrhage.[93] The physical characteristics that affect hemodynamics can potentially affect the type of embolic material used based on flow or possibly even technique (eg, 5% dextrose push, use of endovascular balloon, or adjunct transvenous approaches).

TREATMENT EFFECTS ON FLOW

Endovascular

Endovascular techniques have been used in multiple forms for treating AVMs, as either solitary obliterative treatment or an adjunct to microsurgery or radiosurgery. In looking purely at the overall efficacy for the treatment of intracerebral AVMs, we find that endovascular monotherapy is associated with a per patient and per session efficacy (obliteration) rate of 32.7% and 18.4%, respectively, and with a morbidity rate of 4.1% for patient-related events and 2.3% for procedure-related events.[118] After reviewing the cases of 49 AVM patients who were treated with endovascular-only therapy, Bradac et al[118] recommended endovascular-only treatment for specific clinical situations, such as preoperative embolization, as a curative measure for small AVMs with a limited number of feeders, in patients with comorbidities that preclude surgical treatment, and for palliation only in higher grades. The recommendations are based, in part, on the high recanalization and hemorrhage rates and on the lower clinical efficacy of microsurgical resection or radiosurgery alone. However, other authors propose more aggressive use of endovascular-only treatment of cerebral AVMs.[12,24,45]

The risk of hemorrhage continues to be a concern in endovascular monotherapy. In their study of 408 patients with AVMs treated endovascularly, Baharvahdat et al[94] noted an 11% hemorrhagic complication rate associated with treatment. Of the hemorrhagic complications, 48% were associated with periprocedural arterial perforation. The hemorrhagic complications that were not associated with arterial perforation were commonly intraparenchymal. Baharvahdat et al[94] noted that patients with parenchymal hemorrhages had more neurological deficits and worse prognoses than patients in the arterial-rupture group. The rate of premature venous occlusion was the only independent predictor of hemorrhage in the nonperforation cohort. They also noted a venous occlusion rate that was related to the overall volume of obliterative agent.[94]

It would seem that venous occlusion and disruption of outflow, before arterial obliteration, contribute to increases in hemorrhage, which is a well-understood microsurgical tenet.[28,29,32,94] However, others challenge the transvenous notion. Pereira et al[45] reported successful transvenous embolization and cure of a ruptured AVM, challenging this long-held microsurgical tenet. To date, no clear clinical paradigm exists for the hemodynamics associated with endovascular-only treatment of AVMs.[116] Theoretical mathematical models, based on the movement of endovascular obliterative agents through AVMs, provide some guidance.[12,35,37,38,116]

In 2014, Kaspera et al[26] used transcranial color Doppler to assess for flow within AVMs after endovascular embolization. They built on the 1986 pivotal work by Lindegaard et al,[119] who initially used transcranial Doppler to quantify high-flow velocities within AVM feeding arteries and associated lower perfusion pressures in the perilesional cortex, believed to be responsible for steal phenomenon. Kaspera et al[26] observed decreased flow in embolized arterial feeders; however, this decreased flow did not correlate with the extent of AVM volume reduction after a single embolization session, which they attributed to redistribution of AVM blood flow through newly recruited feeding arteries. Using 4-dimensional MR imaging and spin-labeled MR angiography, Ansari et al[117] evaluated AVM flow in 2013 in a series of 20 patients, 4 of whom had undergone staged Onyx embolization. Their evaluation noted that Spetzler-Martin high-grade AVMs tended to have increased venous outflow velocities, rather than increased arterial velocities. The flow in their post-Onyx embolization cohort showed successively more compact AVMs with redistribution within the feeding arteries. In 2015, Alaraj et al[120] used quantitative MR angiography to assess flow before and after AVM embolization with NBCA. They noted that the mean flow decreased 29% after a single session and 75% after the last session. The predictors of decreased flow after AVM embolization on both multivariate and univariate analysis were the total number of pedicles embolized and the total number of intranidal fistulas occluded. Noteworthy in their analysis was that the drop in flow per session did not correlate with the number of pedicles or intranidal fistulas occluded in that individual session. They therefore concluded that this finding suggested the redistribution of flow through the remaining compartments in patients with partial embolization. This finding seems to bolster the similar findings of Kaspera et al.[26] The observations and quantifications of postembolization AVM flow by Alaraj et al[120] essentially concluded that the total number of pedicles and not the number of pedicles per embolization session is a more accurate predictor of decreasing AVM flow.

Radiosurgery

Radiosurgery has been implemented in AVM treatment as monotherapy or as part of dual therapy. Radiosurgery has made it possible to limit microsurgical resection in some instances. However, this treatment does carry the risk of injury to adjacent normal cerebral parenchyma, in addition to a persistent hemorrhage risk until complete obliteration is obtained.[121-123] Complete obliteration times in radiosurgical patients can range from 15 to 30 mo.[96,124] Although the possibility exists of an increased risk of hemorrhage (11%-16%) in the first 6 mo of radiosurgical treatment,[96,124] radiosurgery can result in an angiographic cure in select AVMs[11,96,118] The optimal lesion size for radiosurgical treatment should be less than 10 mL of total volume.[96,121,122] The overall rate of cure with radiosurgery

TABLE 2. AVM Hemodynamic Changes With Treatment[a]

Treatment Modality	Feeding Arteries				Draining Veins	
	Morphology	Pressure	Velocity	CO_2 Reactivity	Morphology	Pressure
Microsurgery	Pre—dilated	Pre—increased	Pre—increased	Pre—impaired	Pre—variable (dilated, stenotic, thrombotic)	Pre—increased
	Post—thrombosed	Post—normal	Post—decreased	Post—normal	Post—stenotic, thrombotic	Post—decreased
Endovascular embolization	Pre—dilated Post—thrombosed	Pre—increased Post—decreased	Pre—mean flow increased Post—mean flow decreased	NA	Pre—variable Post—variable	Pre—increased Post—decreased
Radiosurgery	Pre—dilated Post—partially thrombosed	Pre—increased Post—partially decreased over time	Pre—increased Post—decreases over time	NA	Pre—variable Post—stenotic, thrombotic	Pre—increased Post—decreased, variable

NA = not applicable; Pre = preoperative; Post = postoperative.
[a]Data from Alaraj et al,[120] al-Rodhan et al,[100] Ansari et al,[117] Kojima et al,[113] and Wowra et al.[60]

in lesions less than 2.5 cm in diameter is generally quoted as 75% to 80%, and it decreases with increasing AVM size.[96,124] Lesions greater than 2.5 cm can have a 50% decrease in cure rate compared with that of lesions less than 2.5 cm.[96,124]

From a hemodynamic perspective, Gamma Knife (Leksell; Elekta AB, Stockholm, Sweden) radiosurgical obliteration of AVMs relies on the occlusion of feeding arteries and decreases in the size of the nidus.[96,121,122,124,125] Colloquial theories propose that adding digital subtraction angiography to MR imaging for radiosurgical planning may improve obliteration rates. This theory is underpinned by the idea that obliteration can be improved by improved visualization of feeding arteries, a relative decrease in the planning area with improved precision, and the ability to induce higher doses.[125] This theory has yet to be actualized in a recent cohort of 46 patients.[125] This finding runs somewhat counter to the current understanding of AVM hemodynamics, in which complete occlusion of the feeding arteries should result in radiographic cure of an AVM.[35,121,122,124,125]

Additional physiological, humoral, and anatomical factors also potentially influence the incomplete obliteration observed in radiosurgically treated AVMs.[35,105,125,126] The general understanding is that radiosurgically treated AVMs have perfusion to the nidus impaired on at least 2 levels.[125] Fiehler et al[127] described both territorial and microvascular perfusion impairment as part of the hemodynamics of AVMs. Using spin-labeling MR imaging, they identified a decrease in perfusion for AVMs of >20% from baseline in the immediate and adjacent area of the brain. The proposed decrease in perfusion was due to low flow in arteries and arterioles.[127] In trying to determine the hemodynamic effects of radiosurgery on AVMs, Guo et al[128] noted initial high transnidal flow and perinidal perfusion disturbances in the early stages after radiosurgical treatment. In the 19 patients they studied, they documented decreasing nidus size, from a complete to a partial reduction and perilesional radiation-induced edema. They also noted hemodynamic decreases in cerebral blood flow and cerebral blood volume ratios and increases in perilesional mean transit times. Of note, they determined a local deterioration in perinidal perfusion with respect to the contralateral hemisphere. Although such studies offer some clue as to the hemodynamics associated with radiosurgical treatment of AVMs, they do not fully elucidate the underlying factors that result in reduction but not cure of AVMs or the persistence or even worsening of nonhemorrhagic sequelae.

Microsurgery

Even in the face of rapidly progressing technological advances in radiosurgery and endovascular embolization, microsurgical treatment maintains a critical role in the complete and comprehensive treatment of cerebral AVMs. Microsurgical treatment continues to provide the only definitive and complete cure for AVMs.[38,40,41,58,93,118] The hemodynamic changes after microsurgical resection tend to be immediate and permanent. In reviewing the clinical efficacy of obliteration in the microsurgical treatment of AVMs, Bradac et al[118] reported surgical cure rates ranging from 81.4% to 100%, with a morbidity and mortality rate ranging from 1.2% to 21%. In 2573 microsurgically treated AVMs, they found a total cure rate of 96% and a morbidity/mortality rate of 7.3%. In comparison to an endovascular series of 3836 cases (22.1% cure, 7.1% morbidity/mortality) and a radiosurgical series of 6016 cases (67.4% cure, 6.8% morbidity/mortality), microsurgical treatment of AVMs appeared to be superior. Bradac et al[118] found that lower rates of cure and higher rates of morbidity and mortality were observed primarily in patients with Spetzler-Martin grades IV-V AVMs. The utility of microsurgical resection is the immediate elimination of abnormal feeding vessels, the simplification of hemodynamics

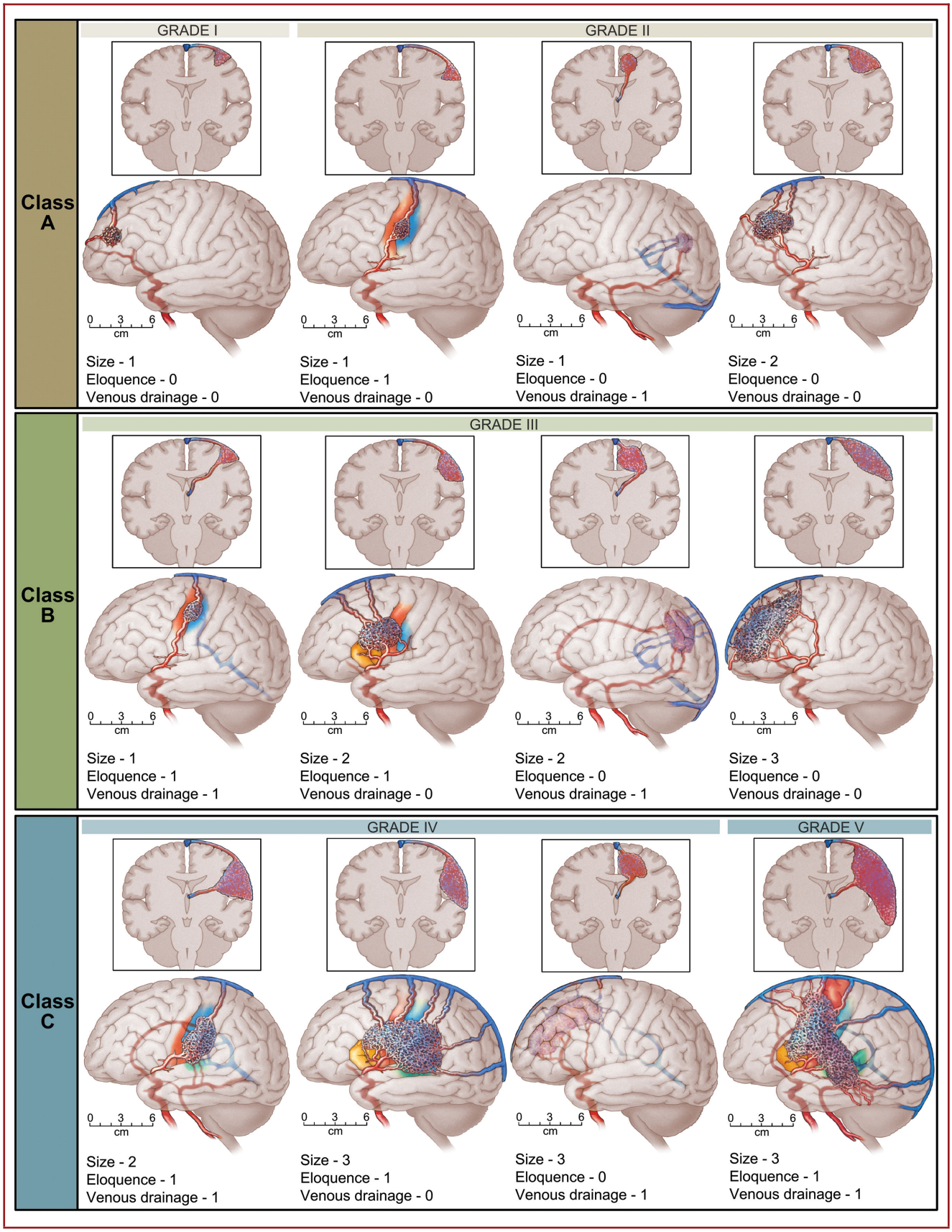

FIGURE. *Cerebral AVMs are classified as class A, B, or C in the Spetzler-Ponce system. This system combines the Spetzler-Martin grades I-V for AVMs. In the Spetzler-Ponce system, Spetzler-Martin grades I and II compose class A, grade III is equivalent to class B, and grades IV and V compose class C. The Spetzler-Martin grading system assigns grades based on the total scores given for the size of the AVM (1 = small, < 3 cm; 2 = medium, 3–6 cm; and 3 = large, > 6 cm); the eloquence of adjacent brain (0 = noneloquent, 1 = eloquent); and venous drainage (0 = superficial only, 1 = drainage to the deep cerebral veins). Reprinted from Spetzler and Ponce[129] with permission from* Journal of Neurosurgery.

with complete resection, and the possible return to favorable cerebral hemodynamics.[18] Depending on microsurgical resection technique and AVM characteristics, the postresection hemodynamics can vary slightly (Table 2).[60,100,113,117,120] In evaluating postmicrosurgical resection of AVMs in 1993, al-Rodhan et al[100] noted that feeding artery pressure and CO_2 reactivity return to normal after resection, with a decrease in feeding artery velocity. The elevated draining venous pressure may also be decreased after resection and is dependent on multiple architectural factors, especially the number of draining veins.

DISCUSSION

The hemodynamics associated with intracranial AVMs is complex and changes over time as the physical morphology changes, particularly with differing treatment modalities. Understanding the hemodynamics associated with each treatment should play a prominent role in treatment management strategies. Current data and a broad review of the literature do not explicitly purport a global advantage of one modality of treatment over another. However, understanding the impact of any one treatment on hemodynamics may prevent morbidity and ultimately improve outcomes. In light of the understanding that small AVMs may have a higher risk of rupture and any partial treatment may also increase the rupture risk, a treatment algorithm should include the following considerations,[36,118] which have been outlined in part in the Spetzler-Ponce revised 3-tier grading scale for AVMs[129]:

1. Microsurgical resection for Spetzler-Martin grades I-II, Spetzler-Ponce class A (Figure), and superficial grade III/class B.
2. Endovascular treatment mainly as a preoperative adjunct to microsurgical resection, and a possible cure for low-grade AVMs in high-risk patients with multiple comorbidities.
3. Stereotactic radiosurgery with or without multimodality treatment for deep-seated Spetzler-Martin grade III or Spetzler-Ponce class B AVMs.
4. Observation for unruptured Spetzler-Martin grades IV-V or Spetzler-Ponce class C AVMs when intervention is a greater risk than the natural course. Exceptions include recurrent hemorrhages, progressive neurological deficits, steal-related symptoms, and AVM-related aneurysms.

The Spetzler-Ponce modification of the Spetzler-Martin AVM grading system serves as an even more streamlined adjunct surgical decision-making tool based on the relative grade of the AVM and the potential treatment strategies.[129] In 672 published articles that have referenced the Spetzler-Martin 5-tier classification system, similarity was found in the routine pairing of grades I and II and in the routine pairing of grades IV and V when the relative risk of surgical treatment was similar, whereas variability was noted in the grade III AVMs. As a result of the similar results of the pooled data, treatment options should take into consideration the revised 3-tier classification.

CONCLUSION

The hemodynamics associated with intracranial AVMs is complex and changes over time with changes in the physical morphology of the lesions, particularly with different treatment modalities. An understanding of AVM hemodynamics associated with the different treatment modalities can affect treatment strategies and should be considered for optimal clinical outcomes.

Disclosure

The authors have no personal, financial, or institutional interest in any of the drugs, materials, or devices described in this article.

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