A Supplementary Grading Scale for Selecting Patients With Brain Arteriovenous Malformations for Surgery

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BACKGROUND: Patient age, hemorrhagic presentation, nidal diffuseness, and deep perforating artery supply are important factors when selecting patients with brain arteriovenous malformations (AVMs) for surgery.

OBJECTIVE: We hypothesized that these factors outside of the Spetzler-Martin grading system could be combined into a simple, supplementary grading system that would accurately predict neurologic outcome and refine patient selection.

METHODS: A consecutive, single-surgeon series of 300 patients with AVMs treated microsurgically was analyzed in terms of change between preoperative and final postoperative modified Rankin Scale scores. Three different multivariable logistic models (full, Spetzler-Martin, and supplementary models) were constructed to test the association of combined predictor variables with the change in modified Rankin Scale score. A simplified supplementary grading system was developed from the data with points assigned according to each variable and added together for a supplementary AVM grade.

RESULTS: Predictive accuracy was highest for the full multivariable model (receiver operating characteristic curve area, 0.78), followed by the supplementary model (0.73), and least for the Spetzler-Martin model (0.66). Predictive accuracy of the simplified supplementary grade was significantly better than that of the Spetzler-Martin grade ($P = .042$), with receiver operating characteristic curve areas of 0.73 and 0.65, respectively.

CONCLUSION: This new AVM grading system supplements rather than replaces the well-established Spetzler-Martin grading system and is a better predictor of neurologic outcomes after AVM surgery. The supplementary grading scale has high predictive accuracy on its own and stratifies surgical risk more evenly. The supplementary grading system is easily applicable at the bedside, where it is intended to improve preoperative risk prediction and patient selection for surgery.

KEY WORDS: Arteriovenous malformation, Microsurgery, Patient selection, Prediction models, Spetzler-Martin grading system, Supplementary grading system

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Judicious patient selection is essential for avoiding surgical complications and poor neurologic outcomes with microsurgical resection of brain arteriovenous malformations (AVMs). The combination of nidus size, deep venous drainage, and eloquence of adjacent brain that comprises the Spetzler-Martin grading scale provides a preliminary assessment of surgical risks,[1] with low-grade AVMs (grades I–III) having acceptably low morbidity rates and high-grade AVMs (grades IV–V) having unacceptably high morbidity and mortality rates. As helpful as this simple grading scale is, it is crude at best, and the recommendation to operate may be strengthened by considering additional risk factors.

ABBREVIATIONS: AVM, arteriovenous malformation; **CI**, confidence interval; **MRI**, magnetic resonance imaging; **mRS**, modified Rankin Scale; **OR**, odds ratio; **ROC**, receiver operating characteristic

Some of these factors are embedded within the Spetzler-Martin grading scale, like grade III subtype and functional eloquence. The dividing line between operability and nonoperability does not run cleanly between grades III and IV, but rather between subtypes of grade III. Our experience has demonstrated that medium-sized AVMs (3–6 cm in diameter) in eloquent locations have morbidity rates that are higher than expected for grade III lesions (more like grade IV AVMs), whereas small-sized AVMs (<3 cm in diameter) with deep venous drainage in eloquent locations have morbidity rates that are lower than expected (more like grade II AVMs).[2] Similarly, structural anatomy defined by the Spetzler-Martin system as eloquent does not always equate with functional anatomy, because brain inhabited by an AVM often relocates functions that lie too close to the nidus. We have found that preoperative functional magnetic resonance imaging (MRI) more precisely localizes neurologic function and allows us to individualize a patient's eloquence.[3]

Other factors important to patient selection that are not part of the Spetzler-Martin grading scale include patient presentation, age, deep perforating artery supply, and diffuseness. Presentation with hemorrhage not only indicates AVMs with high risk of rehemorrhage[4-6] but also facilitates surgery.[7] Hematomas help separate AVMs from adjacent brain; evacuation of hematoma creates a working space around the AVM that can minimize transgression of normal brain or provides access to a deep nidus that might otherwise have been unreachable; and hemorrhage can obliterate some of the AVM's arterial supply to reduce its flow during resection. AVM hemorrhage and microsurgery can injure brain tissue, but young age and plasticity can enhance a patient's ability to recover neurologic function.[8] Compact AVMs with tightly woven arteries and veins often have distinct borders that separate cleanly from the adjacent brain, whereas diffuse AVMs with ragged borders and intermixed brain force the neurosurgeon to establish dissection planes that can extend into normal brain.[9] Deep perforating arteries are thin, fragile, and difficult to occlude with cautery. Bleeding during surgery can escape into deep white matter tracts and cause significant deficits. All of these factors, hemorrhagic presentation, young age, compactness, and absence of deep perforator supply have been identified as predictors of good outcome after microsurgical resection.[7,9]

We hypothesized that these factors outside the Spetzler-Martin grading system could be combined into a supplementary grading system that would accurately predict neurologic outcome. We analyzed a consecutive surgical series of 300 patients to compare the predictive accuracy using the Spetzler-Martin scale and a new supplementary scale. We propose that this simple supplementary grading system can be used to improve and refine patient selection for AVM surgery.

PATIENTS AND METHODS

Study Population

The study was approved by the University of California, San Francisco, Committee on Human Research and conducted in compliance with Health Insurance Portability and Accountability Act regulations. During an 11-year period, 392 patients underwent microsurgical resection of their AVMs by a single neurosurgeon (M.T.L.). Since 2000, all patients with brain AVMs evaluated or treated at University of California, San Francisco, were enrolled prospectively in the institution's brain AVM registry. The study sample consisted of patients with AVMs treated with microsurgical resection from 2000 through 2007, of which 300 had complete demographic, anatomic, and clinical data.

Study Variables

Patient demographics included age (decade), sex, and race/ethnicity. Nidus size (diameter in cm), venous drainage (superficial, deep, or both), and eloquence were determined from preoperative angiograms, computed tomographic scans, and MRI scans for each AVM, according to the Spetzler-Martin grading system. Presence of deep perforating arterial feeders was also determined from preoperative angiograms and included lateral lenticulostriate arteries from the M1 segment of the middle cerebral artery, medial lenticulostriates from the A1 segment of the anterior cerebral artery, anterior and posterior choroidal arteries, thalamoperforators from the posterior communicating artery and P1 segment of the posterior cerebral artery, and brainstem perforators from the basilar trunk and vertebral arteries. Compact or diffuse AVM morphology was determined from preoperative angiograms, with computed tomographic and MRI scans used to identify intervening brain parenchyma within the nidus. Hemorrhagic presentation was defined as radiographic evidence of hemorrhage on computed tomography or MRI, regardless of signs or symptoms.

The modified Rankin Scale (mRS) was used to grade outcomes.[10] A nurse clinician, under the supervision of a neurologist, performed mRS assessments at presentation, preoperatively, 3 months postoperatively, and up to 2 years postoperatively. Follow-up information was obtained during routine clinic visits or telephone interviews. Outcomes were analyzed in terms of change between preoperative and final postoperative mRS scores (mRS final – mRS preoperative). A final mRS score of 0 to 2 was considered a good outcome, and a final mRS score of more than 2 was considered a poor outcome. Improvement was defined as a change in mRS score of less than or equal to 0 (improved or unchanged), and deterioration was defined as a change in mRS score of greater than 0 (worse or dead).[7]

Statistical Analysis

Data were analyzed using Intercooled Stata, version 9 (Stata Corp, College Station, TX). Descriptive statistics included t tests and χ^2 tests for comparison between the change in mRS score and continuous and dichotomous variables, respectively. Univariable logistic regression analysis tested the association of each predictor with the change in mRS score, dichotomized into deterioration (mRS change of 1–6) vs no change or improvement (mRS change ≤0). Three different multivariable logistic models were constructed to test the association of combined predictor variables with the change in mRS score:

Full Model

$$\text{Logit (mRS change)} = \beta_0 + \beta_1(\text{unruptured presentation}) + \beta_2(\text{age decade}) + \beta_3(\text{eloquent location}) + \beta_4(\text{size}) + \beta_5(\text{diffuse}) + \beta_6(\text{deep venous drainage}) + \beta_7(\text{deep perforating artery}) + \beta_8(\text{logtime})$$

Spetzler-Martin Score Model

$$\text{Logit (mRS change)} = \beta_0 + \beta_1(\text{eloquent location}) + \beta_2(\text{size}) + \beta_3(\text{deep venous drainage}) + \beta_4(\text{logtime})$$

Supplementary Score Model

$$\text{Logit (mRS change)} = \beta_0 + \beta_1(\text{unruptured presentation}) + \beta_2(\text{age decade}) + \beta_3(\text{diffuse}) + \beta_4(\text{deep perforating artery}) + \beta_5(\text{logtime})$$

The full model included all prespecified predictor variables. The Spetzler-Martin score model included the components of this grading system.[1] The supplementary score model included nonhemorrhagic presentation, age, diffuseness, and deep perforating artery supply. All multivariable models included adjustment for the duration of follow-up (log transformed time), which influenced final mRS assessments. Statistical significance was set at $P < .05$.

Predictive accuracy is the ability of a grading system to correctly classify patients into those who will be worse after surgery and those who will not. Receiver operating characteristic (ROC) analyses were performed after each multivariable logistic regression model, and the areas under the ROC curves of the 3 models were compared for accuracy in predicting change in mRS score. An area under the ROC curve of 1.0 indicates perfect discrimination, whereas an area of 0.5 indicates no discrimination. Generally, an area under the ROC curve of 0.70 or more is considered a clinically useful predictive model.[11]

Supplementary AVM Grading System

A point scoring system was developed from the data that used the β coefficients from the multivariable logistic regression models to weight the clinical and AVM characteristic values for each patient. These points were added together to obtain a total point score for each patient (Table 1). A simplified supplementary grading system was developed from the data, which included significant clinical and AVM characteristics not already expressed in the Spetzler-Martin scoring system. In a manner analogous to the Spetzler-Martin scoring system, points were assigned according to these variables and added together for a supplementary AVM grade (Table 1).

The total point score, supplementary grade score, and Spetzler-Martin grade score were then analyzed as predictor variables in separate logistic regression models, adjusting again for the duration of follow-up, and ROC analyses were repeated. Areas under the ROC curves were tested for equality using a χ^2 test.

Because we used all of the data to build our prediction models, which could result in overly optimistic predictions, we performed a 10-fold cross-validation.[12] In this approach, the dataset is randomly split into 10 groups; the model is then constructed on the first 9 groups and applied to the remaining group. The model building and validation process is repeated 10 times with each sample used only once as the validation set, ie, no patient is used both to develop and test the model. The area under the ROC curve is then estimated using data from the 10 validation sets.

RESULTS

Patient Demographics and AVM Characteristics

Patient demographics and AVM characteristics are summarized in Table 2. A total of 194 patients (65%) had embolization, radiosurgery, or both, before undergoing microsurgical resection.

Good outcomes after AVM resection were observed in 239 of the 300 patients (80%, mRS scores 0–2) (Fig. 1). On the basis of changes in mRS score, 227 patients (76%) were unchanged or improved, 55 patients (18%) were worse, and 18 patients (6%) died. Of the patients who were worse after treatment, the largest groups were those presenting with preoperative mRS scores of 0 (35

TABLE 1. Point Scoring System According to Variables Included in the Full Model, Spetzler-Martin Grading Scale, and Supplementary Grading Scale[a]

Variable	Point Score, Full Model		Spetzler-Martin Grading Scale		Supplementary Grading Scale	
	Definition	Weighting[b]	Definition	Points	Definition	Points
AVM size	Diameter, cm	×1	<3 cm	1		
			3–6 cm	2		
			>6 cm	3		
Deep venous drainage	No	0	No	0		
	Yes	3	Yes	1		
Eloquence	No	0	No	0		
	Yes	2	Yes	1		
Age	Decades	×1			<20 y	1
					20–40 y	2
					>40 y	3
Unruptured presentation	No	0			No	0
	Yes	4			Yes	1
Diffuse	No	0			No	0
	Yes	2			Yes	1
Perforating artery supply	No	0				
	Yes	0				
Grade		Total		Total (1–5)		Total (1–5)

[a] AVM, arteriovenous malformation.
[b] Weighting ×1 for continuous variables = actual value × 1.

TABLE 2. Patient Outcomes After Resection of Arteriovenous Malformations[a]

Variable	mRS Outcome				P Value[b]
	Improved, Unchanged		Worse, Dead		
	No.	%	No.	%	
Total patients	227	76	73	24	
Age, y	35.9 ± 16.9		45.3 ± 14.8		<.001
Sex					.081
Female	123	54	31	42	
Male	104	46	42	58	
Unruptured presentation					.005
No	121	53	25	34	
Yes	106	47	48	66	
AVM size, cm	2.4 ± 1.3		3.0 ± 1.4		.001
Venous drainage					.084
Superficial only	135	59	35	48	
Any deep	92	41	38	52	
Eloquence					.057
Noneloquent	113	50	27	37	
Eloquent	114	50	46	63	
Diffuse					.014
No	205	90	58	79	
Yes	22	10	15	21	
Deep perforator supply					.614
No	187	82	62	85	
Yes	40	18	11	15	
mRS score, initial					<.001
0	50	22	35	48	
1	51	22	14	19	
2	25	11	8	11	
3	46	20	9	12	
4	32	14	1	1	
5	23	10	6	8	
mRS score, final					<.001
0	98	43	0	0	
1	57	25	27	37	
2	44	19	13	18	
3	18	8	7	10	
4	9	4	7	10	
5	1	0	1	1	
6	0	0	18	25	
Follow-up duration, y	1.5 ± 1.3		1.1 ± 1.2		.022

[a] mRS, modified Rankin Scale; AVM, arteriovenous malformation.
[b] *t* test for continuous variables (presented as mean ± standard deviation) and χ^2 for categorical variables.

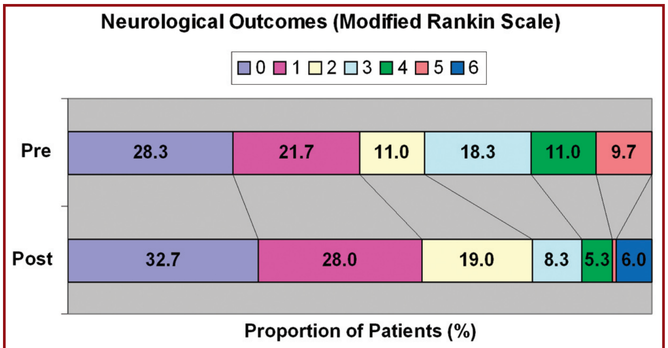


FIGURE 1. *Neurological outcomes. Graph showing pre- and postoperative modified Rankin Scale scores.*

patients, 48%) or 1 (14 patients, 19%). Six of the patients who died presented in coma (preoperative mRS score 5, 8%) and failed to improve with aggressive management.

Patients who did worse after treatment were older and male, and they had a greater frequency of unruptured presentation compared with patients who improved or remained unchanged (Table 2). In addition, patients who did worse had AVMs that were larger, diffuse, in eloquent location, and with deep venous drainage. There was no difference in the proportion of patients with deep perforating artery supply ($P = .614$).

Logistic Regression Analysis

Univariable logistic regression analysis identified age ($P < .001$), AVM size ($P = .001$), unruptured presentation ($P = .005$), and diffuse nidus ($P = .016$) as significant predictors of worsened mRS score (Table 3). Eloquence ($P = .058$) and deep venous drainage ($P = .085$) were borderline significant, whereas deep perforating artery supply was not associated with worsened mRS score ($P = .614$).

Multivariable logistic regression analysis using the full model containing all variables identified unruptured presentation (odds ratio [OR], 2.7), age (OR, 1.4), and deep venous drainage (OR, 2.0) as independent and significant predictors of worsened mRS score ($P < .05$) (Table 4). In the Spetzler-Martin score model,

TABLE 3. Univariable Logistic Regression Analysis[a]

Variable	OR	95% CI	P Value
AVM size, cm	1.38	1.13–1.69	.001
Deep venous drainage	1.59	0.94–2.71	.085
Eloquence	1.69	0.98–2.90	.058
Age, per 10 y	1.41	1.19–1.66	.0000
Unruptured presentation	2.19	1.27–3.80	.005
Diffuse	2.41	1.18–4.94	.016
Deep perforating artery supply	0.83	0.40–1.72	.614

[a] AVM, arteriovenous malformation; OR, odds ratio; CI, confidence interval.

TABLE 4. Multivariable Logistic Regression Analysis[a]

Variable	Model 1: Full Model			Model 2: S-M Score Model			Model 3: Supplementary Score Model		
	OR	95% CI	*P* Value	OR	95% CI	*P* Value	OR	95% CI	*P* Value
AVM size, cm	1.23	0.98–1.55	.068	1.31	1.07–1.62	.009			
Deep venous drainage	2.12	1.10–4.08	.025	1.31	0.75–2.29	.344			
Eloquence	1.71	0.94–3.10	.079	1.60	0.92–2.80	.099			
Age, per 10 y	1.42	1.18–1.70	<.001				1.40	1.17–1.67	<.001
Unruptured presentation	2.68	1.40–5.15	.003				2.21	1.22–4.01	.009
Diffuse	1.79	0.78–4.10	.171				2.33	1.06–5.14	.035
Deep perforating artery supply	0.62	0.27–1.45	.270				0.89	0.40–2.00	.784
Logtime since last surgery, y	0.78	0.67–0.91	.002	0.83	0.72–0.95	.009	0.76	0.65–0.88	<.001
Area under the ROC curve (95% CI)	0.78 (0.72–0.83)			0.66 (0.59–0.73)			0.73 (0.67–0.80)		

[a] S-M, Spetzler-Martin; OR, odds ratio; CI, confidence interval; AVM, arteriovenous malformation; ROC receiver operating characteristic.

AVM size (OR, 1.3) was the only significant predictor of worsened mRS score (Table 4). In the supplementary score model, age (OR, 1.4), unruptured presentation (OR, 2.3), and diffuseness (OR, 2.3) were all independent predictors of worsened outcome ($P < .05$) (Table 4).

ROC Analysis

The area under the ROC curve, indicating the predictive accuracy of each model, was highest for the full multivariable model (0.78), followed by the supplementary score model (0.73) (Table 4). The Spetzler-Martin score model had the lowest area under the ROC curve (0.66). The ROC curve areas of the 3 models were significantly different ($P < .001$).

Patient outcome is predicted better using all 7 variables in the full multivariable model than with the 3 variables in the Spetzler-Martin scale, with increased specificity for the same sensitivity and increased sensitivity for the same specificity. For example, the sensitivity and specificity of predicting clinical deterioration is 52% and 63%, respectively, for an AVM with Spetzler-Martin grade III or higher. With the same sensitivity, the specificity increases to 81% when combining the Spetzler-Martin variables with other supplementary variables. Similarly, for the same specificity of the Spetzler-Martin score, the sensitivity increases to 75% when using all variables.

Supplementary AVM Grading Scale

Next, we constructed a supplementary grading system, which included only statistically significant variables from model 3 (Table 4) that were not already expressed in the Spetzler-Martin scoring system. Therefore, points were assigned for patient age, presentation, and AVM diffuseness, analogous to the Spetzler-Martin scoring system (Table 1). These points were added together for a supplementary AVM grade that ranged from 1 to 5. Supplementary AVM grades were assigned immediately before surgical treatment. There was only 1 patient whose supplementary grade changed during treatment owing to an intraprocedural hemorrhage during embolization of a previously unruptured AVM. Supplementary AVM grades were normally distributed, without the selection bias against higher grades seen in the distribution of Spetzler-Martin grades (Fig. 2).

Neurologic outcomes by Spetzler-Martin grade and the new supplementary grade are shown in Table 5. Adding the Spetzler-Martin grade and the supplementary grade for each patient yielded a combined grade ranging from 1 to 10. A greater percentage of patients had improved neurologic outcomes with decreasing combined grade, with stratification into low-risk (grades 1–3), moderate-risk (grades 4–6), and high-risk groups (grades 7–10) (Table 5).

The predictive accuracy of the new supplementary grade was significantly better than that of the Spetzler-Martin grade ($P = .042$), with areas under the ROC curve of 0.73 (95% confidence interval [CI], 0.67–0.79) vs 0.65 (95% CI, 0.58–0.72), respectively (Fig. 3). The predictive accuracy of the supplementary grade was only slightly less than the combined score ($P = .364$), with areas

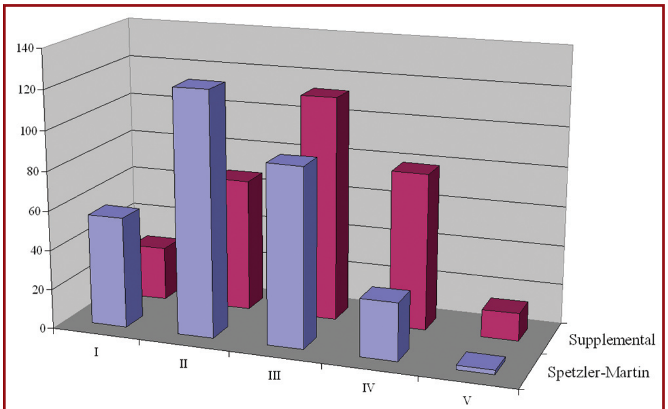


FIGURE 2. *Graph showing distribution of Spetzler-Martin grades and supplementary grades, as applied to 300 patients.*

TABLE 5. Neurologic Outcomes by Spetzler-Martin Grade and the New Supplementary Grade[a]

Variable	Neurologic Outcome: Worse, Dead No.	Worse, Dead %	Improved, Unchanged No.	Improved, Unchanged %
Spetzler-Martin Grade				
I	5	8.9	51	91.1
II	30	24.4	93	75.6
III	27	30.0	63	70.0
IV	9	31.0	20	69.0
V	2	100.0	0	0.0
Supplemental Grade				
I	1	3.7	26	96.3
II	8	11.9	59	88.1
III	25	22.1	88	77.9
IV	32	40.5	47	59.5
V	7	50.0	7	50.0
Combined Grade				
1	0	0.0	0	0.0
2	0	0.0	7	100.0
3	0	0.0	21	100.0
4	5	9.1	50	90.9
5	19	21.1	71	78.9
6	19	27.1	51	72.9
7	24	54.5	20	45.5
8	4	50.0	4	50.0
9	2	40.0	3	60.0
10	0	0.0	0	0.0

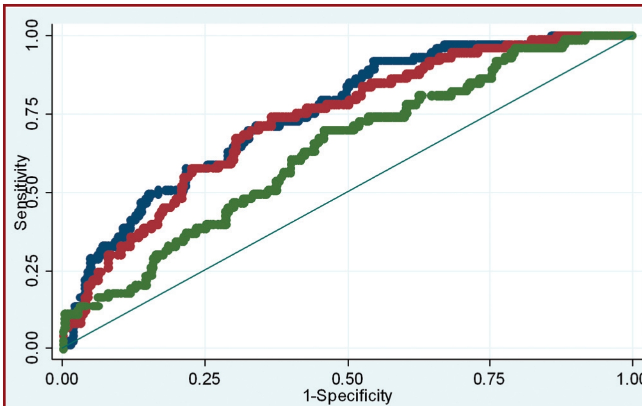


FIGURE 3. *Graph showing receiver operating characteristic (ROC) analyses for the weighted point scores using all 7 variables (blue curve), the Spetzler-Martin grading system (green curve), and the supplementary grading system (red curve) (reference line shown in teal). The predictive accuracy of supplementary grades was similar to that of weighted point scores (ROC areas, 0.75 and 0.73, respectively), and both were greater than that of Spetzler-Martin scores (ROC area, 0.65).*

under the ROC curve of 0.73 (95% CI, 0.67–0.79) and 0.75 (95% CI, 0.69–0.81), respectively.

To evaluate whether the predictive accuracy of our supplementary grade was overly optimistic, we performed a 10-fold cross-validation of the data so that no patient was used to both build and test the model. The 10-fold cross-validation resulted in similar estimates, with an area under the ROC curve of 0.72 compared with 0.73, suggesting that the model was not overly optimistic.

DISCUSSION

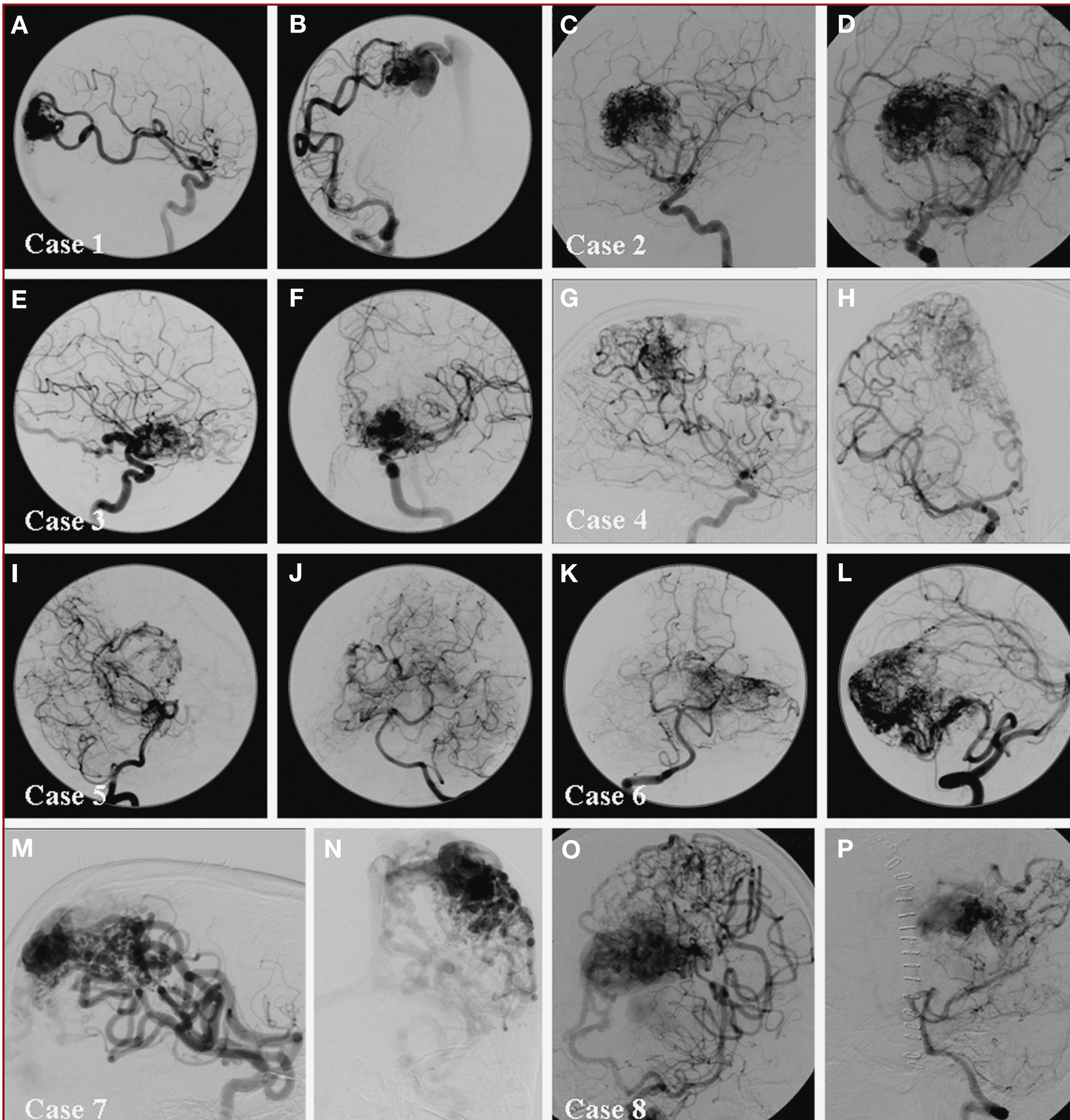
Supplementing the Spetzler-Martin Grading Scale

Our analysis of 300 patients undergoing microsurgical AVM resection demonstrated that the Spetzler-Martin grading system is a crude predictor of neurologic outcomes (ROC area <0.7), as defined by changes in mRS scores. This analysis also demonstrated that a supplementary grading system with 3 other variables (age, hemorrhagic presentation, and diffuseness) was a better predictor of neurologic outcomes, and that the combination of all 6 variables was better still. This supplementary grading system is simple, analogous to the Spetzler-Martin grading system, and easily applicable at the bedside (Table 1).

Our previous research demonstrated that deep perforating artery supply was associated with increased surgical risk,[9] but the current study did not confirm this association. These thin-walled, friable feeders are difficult to coagulate and reside along the deep margin of the nidus, where bleeding can result in intraparenchymal bleeding and dissection into eloquent white matter. Therefore, the lack of a significant association between perforator supply and outcome disagreed with our clinical experience. We attributed the lack of significance of deep perforating artery supply to the differences in patient population and methodology between studies. However, diffuseness was significantly associated with increased surgical risk, and deep perforators often contribute to the ragged borders of diffuse AVMs. Diffuseness may therefore indirectly address deep perforating artery supply in the supplementary grading scale.

Compact AVMs are easily recognized as a tight tangle of vessels on angiography, with little brain tissue within the nidus on MRI scans and well-defined margins between brain and AVM. However, diffuseness remains somewhat vague. Margins are ragged and irregular, as if the arteriovenous tangle was loosened and unraveled, with intervening brain parenchyma intermixed within the nidus. Diffuseness is easy to recognize on angiography (Fig. 4), but difficult to quantify. We developed methodology to quantify diffuseness using computer-generated outlines of AVMs on angiograms, contour plots with varying image intensities, and calculations of nidus area-intensity profiles,[9] but this methodology is far too complex for quick bedside application. Therefore, the determination of diffuseness in the supplementary grading system is qualitative.

Nonetheless, diffuseness belongs in the supplementary grading system because this angioarchitecture is critically important to surgical risk assessment. Compact AVMs have distinct dissection planes with clear separation between nidus and brain tissue, whereas diffuse AVMs have obscure planes that can draw the dissection too close to the nidus, resulting in hemorrhagic complications, or can force the dissection away from the nidus, compromising interspersed brain. Experienced neurosurgeons, who are trained to analyze dissection planes on preoperative angiograms, can identify diffuse AVMs reliably. Spears et al[11] examined interobserver variability in grading 233 brain AVMs and found substantial agreement when separate clinicians determined diffuseness (κ value = 0.67).



Age categories in the supplementary grading system are somewhat arbitrary. The 20-year cutoff was intended to capture pediatric patients, who fare better than adults after AVM resection owing to increased tolerance for surgery, increased neurologic recovery, and/or neural plasticity.[8] The 40-year cutoff was intended to separate adults into those with and without other medical comorbidities. As with size categories in the Spetzler-Martin grading system, minor changes in the cutoffs in age categories did not diminish the predictive accuracy or utility of the supplementary scale.

Like the Spetzler-Martin grading system, the supplementary grading system is a tool to assess the risk of AVM resection. It is applied when analyzing a particular patient's AVM and formulating a management recommendation. However, unlike the Spetzler-Martin score, the supplementary score can change with other treatments or with time. After radiosurgery, an AVM can lose its diffuseness, it can rupture during the latency period, and a pediatric patient can transition to an adult patient. In this example, one would subtract 2 points and add 1 point to the supplementary score. Similarly, embolization can cause hemorrhage in a previously unruptured AVM, and one would subtract 1 point (as in one of our patients). We did not encounter cases in which embolization changed diffuseness in the supplementary score. In these examples, the supplementary score decreases to reflect the effects of previous treatment and thereby encourage surgical intervention. Therefore, the supplementary score is dynamic and must be reevaluated as the patient's clinical circumstances change, whereas the Spetzler-Martin score is determined at initial diagnosis and carried throughout subsequent treatments or clinical events.

FIGURE 4. *Angiograms showing examples of compact and diffuse arteriovenous malformations (AVMs).* **A** *and* **B***, case 1, internal carotid artery angiograms demonstrating a compact nidus in the right parieto-occipital region with distinct borders and a tight tangle of arteries and veins (***A***, lateral view;* **B***, anteroposterior view).* **C** *and* **D***, case 2, left internal carotid artery (ICA) angiograms showing that large AVMs fed by numerous deep perforating arteries can nonetheless have distinct borders, like this AVM in the anterior insula (***C***, lateral view;* **D***, anterior oblique view).* **E** *and* **F***, case 3, left ICA angiograms showing that even 1 diffuse border is sufficient to assign 1 point for diffuseness, as in case 3, with defined borders everywhere but anteriorly (***E***, lateral view;* **F***, anteroposterior view).* **G** *and* **H***, case 4, right ICA angiograms showing that the AVM in case 4 has a small central core of compact nidus, but a loose fringe of surrounding arteries makes it diffuse (***G***, lateral view;* **H***, anterior oblique view).* **I** *and* **J***, case 5, left vertebral artery angiograms showing a diffuse thalamic AVM that appears "pulled apart" or loosened in the direction of its anterior, inferior, and posterior feeding arteries (***I***, lateral view;* **J***, anterior oblique view).* **K** *and* **L***, case 6, right vertebral artery (VA) angiograms showing that ragged and irregular borders comprised of fine, lacy arteries make this left cerebellar AVM diffuse (***K***, anteroposterior view;* **L***, lateral view).* **M** *and* **N***, case 7, left ICA angiograms showing that ragged and irregular borders comprised of dilated, high-flow arteries make large AVMs occupying entire lobes of brain diffuse (***M***, lateral view;* **N***, anteroposterior view).* **O** *and* **P***, case 8, angiograms showing that AVMs in watershed areas can have a diffuse network of feeding arteries, like this parietal nidus fed from the anterior cerebral artery, middle cerebral artery (***O***, left ICA angiogram, anterior oblique view), and posterior cerebral artery (***P***, left VA angiogram, lateral view).*

Other AVM Grading Systems

Other AVM grading systems have been proposed to improve surgical risk prediction and patient selection since the introduction of the Spetzler-Martin grading system in 1986.[1] Tamaki et al[13] assigned points for size (small or large), number of feeding artery systems (1–2 or ≥3), and location (superficial or deep), stratifying AVMs into 5 grades ranging from 0 to 4 that correlated with surgical difficulty, as measured by rate of total AVM excision and patients' Karnofsky scale score.[14] These authors identified age as a significant predictor of outcome but did not include it in the grading system. Their grading system was too similar to the Spetzler-Martin system and failed to gain acceptance.

After finding that neither AVM size nor venous drainage pattern influenced outcome in their experience, Hollerhage et al[15] proposed a grading system based on 5 territories of feeding artery supply (anterior cerebral artery, middle cerebral artery, posterior cerebral artery, rolandic branches, and anterior communicating artery shunt flow). Their grading system was among the first to incorporate a clinical variable in addition to these anatomic variables, assigning 1 point for Hunt and Hess grades I to II and 2 points for Hunt and Hess grades III to V. The Hunt and Hess grade contained within this AVM grading system may be a surrogate for hemorrhagic presentation, but Hunt and Hess[16] designed their scale for aneurysm patients with subarachnoid hemorrhage, and its application to AVM patients was awkward. Despite the possibility of an AVM grade as high as 7, grades ranged from 1 to 4 in this study and correlated with Glasgow Outcome Scale scores.[17] However, by measuring surgical results by final Glasgow Outcome Scale score rather than changes in the score, this grading scale failed to recognize the surgical advantages associated with hemorrhagic presentation.

Perhaps the most comprehensive grading system for AVMs was proposed by Pertuiset et al.[18] In addition to angiographic factors like AVM location and feeding artery supply, this system analyzed the number of AVM sectors and the caliber and straightening of feeding arteries. Hemodynamic factors included nidus volume, cerebral steal, and circulatory velocity of radiolabeled red blood cells. Notably, this system included age and previous hemorrhage in its clinical variables. With the use of elaborate tables, each variable was coded, and these codes were added to generate operability scores ranging between 3 and 69, with AVMs scores of less than 30 considered operable. The authors concluded that "the score system is a little too complicated. . . . It will not take more than 15 minutes to get the sum of the code numbers but it is absolutely necessary to choose a team of scrutators with more than one neurosurgeon; it is also necessary to add to the scrutators a biophysicist." This system contained 2 of the variables in our supplementary grading system, but it was too impractical for clinical use.

The University of Toronto Brain AVM Study Group developed a discriminative prediction model of neurologic outcomes associated with AVM resection that recognized nidus diffuseness as a critical predictor variable, weighted predictor variables according to their statistical significance, and used the mRS score to measure outcomes.[11] The Toronto model incorporated just 3 variables, weighted them with rounded ORs (eloquence = 4, diffuseness = 3, and deep venous drainage = 2), and added points to form a 9-point stratified risk score. Discrimination of this model for predicting permanent disabling neurologic outcomes was high (area under the ROC curve, 0.79) and better than the Spetzler-Martin scale (area under the ROC curve, 0.69). Our full model point score was derived with a similar statistical approach, incorporating 7 variables weighted according to the β coefficients from multivariable logistic regression models. The predictive accuracy of this grading system was high also (area under the ROC curve, 0.78), but such a grading system is too cumbersome to be practical. The weighted grading system of the Toronto group is much simpler, but it has not been widely applied in the years since its publication. In addition, it competes with the Spetzler-Martin grading system, reaffiliating eloquence and venous drainage with the newer scale. Our supplementary grading system, with its own unique variables, remains separate from the Spetzler-Martin scale and avoids this problem.

We envisioned a grading system that would supplement rather than replace the already entrenched Spetzler-Martin grading system. Simplicity is a critical aspect of a popular grading scale, and our supplementary grading scale is designed with this in mind. In addition, the 2 grading systems are analogous in their structure, which we hope will make the supplementary grading scale memorable. The supplementary grading scale has high predictive accuracy on its own (area under the ROC curve, 0.73 vs 0.65 for the Spetzler-Martin grading system), and it stratified surgical risk more evenly in our series (Table 5). Therefore, the supplementary grade can be considered separately, or it can be combined with the Spetzler-Martin grade. Patients with supplementary grades of 3 or less, or combined grades of 6 or less, stratify into low- or moderate-risk groups that predict acceptably low surgical morbidity.

Application of Supplementary AVM Grading System

Clinical decisions begin with an analysis of nidus size, venous drainage, and location. An analysis of supplementary factors can impact a management decision by confirming the risk predicted by the Spetzler-Martin grade. For example, an AVM with a low Spetzler-Martin grade (grade I–III) may be favorable for microsurgical resection, and a low supplementary grade (I–III) may strengthen the recommendation for surgery. In our experience, 186 patients (62%) had low-grade AVMs according to both grading systems, and 158 patients (85%) were improved or unchanged after surgery (Table 6). Conversely, an AVM with a high Spetzler-Martin grade (IV–V) may be unfavorable for microsurgical resection, and an AVM with a high supplementary grade (IV–V) may strengthen the recommendation for nonoperative management. This experience included only surgical patients, and, therefore, there were only 10 such patients (3%), of which half were worse after surgery. In these cases of matched Spetzler-Martin and supplementary grades, the supplementary grading system has a confirmatory role and may not alter management decisions. However, in cases of mismatched Spetzler-Martin and supplementary grades, the supplementary grading system may alter management decisions and therefore has a more important role.

In our data, 83 patients (28%) had low Spetzler-Martin grades and high supplementary grades, and 34 of these patients (41%) were neurologically worse after surgery (Table 6), which is a higher morbidity than that of Spetzler-Martin grade IV AVMs (31%). Insight provided by the supplementary grade might have discouraged the recommendation for surgery in some of these patients (Fig. 5). Similarly, 21 patients (7%) had high Spetzler-Martin grades and low supplementary grades, and 6 of these patients (29%) were neurologically worse after surgery (Table 6). This proportion of worsening was lower than the 35% morbidity for the overall group of Spetzler-Martin grade IV and V AVMs and equivalent to the 30% morbidity seen for grade III AVMs. Again, insight provided by the supplementary grade might have encouraged the recommendation for surgery in some of these patients (Fig. 6). Spetzler-Martin grade III AVMs have surgical risks that depend on the subtype, with small-sized/deep/eloquent AVMs (S1V1E1) associated with lower risk and medium-sized/eloquent AVMs (S2V0E1) associated with higher risk. In addition to considering the grade III subtype, considering the supplementary grade may influence surgical decisions for AVM patients at the borderline between high and low risk (Fig. 7).

Limitations

These 2 grading systems analyze just 6 variables, and there may be other factors that influence surgical outcomes. For example, previous radiation has been shown to reduce surgical morbidity, in part because radiation changes AVM tissue to facilitate its resection.[19] Although previous radiation is not assigned points from

TABLE 6. Matched and Unmatched Prediction of Risk for Morbidity After Surgery

	Total		Improved, Unchanged		Worse, Dead	
	No.	%	No.	%	No.	%
Matched risk prediction						
Low grade, Spetzler-Martin and supplementary scores	186	62%	158	85%	28	15%
High grade, Spetzler-Martin and supplementary scores	10	3%	5	50%	5	50%
Mismatched risk prediction						
Low Spetzler-Martin, high supplementary scores	83	28%	49	59%	34	41%
High Spetzler-Martin, low supplementary scores	21	7%	15	71%	6	29%
Total	300	100%	227		73	

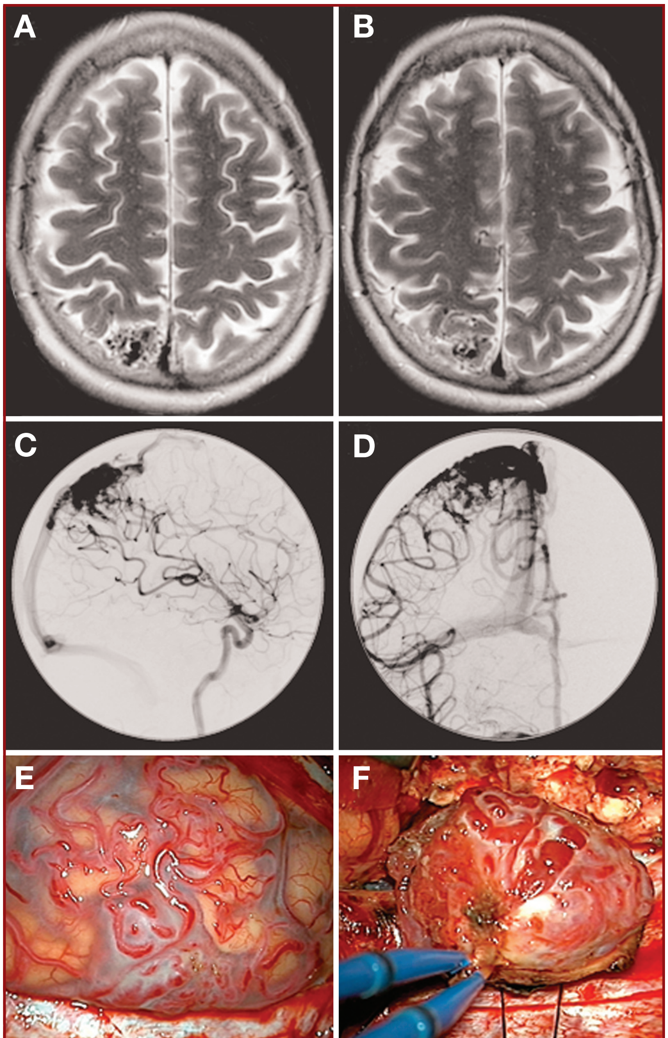


FIGURE 5. *A 56-year-old woman who presented with an incidental, unruptured AVM in the right medial parietal lobe, just posterior to the somatosensory strip.* **A** *and* **B**, *axial T2-weighted magnetic resonance imaging (MRI) scans showing the AVM.* **C** *and* **D**, *angiograms (right ICA injection;* **C**, *lateral view;* **D**, *anteroposterior view) demonstrating superficial venous drainage and confirming a diffuse border laterally and posteriorly. Therefore, this patient had a Spetzler-Martin grade II AVM (S2V0E0) and a supplementary grade V (A3U1D1) (mismatched grades).* **E** *and* **F**, *intraoperative photographs showing resection of her AVM through a biparietal craniotomy. Although the resection was uncomplicated, she had new numbness in the left shoulder postoperatively. The supplementary grade was more predictive of her final outcome.*

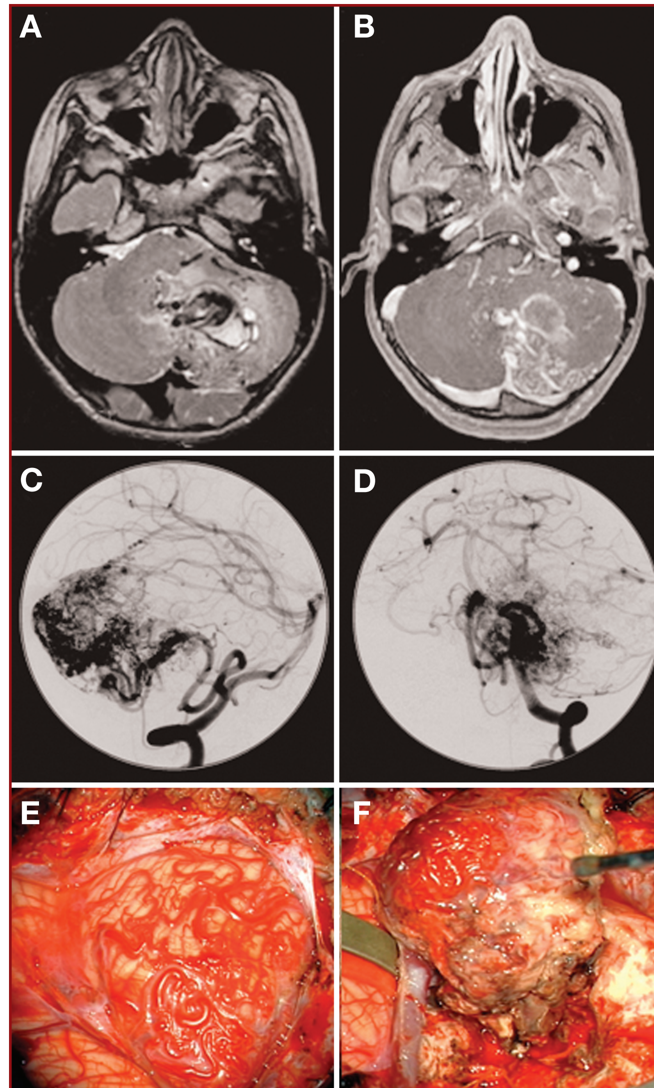


FIGURE 6. *A 6-year-old boy who presented with a cerebellar hemorrhage.* **A** *and* **B**, *axial T2-weighted (***A***) and gadolinium-enhanced T1-weighted MRI scans (***B***) showing the associated AVM, which extended down to the deep cerebellar nuclei.* **C** *and* **D**, *angiograms (left VA injection;* **C**, *lateral view;* **D**, *anteroposterior view) demonstrating a diffuse nidus with deep venous drainage. Therefore, this patient had a Spetzler-Martin grade IV AVM (S2V1E1) and a supplementary grade II (A1U0D1) (mismatched grades).* **E** *and* **F**, *intraoperative photographs showing that resection of his AVM through a torcular craniotomy was uncomplicated. He recovered fully. The supplementary grade was more predictive of his final outcome.*

the supplementary grading scale, it may still influence the supplementary score if it has changed an AVM's diffuseness or bled during the latency period. We limited the supplementary grading scale to 3 variables, but there may be other variables of importance.

The supplementary grading system was derived from a surgical series that includes only operated AVMs and therefore contains selection biases. However, we performed a 10-fold cross-validation of our prediction model, and the results were similar, suggesting that the model was not overly optimistic. Nevertheless, we encourage the broader application of this grading system outside our institution to validate it on different cohorts of AVM patients.

The decision to resect a brain AVM is a complex art that requires a thorough appreciation of the lesion's anatomy, patient's history, neurosurgeon's skills, and family's preferences. No grading system, combination of grading systems, or simple algorithm

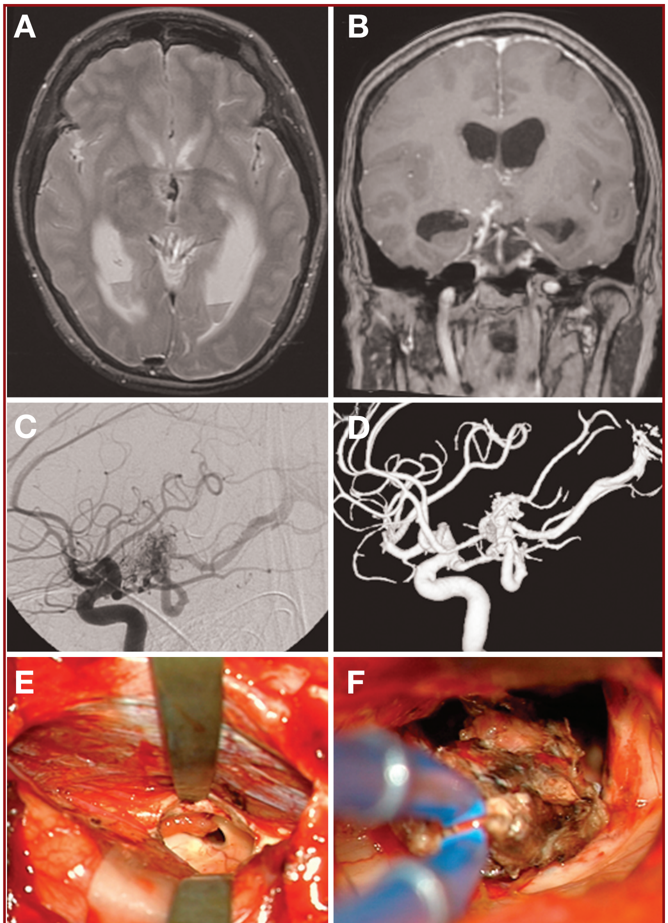


FIGURE 7. *A 54-year-old woman who presented with an intraventricular hemorrhage from a right anteromedial thalamic AVM.* **A** *and* **B**, *axial T2-weighted (***A***) and coronal T1-weighted MRI scans (***B***) showing the AVM.* **C** *and* **D**, *angiograms (right ICA injection;* **C**, *lateral view;* **D**, *3-dimensional rotational view) demonstrating a small, compact nidus with drainage to the basal vein of Rosenthal. Therefore, this patient had a Spetzler-Martin grade III AVM (S1V1E1) and a supplementary grade III (A3U0D0). This borderline AVM had a combined grade of 6, and surgery was selected.* **E** *and* **F**, *intraoperative photographs showing resection of the AVM through a transcallosal-transchoroidal fissure approach, which was uncomplicated. She recovered fully.*

can replace the discriminating process of patient selection. We offer this supplementary grading system as just another tool to guide the process of analyzing some of the critical factors that influence patient outcome, to make more rational choices when weighing known risk factors for spontaneous AVM rupture[4] against risk of intervention. The supplementary grading system is intended to improve preoperative risk prediction, and we expect that it will assist in patient selection for surgery. We anticipate that other grading systems will be developed to predict radiosurgical risks, embolization risks, and natural history risks. The clinician will be required to use these different scales and synthesize their insights to generate the best management plan for each individual patient.

Disclosures

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V. Halbach, MD, Randall T. Higashida, MD, S. Claiborne Johnston, MD, PhD, Nerissa Ko, MD, Nancy Quinnine, RN, Brad Dispena, BS, and Phillip Jolivalt, BS.

COMMENTS

This is a very interesting article describing a large series of a single neurosurgeon's experience in microneurosurgical treatment of brain arteriovenous malformations (AVMs), with a retrospective application of a novel grading system to predict outcome. The most widely applied surgical classification of brain AVMs is obviously the Spetzler-Martin grading scale, which was introduced more than 20 years ago. Modifications of this scale, as well as completely separate grading systems, have been published previously.[1] The fact that the grading system proposed by Lawton et al is designed to supplement, rather than to replace, the Spetzler-Martin grading scale will probably increase the likelihood that this novel grading system will be adopted by the neurosurgical community. Importantly, while increasing the accuracy of the original Spetzler-Martin grading scale (at least in this retrospective setting), the proposed system is still simple enough to gain popularity in daily clinical practice. Naturally, the ultimate test for the proposed grading system will be its application to a prospective patient series, something we expect will undoubtedly take place in the near future.

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1. Hernesniemi J, Keränen T. Microsurgical treatment of arteriovenous malformations of the brain in a defined population. *Surg Neurol.* 1990;33(6):384-390.

In a continued effort to analyze surgical aspects of AVM management, the University of California, San Francisco, Brain AVM Study Project presents a retrospective analysis of 300 surgically resected lesions using a supplementary grading scale that was developed at their institution. The goal of this grading scale is to more accurately predict neurosurgical outcome and thus further refine the selection of surgical patients. The authors are sensible in that they propose to augment the predictive value of the Spetzler-Martin scale while emphasizing the maintenance of bedside applicability.

The authors incorporate the recognized reductions in surgical mortality associated with hemorrhagic presentation, young age, and the absence of a diffuse nidus. In the initial stages of the supplementary grading scale, an attempt was made to include a parameter for deep perforator feeding. However, in the ensuing analysis, the authors encountered a surprising lack of morbidity associated with these perforators and consequently deleted this parameter from their final formulation. As a predictor of good outcome, the supplementary scale was superior to the Spetzler-Martin scale. When combined, these scales outperformed their individual results.

We found this article to be insightful and a good contribution to the neurosurgical literature. We read with interest the conflicting data on the contribution of deep perforating arteries to the surgical outcomes. The authors mention the possibility that this experimental finding is better represented by other parameters, such as the nature of the AVM nidus. It is our experience that a higher morbidity is encountered when the posterior circulation perforators are involved. The actual description of the nidus is obviously the weakest and most subjective aspect of the supplemental system. Perhaps, as was first said in reference to pornography, the experienced observer simply "knows it when he sees it."

Although some question the need for frequent surgical resection of AVMs, it is fair to say that none question the need to resect them safely. Adjunctive therapies, such as radiosurgery and embolization, may be better applied to those lesions for which higher morbidities are expected. A grading system for the adjunctive therapies or a refinement of current systems to reflect the effects of prior radiation and, especially, embolization on subsequent surgical morbidity would be useful. The authors have performed a rigorous evaluation. We look forward to their comments on the use of functional magnetic resonance imaging when evaluating diffuse or compact lesions.

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In this study, the authors examined the value of 4 additional factors that may influence the outcome of AVM resections, in addition to the well-accepted Spetzler-Martin grading system; these included age, hemorrhagic presentation, diffuseness of the nidus, and deep perforating arterial supply. Of these, deep perforating arterial supply was not found to be a significant factor. The combination of the other 3 factors in a multivariate model, along with the Spetzler-Martin classification system, had the best predictive accuracy of outcome. Therefore, the authors recommend the consideration of this supplemental system in evaluating the risk of AVM resection. The authors present an exceptional analysis of their experience and their attempt to develop a system to provide a better measure of surgical treatment.

Published in 1986, the Spetzler-Martin classification system has withstood the test of time until now, and it is widely used by all physicians who treat AVMs. However, some flaws in the system have become apparent to many treating surgeons. These concern microsurgical resection, embolization, and radiosurgery. In respect to microsurgery, I think that size and location are the most important variables. The importance of size increases especially above a diameter of 3 cm, and I believe that each additional centimeter increases the treatment risk. The Spetzler-Martin system assigns only 3 grades to size, and I believe that this is an underestimation. In respect to location, I believe that posterior fossa location (including the brainstem) and location anywhere in the depth of the brain without reaching the pial surface increase the surgical risk. The Spetzler-Martin classification system attempts to correct for this by adding deep venous drainage, but I believe it is better to address it directly. Third, "eloquence" is hard to define. This was a term coined by Charles Drake, after he listened to a lecture by Wilder Penfield. However, as pointed out by M. Gazi Yaşargil, all areas of brain are eloquent, some more obviously than others. Perhaps, "eloquence" should be restricted to the motor sensory areas. Lastly, one cannot underestimate the importance of the experience and expertise of the team that is treating the patient.

Enter embolization with Onyx (ev3, Inc., Irvine, CA), which is further changing the nature of AVM treatment. Some small AVMs can be "cured" by such embolization. Some large AVMs can be considerably reduced by staged embolization with Onyx, making them amenable for radiosurgery. The efficacy of this combined treatment over the long term is unknown at present. However, in cases of some Spetzler-Martin grade 4 AVMs, we are doing staged embolization with Onyx and then deciding whether to resect the AVM or to treat the remnant with radiosurgery. The factors that make an AVM easily amenable to Onyx embolization (and the risk) are somewhat different from the factors concerning microsurgery. Finally, radiosurgery, either primarily, or in combination with Onyx, also has a different set of risk factors.

Perhaps, the only risk factors that are similar for all 3 current treatment modalities are AVM size, location, and the experience of the center. It is apparent that multidisciplinary evaluation, treatment, and outcomes assessment are very important in the management of AVMs in the present era.

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