

A proposed radiosurgery-based grading system for arteriovenous malformations

BRUCE E. POLLOCK, M.D., AND JOHN C. FLICKINGER, M.D.

Department of Neurological Surgery, Mayo Clinic and Foundation, Rochester, Minnesota; and Department of Radiation Oncology, University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania

Object. Radiosurgery is an effective treatment strategy for properly selected patients harboring arteriovenous malformations (AVMs). Grading scales that are currently used to predict patient outcomes after AVM resection are unreliable tools for the prediction of the results of AVM radiosurgery.

Methods. A grading system was developed to predict outcomes following AVM radiosurgery, based on the multivariate analysis of data obtained in 220 patients treated between 1987 and 1991 (Group 1). The dependent variable in all analyses was excellent patient outcome (complete AVM obliteration without any new neurological deficit). The grading scale was tested on a separate set of 136 patients with AVMs treated between 1990 and 1996 at a different center (Group 2).

One hundred twenty-one (55%) of 220 Group 1 patients had excellent outcomes. Multivariate analysis identified five variables related to excellent patient outcomes: AVM volume ($p = 0.001$), patient age ($p < 0.001$), AVM location ($p < 0.001$), previous embolization ($p = 0.02$), and number of draining veins ($p < 0.001$). Regression analysis modeling permitted removal of two significant variables (previous embolization and number of draining veins) and resulted in the following equation to predict patient outcomes after AVM radiosurgery: $\text{AVM score} = (0.1)(\text{AVM volume in cm}^3) + (0.02)(\text{patient age in years}) + (0.3)(\text{location of lesion: frontal or temporal} = 0; \text{parietal, occipital, intraventricular, corpus callosum, cerebellar} = 1; \text{or basal ganglia, thalamic, or brainstem} = 2)$. Seventy-nine (58%) of 136 Group 2 patients had excellent outcomes. All variables in the model remained significant for the Group 2 patients: AVM volume ($p = 0.01$), patient age ($p = 0.01$), and AVM location ($p < 0.001$). Testing of the entire model on the Group 2 patients demonstrated that the AVM score could be used to predict patient outcomes after radiosurgery ($p < 0.0001$). All patients with an AVM score of 1 or lower had an excellent outcome compared with only 39% of patients with an AVM score higher than 2. The Spetzler–Martin grade ($p = 0.13$), the K index ($p = 0.26$), and the obliteration prediction index ($p = 0.21$) did not correlate with excellent patient outcomes.

Conclusions. Despite significant differences in preoperative patient characteristics and dose prescription guidelines at the two centers, the proposed AVM grading system strongly correlated with patient outcomes after single-session radiosurgery for both patient groups. Although further testing of this model by independent centers using prospective methodology is still required, this system allows a more accurate prediction of outcomes from radiosurgery to guide choices between surgical and radiosurgical management for individual patients with AVMs.

KEY WORDS • arteriovenous malformation • arteriovenous malformation grading • radiosurgery • prognosis

THE treatment of patients with small to medium-sized AVMs remains controversial. Proponents of microsurgery for the management of AVMs posit that complete nidus excision provides immediate protection against future hemorrhage and that this can be achieved with a low risk of morbidity for the vast majority of patients.^{11,13,24–26,35,38,39} In contrast, supporters of radiosurgery for the management of AVMs contend that complete obliteration occurs in approximately 65 to 90% of patients after a latency interval of 1 to 3 years and that this is also associated with a low risk of treatment-related complications.^{2,9,20,23,28,36,40,43} The authors of two studies in which outcomes for

patients with small AVMs were compared have concluded that resection confers a large clinical benefit over radiosurgery and is more cost effective.^{26,33} These studies have been criticized, however, because in many patients who undergo radiosurgery the AVMs are located in critical areas of the brain and, as such, are considered to be at high risk for surgical resection.^{1,27} Because a prospective randomized trial in which these two management strategies could be compared is extremely unlikely, physicians and their patients must choose the most appropriate treatment based on the available data.

The Spetzler–Martin grading system³⁹ has become widely accepted as an accurate method to predict patient outcomes after resection of AVMs. Composed of three components (AVM size, location [eloquence of adjacent brain], and pattern of venous drainage), this system has been vali-

Abbreviations used in this paper: AVM = arteriovenous malformation; MR = magnetic resonance; OPI = obliteration prediction index.

TABLE 1
Characteristics of the patient groups

| Characteristic | No. of Patients | | p Value |
|--|---------------------------|---------------------------|---------|
| | Group 1 (220 patients) | Group 2 (136 patients) | |
| mean patient age in yrs (range) | 32.9 (3–77) | 38.1 (9–82) | <0.001 |
| previous hemorrhage | 61% | 36% | <0.001 |
| previous surgery | 13% | 12% | 0.82 |
| previous embolization | 18% | 5% | 0.001 |
| deep AVM location* | 30% | 26% | 0.36 |
| mean AVM volume in cm ³ (range) | 4.1 (0.1–18) | 7.9 (0.2–40.2) | <0.001 |
| Spetzler–Martin grade† | | | |
| I–II | 93 (42%) | 31 (23%) | 0.001 |
| IIIA | 3 (1%) | 16 (12%) | <0.001 |
| IIIB | 104 (47%) | 59 (43%) | 0.54 |
| IV | 20 (9%) | 30 (22%) | 0.001 |

* Basal ganglia, thalamic, or brainstem.

† The Spetzler–Martin classification has been modified to include Grade IIIA (> 3-cm AVMs) and Grade IIIB (< 3-cm AVMs in eloquent areas), as suggested by de Oliveira, et al.

dated prospectively¹¹ and by personnel at numerous cerebrovascular centers of excellence.^{13,24,25,35} Although some authors have noted discrepancies between the Spetzler–Martin AVM grade and patient outcomes, especially with regard to Grade III AVMs,^{3,24} the general consensus supports this grading scale as practical and reliable. Unfortunately, this grading scale does not seem to correlate with successful AVM radiosurgery.^{22,28} This should not be surprising because the Spetzler–Martin grading system is insensitive to important factors such as AVM volume and specific location. For example, a 1-cm diameter lesion has an approximate volume of 0.6 cm³, whereas a 3-cm diameter lesion has an approximate volume of 14 cm³; the expected obliteration rates for these AVMs should be 85 to 95% and 40 to 50%, respectively.^{7,9,16,37} Nevertheless, both AVMs would be considered small (< 3 cm) according to the Spetzler–Martin system. Similarly, deep structures (thalamus, basal ganglia, or brainstem) and critical cortical areas are both considered eloquent brain regions; however, radiation-related complications are more likely to occur in patients with deeply located AVMs than in those harboring hemispheric malformations.^{6,19} Consequently, a valid instrument capable of the accurate prediction of outcomes after AVM radiosurgery is necessary to compare adequately the expected results of microsurgery and radiosurgery for individual patients with AVMs.

Successful AVM radiosurgery results in complete nidus obliteration without new or worsened neurological deficits. Karlsson, et al.,¹⁶ posited the K index as a method to predict obliteration after AVM radiosurgery. In a similar fashion, Schwartz, et al.,³⁷ proposed the OPI as a means to estimate the chance of AVM obliteration for individual patients. Although both correlate with AVM elimination, neither index takes into account the likelihood of producing radiation-related complications for a given radiation dose. Also, the K index and the OPI are based on the radiation dosimetry used (that is, the dose delivered to the AVM margin) at the time of treatment and not on patient and AVM characteristics alone. In this study, we propose a system that can

be used to account for these shortcomings and to predict the chance of successful, single-session AVM radiosurgery, based solely on patient and AVM variables.

Clinical Material and Methods

Study Design

A radiosurgical AVM grading system was developed based on a multivariate analysis of patients with AVMs undergoing stereotactic radiosurgery at the University of Pittsburgh Medical Center between August 1987 and January 1992 (Group 1). The grading system was later tested on patients who underwent AVM radiosurgery at the Mayo Clinic, Rochester, Minnesota, between January 1990 and March 1997 (Group 2).

Patient Population

To be included in the study patients had to have undergone follow-up angiography 2 or more years after radiosurgery, undergone AVM resection after radiosurgery, or died. In addition, all patients in whom a neurological deficit developed in the absence of follow-up angiography were included in the analysis and were considered to harbor a patent AVM. Thus, no patient who had been excluded experienced a new or worsened neurological deficit after radiosurgery. Two hundred twenty (70%) of 315 Group 1 patients comprised the patient population that was analyzed. Three patients (1%) were lost to follow-up review, and 92 other patients (29%) did not undergo postradiosurgical angiography. One hundred thirty-six (72%) of 189 Group 2 patients met the study criteria. Sixteen patients (8%) were lost to follow-up review and 32 (17%) only underwent MR imaging as a result of follow-up examination postradiosurgery. Five more patients were excluded because they died either of unrelated medical causes (four patients) or committed suicide (one patient) less than 2 years after undergoing radiosurgery: all these patients were neurologically unchanged at the time of their deaths. A comparison of study patients with those patients who were excluded because of a lack of angiographic studies showed no difference in AVM volumes, history of hemorrhage, AVM locations, or evidence of AVM obliteration on MR images. Excluded Group 1 patients were older than the study population ($p = 0.0003$), but there was no difference in the age of the excluded Group 2 patients. Table 1 outlines the patient characteristics for both patient groups. Of note, the groups were significantly different with respect to patient age, mode of presentation, previous embolization, and AVM size.

Radiosurgical Technique

All patients underwent radiosurgery that was performed using the Leksell gamma knife (Elekta Instruments, Norcross, GA). Dose planning for Group 1 patients was based on biplanar stereotactic angiography. The radiation dose prescription was based primarily on the risk of developing radiation-related complications, as predicted by the integrated logistical equation.⁵ Thus, AVM margin doses of 25, 20, 18, 16, and less than 16 Gy were typically administered for AVM volumes smaller than 2, 2 to 4, 4 to 8, 8 to 12, and greater than 12 cm³, respectively. The mean radiation dose

Arteriovenous malformation grading scale

delivered to the AVM margin was 21 Gy, and the mean maximum radiation dose was 36.7 Gy. Dose planning for Group 2 patients was based on findings of both stereotactic angiography and either contrast-enhanced computerized tomography scanning before 1992 or MR imaging after 1992. The selected dose directed to the AVM margin for Group 2 patients was 20 Gy (AVM volumes $\leq 4 \text{ cm}^3$), 18 Gy (AVM volumes 4–14 cm^3), and 16 Gy (AVM volumes $> 14 \text{ cm}^3$). The mean radiation dose delivered to the AVM margin was 18.6 Gy and the mean maximum radiation dose was 35.8 Gy.

Patient Outcomes

Patient outcomes after radiosurgery were excellent, good, fair, unchanged, poor, or death²⁸ and were determined at the patient's last follow-up review, time of resection or repeated radiosurgery, or death. An excellent patient outcome consisted of complete nidus obliteration and no new development of a neurological deficit. In patients with good or fair outcomes AVM obliteration was also achieved, but was associated with the development of a minor deficit (for example, partial quadrantanopsia, ataxia, or cranial nerve injury) that did not interfere with the patient's normal level of activities or a major deficit (for example, hemiparesis, aphasia, or homonymous hemianopsia) that resulted in a decline in the patient's level of functioning. Patients were considered unchanged if they continued to have any persistent arteriovenous shunting, but had no new neurological deficits. Any patient with a new neurological deficit and incomplete nidus obliteration was deemed to have a poor outcome. As mentioned previously, any patient who exhibited a new deficit without undergoing follow-up angiography was classified as having a poor outcome in this study.

Statistical Analysis

Continuous variables were compared using the Student t-test and ratio comparisons were made using the chi-square test. Multivariate linear regression analysis in which the relationship between patient and AVM factors and patient outcomes were evaluated was performed using statistical computer software (SAS Language Reference, Version 6.12; SAS Institute, Cary, NC). The dependent variable for both model development and testing was excellent patient outcome after single-session AVM radiosurgery. The location of the AVM was categorized according to the likelihood of permanent symptomatic injury postradiosurgery. Previously, we found locations in increasing order of risk to be as follows: frontal, temporal, intraventricular, parietal, cerebellar, corpus callosum, occipital, medulla, thalamic, basal ganglia, and pons/midbrain.⁶ Assignment of relative risk in our analysis was based on regression coefficients related to the different locations. Thus, frontal or temporal AVMs were given a score of 0 (coefficient range 2.35–3.48), whereas intraventricular, parietal, cerebellar, or occipital AVMs were assigned a score of 1 (coefficient range 4.57–5.96), and thalamic, basal ganglia, or brainstem AVMs were given a score of 2 (coefficient range 6.96–8.33). For AVMs involving multiple locations, fractional values were used according to the number of sites (0.5 for two sites and 0.33 for three sites).

TABLE 2
Results after radiosurgery

| Results | No. of Patients (%) | | p Value |
|--------------------------------|---------------------------|---------------------------|---------|
| | Group 1 (220 patients) | Group 2 (136 patients) | |
| AVM obliteration* | 134 (66) | 88 (74) | 0.17 |
| radiation-related complication | 14 (6) | 20 (15) | 0.02 |
| major | 4 (2) | 9 (7) | |
| minor | 9 (4) | 11 (8) | |
| death | 1 (0.5) | 0 | |
| postradiosurgery hemorrhage† | 23 (10) | 12 (9) | 0.75 |
| no deficit | 8 (4) | 4 (3) | |
| major | 4 (2) | 3 (2) | |
| minor | 2 (1) | 1 (1) | |
| death | 9 (4) | 4 (3) | |
| patient outcome | | | |
| excellent | 121 (55) | 79 (58) | 0.65 |
| good | 11 (5) | 6 (4) | |
| fair | 2 (1) | 3 (2) | |
| unchanged | 70 (32) | 29 (21) | 0.04 |
| poor | 6 (3) | 15 (11) | |
| death | 10 (5) | 4 (3) | |

* Based on patients in whom angiographic follow-up data were available: 203 patients in Group 1 and 136 patients in Group 2.

† Three patients (two in Group 1 and one in Group 2) sustained intracranial hemorrhages from associated aneurysms.

Results

Patient Outcomes

Table 2 shows the results of single-session radiosurgery for both patient groups. No difference was noted between patient groups with respect to obliteration of the AVM nidus, postradiosurgery hemorrhage, or percentage of patients in whom excellent outcomes were achieved. Group 2 patients more commonly experienced radiation-related complications (15% compared with 6% of Group 1 patients, $p = 0.02$), whereas Group 1 patients were more likely to be unchanged after radiosurgery (32% compared with 21% of Group 2 patients, $p = 0.04$).

Development of the Grading System

Multivariate linear regression analysis of the Group 1 patients revealed five factors that correlated with excellent patient outcomes: AVM volume ($p = 0.002$), patient age ($p = 0.0002$), AVM location ($p = 0.002$), no previous embolization ($p = 0.02$), and the number of draining veins ($p = 0.001$). Insertion of the y intercept (0.13) and regression coefficients for the significant variables resulted in the following equation: AVM score = $0.13 + (0.1)(\text{AVM volume in cm}^3) + (0.03)(\text{patient age in years}) + (0.64)(\text{AVM location}) + (0.67)(\text{prior embolization}) + (0.35)(\text{number of draining veins})$, in which the number designating AVM location was 0 (frontal or temporal), 1 (parietal, occipital, intraventricular, corpus callosum, or cerebellar), or 2 (basal ganglia, thalamic, or brainstem) and the number designating previous embolization was 0 (no) or 1 (yes).

For ease of use, the y intercept was eliminated from all subsequent testing. Regression analysis modeling designed to maximize the R^2 coefficient yielded the following: the best one-variable model was patient age ($R^2 = 0.78$, $F = 803.83$, $F > 0.0001$); the best two-variable model consist-

TABLE 3
Determination of AVM score*

| Characteristic | Coefficient |
|---|-------------|
| AVM volume (cm ³) | 0.1 |
| patient age (yrs) | 0.02 |
| AVM location† | 0.3 |
| frontal or temporal = 0 | |
| parietal, occipital, intraventricular, corpus callosum, or cerebellar = 1 | |
| basal ganglia, thalamic, or brainstem = 2 | |

* AVM score = (0.1)(AVM volume) + (0.02)(patient age) + (0.3)(AVM location).

† When an AVM involves multiple sites, fractional values are used according to the number of sites (0.5 for two sites, 0.33 for three sites).

ed of patient age and number of draining veins ($R^2 = 0.84$, $F = 624.64$, $F > 0.0001$); the best three-variable model included AVM volume, patient age, and location of lesion ($R^2 = 0.88$, $F = 544.34$, $F > 0.0001$); the best four-variable model included AVM volume, patient age, location of lesion, and number of draining veins ($R^2 = 0.89$, $F = 469.01$, $F > 0.0001$); and the full model included AVM volume, patient age, location of lesion, number of draining veins, and previous embolization ($R^2 = 0.90$, $F = 390.65$, $F > 0.0001$).

Because the R^2 coefficient displayed only minimal improvement beyond the best three-variable model (AVM volume, patient age, and location of lesion), the latter was utilized to calculate the radiosurgery-associated AVM score. Diagnostic evaluation of this three-variable model (adjusted $R^2 = 0.88$) showed no evidence of collinearity between the individual factors; the White test for heteroscedasticity was not significant ($p = 0.12$). Table 3 shows how the AVM score was determined for individual patients. When AVM scores for the Group 1 patients were placed back into a multivariate analysis with the other five significant variables, only the AVM score correlated with excellent patient outcomes ($p < 0.0001$).

Testing the Grading System

Multivariate analysis of the three factors showed that all predicted excellent patient outcomes for Group 2 patients: patient age ($p = 0.01$), AVM volume ($p = 0.01$), and location of lesion ($p < 0.001$). The calculated AVM scores for Group 2 patients correlated significantly with excellent patient outcomes ($p < 0.0001$; Fig. 1). All patients with AVM scores of 1 or lower had excellent outcomes compared with only 39% of patients with AVM scores greater than 2. Testing of the K index¹⁶ and the OPI³⁷ revealed that, although both predicted AVM obliteration in univariate testing ($p < 0.05$), neither correlated with excellent patient outcomes (K index, $p = 0.26$; OPI, $p = 0.21$). The Spetzler–Martin grade³⁹ did not correlate with either AVM obliteration ($p = 0.15$) or excellent patient outcomes ($p = 0.13$) in the univariate analysis.

Discussion

Significance of an AVM Radiosurgery System

It has been 16 years since the seminal publication by Spetzler and Martin,³⁹ in which they proposed a grading

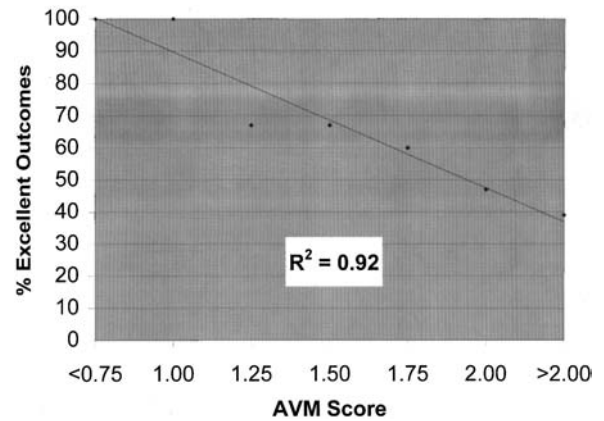


FIG. 1. Graph showing the relationship between the radiosurgery-associated AVM score and the percentage of patients in whom complete obliteration was achieved without new neurological deficits after a single radiosurgical procedure.

scale that could be used to predict patient outcomes after AVM resection. To quote these authors, "Our grading system may be applied to lesions treated either by radiation therapy or by embolization for the purpose of comparing the results of these techniques with those of surgical excision. It is, however, quite possible that this system will not accurately predict the results of embolization or radiation therapy, as the complications of these types of treatment differ from those of surgery."³⁹ During the past several decades, radiosurgery has emerged as an effective treatment strategy for properly selected patients with AVMs.^{2,9,20,23,36,40,43} Thus, the question as to which therapy is the preferred modality for patients with AVMs who are deemed candidates for either technique continues to spark academic debate.^{25,26,31–34} In the present study complete nidus obliteration was achieved in 58% of patients with AVMs who underwent radiosurgery with contemporary imaging techniques, and no new neurological deficits emerged after a single radiosurgical procedure. At first glance, this figure pales when compared with the results of recent microsurgical series of small AVMs (< 3 cm), in which complete resection has been achieved in nearly all cases with less than a 10% morbidity rate and no deaths.^{11,13,25,26,38,39} A comparison between expected outcomes after resection and our series is possible by using the weighted average of complications for 815 patients with Spetzler–Martin Grade I through IV AVMs in the literature.^{3,11,13,25,35,39} Assuming that complete resection was achieved in 99% of patients with no deaths and that the risk of morbidity correlates to the Spetzler–Martin grade (I or II 2%; III 16%; and IV or V 35%), more of our patients (114 [84%] of 136) would have excellent outcomes after microsurgery ($p < 0.001$). In fact, several authors have used such methodology to support microsurgery as the preferred treatment in patients with small AVMs.^{26,33}

A closer inspection of the patient populations comprising published microsurgery and radiosurgery series, however, suggests that the two patient groups are not directly comparable. For example, although the percentage of patients with Spetzler–Martin Grade III AVMs ranges from 18 to 39% in recent microsurgical series (51% in the present series),^{11,13,25,26,37} only 4 to 11% of patients harbored AVMs lo-

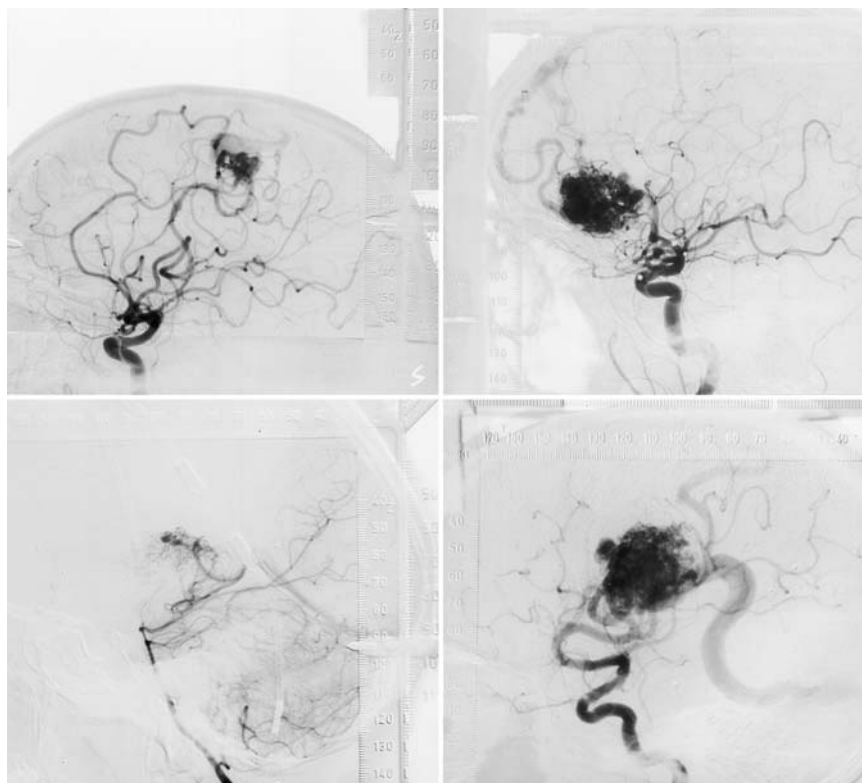


FIG. 2. Lateral cerebral angiograms demonstrating the discrepancy between the Spetzler–Martin grade and the radiosurgery-associated AVM score. *Upper Left:* Angiogram obtained in a 35-year-old woman with a left frontal Spetzler–Martin Grade II AVM (diameter 15 mm, volume 2 cm³) involving the motor strip; the AVM score for radiosurgery is 0.9 (> 95% chance of excellent outcome). *Upper Right:* Angiogram obtained in a 32-year-old woman with a right frontal Spetzler–Martin Grade I AVM (diameter 29 mm, volume 12.8 cm³); the AVM score for radiosurgery is 1.92 (50% chance of excellent outcome). *Lower Left:* Angiogram obtained in a 15-year-old girl with a right thalamic Spetzler–Martin Grade III AVM (diameter 18 mm, volume 2.8 cm³); the AVM score for radiosurgery is 1.18 (80% chance of excellent outcome). *Lower Right:* Angiogram obtained in a 25-year-old woman with a left frontal Spetzler–Martin Grade III AVM (diameter 35 mm, volume 16.2 cm³); the AVM score for radiosurgery is 2.12 (< 40% chance of excellent outcome).

cated in the basal ganglia, thalamus, or brainstem. In contrast, 28% of patients treated by radiosurgery in the current series harbored AVMs in these deep locations. Morgan, et al.,²⁴ analyzed the results of surgery for 92 patients with AVMs supplied by the middle cerebral artery. Morbidity rates for patients with Grade I or II AVMs (56 patients) and Grade III AVMs (26 patients) were 2% and 31%, respectively. Of note, five (83%) of six patients with Grade III AVMs supplied by lenticulostriate arteries suffered a new neurological deficit. As the majority of deep AVMs do receive arterial supply through perforating arteries and many could be considered inoperable (Spetzler–Martin Grade VI AVMs), significant changes would be expected in the hypothetical comparison between microsurgery and radiosurgery. Likewise, de Oliveira and colleagues³ recognized that the morbidity rate associated with the removal of a large AVM from a noncritical location (Grade IIIA) is lower than that associated with small AVMs in critical brain regions (Grade IIIB). In their series, two (5%) of 44 patients with Grade IIIA AVMs experienced new neurological deficits, compared with 29 (30%) of 97 patients with Grade IIIB AVMs. By incorporating these morbidity estimates for patients with Grade IIIB and deeply located AVMs, the percentage of our patients expected to attain excellent out-

comes after microsurgery (66%) is no different from our observed rate of 58% ($p = 0.21$). This illustrates the fact that comparisons that are based solely on grading scales designed to predict patient outcomes after AVM resection, without taking into account patient selection, are fundamentally flawed and misleading.

The disparity between prediction of successful AVM radiosurgery for individual patients and the Spetzler–Martin grading scale is easily demonstrated by a discussion of some specific cases (Fig. 2). For example, a 22-year-old patient with a 2-cm-wide AVM located in the frontal lobe and a 50-year-old patient with a 2.5-cm-wide AVM located in the occipital lobe would have Spetzler–Martin Grade I or II lesions, assuming the lesions only had superficial venous drainage. Yet, the chance of an excellent outcome after a single radiosurgical procedure would exceed 95% for the first patient and be less than 40% in the second. Similarly, a 16-year-old patient with a 1.5-cm-wide thalamic AVM and a 35-year-old patient with a 2.5-cm-wide parietal AVM would both have Spetzler–Martin Grade III AVMs, assuming the lesions had deep venous drainage. Nevertheless, the patient with the thalamic AVM should have approximately a 90% chance of an excellent outcome after radiosurgery compared with only a 55% chance for the patient with the

parietal AVM. Consequently, utilization of the proposed radiosurgical AVM grading system should permit a more accurate comparison with expected results after surgical resection predicted by the Spetzler–Martin grading scale for individual AVM patients.

Strengths of the Proposed System

The literature on AVM radiosurgery tends to provide fragmented information with studies focusing on nidus obliteration,^{7,16,37} radiation-related complications,^{5,6,18,19,41} postradiosurgical hemorrhage,^{8,15,29} or reasons for failed radiosurgery.^{4,10,30} As a result, it is difficult to determine the chance that radiosurgery will result in nidus obliteration without causing a neurological deficit for specific patients. In the current paper we present a large number (356) of consecutively treated patients from two respected radiosurgical centers. We not only provide the rates of nidus obliteration, hemorrhage, and radiation-related complications, but also the number of patients in whom AVM elimination was achieved without the development of new neurological deficits. Although some readers may criticize the fact that only 71% of patients treated are included in the analysis because there was a lack of angiographic follow-up data,¹² clinical and MR imaging follow-up data were available for 486 (96.4%) of 504 patients. The patients who were excluded from the analysis were no different from the study population with respect to patient characteristics, treatment parameters, or MR imaging evidence of obliteration. Nevertheless, because all patients who experienced a neurological decline after radiosurgery were included in the analysis, the results actually overestimated the risk of morbidity associated with radiosurgery. If all patients in whom clinical follow up is available were included, the incidences of major morbidity and death were 3.9% and 2.8%, respectively.

The proposed radiosurgery-associated AVM grading system has a number of features that should promote its clinical application by physicians who commonly treat AVM patients. 1) Its development was based on factors relevant to AVM radiosurgery rather than microsurgery. 2) Calculation and interpretation of the AVM score is relatively simple. The AVM volume can be estimated at the time of consultation based on diagnostic studies (volume = $\pi/6 \times \text{width} \times \text{length} \times \text{height}$) and MR images are most helpful for the accurate determination of AVM volume. The percentages of patients with AVM scores of 1 or less, 1.25, 1.5, 1.75, 2, and greater than 2 for whom excellent outcomes were achieved are greater than 95%, 80%, 70%, 60%, 50%, and lower than 40%, respectively. 3) The AVM score is based entirely on patient and AVM characteristics, unlike earlier attempts to predict obliteration in which treatment parameters (radiation doses) were included as part of the calculations.^{16,37} Attempts to increase the rate of AVM obliteration by using higher doses are offset by a greater risk of developing delayed radiation-related complications. For example, more Group 2 patients achieved AVM obliteration, which was most likely due to the higher margin doses used for larger ($> 10 \text{ cm}^3$) AVMs; however, this was associated with an increased rate of radiation-related complications compared with Group 1. Consequently, no difference was noted in the percentage of patients with excellent outcomes between the two groups. Thus, the likelihood

of an excellent outcome after radiosurgery can be predicted during preoperative consultation and compared with the expected results of surgical resection. 4) Despite significant differences between the patient characteristics of the two groups in this study with regard to age, presentation, previous embolization, and size of the lesions, the model could be used to predict outcomes well for both patient cohorts. Therefore, the system appears to be robust and is sensitive to different dose-planning and radiation-prescription guidelines.

Weaknesses of the Proposed System

The proposed radiosurgery-associated AVM grading system has several limitations worthy of discussion. 1) Although the data used in this study were obtained from prospectively maintained computer spreadsheets, the grading system was developed and applied in a retrospective fashion. This method has been used at the Mayo Clinic since April 1997 to counsel AVM patients and, thus, a prospective application of this grading system should be available within the next several years. 2) This system was created to predict patient outcomes after a single radiosurgery procedure and not the overall results of radiosurgical management. It has been shown that obliteration is accomplished in 60 to 70% of patients after repeated AVM radiosurgery.^{14,21} In addition, complications after AVM radiosurgery, such as cyst formation, may occur many years after angiographically verified obliteration.^{17,42} Hence, the final results of AVM radiosurgery may change with this additional information. We are in the process of gathering long-term follow-up data for patients treated before 1996 to evaluate the predictive value of this system after one or more radiosurgical procedures. 3) Because the grading system was developed and tested at centers at which the gamma knife is used to perform radiosurgery, it remains to be seen whether the system can be used to predict outcomes accurately in patients in whom linear accelerator-based AVM radiosurgery is used.^{2,9,23,36}

Conclusions

The proposed radiosurgical AVM grading scale provides a more accurate prediction of outcomes from radiosurgery to help guide clinical decision making for individual patients with AVMs.

Acknowledgments

The authors are indebted to Drs. L. Dade Lunsford, Robert J. Coffey, and Douglas Kondziolka for their direction and for permitting their patients to be included in this study. The following physicians also contributed patients to this project and should be recognized: Drs. Dudley H. Davis, Patrick J. Kelly, Robert L. Foote, Paula J. Schomberg, Scott L. Stafford, Edward G. Shaw, and John D. Earle. Last, David J. Bissonette, P.A., M.B.A., and Deborah A. Gorman, R.N. maintained the computer databases, thus making this study possible.

References

1. Coffey RJ: Radiosurgery and microsurgery for AVMs. *J Neurosurg* 89:690–693, 1998 (Letter)

Arteriovenous malformation grading scale

2. Columbo F, Pozza F, Chierago G, et al: Linear accelerator radiosurgery of cerebral arteriovenous malformations: an update. **Neurosurgery** 34:14–21, 1994
3. de Oliveira E, Tedeschi H, Raso J: Comprehensive management of arteriovenous malformations. **Neurol Res** 20:673–683, 1998
4. Ellis TL, Friedman WA, Bova FJ, et al: Analysis of treatment failure after radiosurgery for arteriovenous malformations. **J Neurosurg** 89:104–110, 1998
5. Flickinger JC: An integrated logistic formula and prediction of complications from radiosurgery. **Int J Radiat Oncol Biol Phys** 17:879–885, 1989
6. Flickinger JC, Kondziolka D, Lunsford LD, et al: Development of a model to predict permanent symptomatic postradiosurgery injury for arteriovenous malformation patients. Arteriovenous Malformation Radiosurgery Study Group. **Int J Radiat Oncol Biol Phys** 46:1143–1148, 2000
7. Flickinger JC, Pollock BE, Kondziolka D, et al: A dose-response analysis of arteriovenous malformation obliteration by radiosurgery. **Int J Radiat Oncol Biol Phys** 36:873–879, 1996
8. Friedman WA, Blatt DL, Bova FJ, et al: The risk of hemorrhage after radiosurgery for arteriovenous malformations. **J Neurosurg** 84:912–919, 1996
9. Friedman WA, Bova FJ, Mendenhall WM: Linear accelerator radiosurgery for arteriovenous malformations: the relationship of size to outcome. **J Neurosurg** 82:180–189, 1995
10. Gallina P, Merienne L, Meder JF, et al: Failure in radiosurgery treatment of cerebral arteriovenous malformations. **Neurosurgery** 42:996–1004, 1998
11. Hamilton MG, Spetzler RF: The prospective application of a grading system for arteriovenous malformations. **Neurosurgery** 34:2–7, 1994
12. Heffez DS, Osterdock RJ, Alderete L, et al: The effect of incomplete patient follow-up on the reported results of AVM radiosurgery. **Surg Neurol** 49:373–384, 1998
13. Heros RC, Korosue K, Diebold PM: Surgical excision of cerebral arteriovenous malformations: late results. **Neurosurgery** 26:570–578, 1990
14. Karlsson B, Kihlstrom L, Lindquist C, et al: Gamma knife surgery for previously irradiated arteriovenous malformations. **Neurosurgery** 42:1–6, 1998
15. Karlsson B, Lindquist C, Steiner L: Effect of gamma knife surgery on the risk of rupture prior to AVM obliteration. **Minim Invasive Neurosurg** 39:21–27, 1996
16. Karlsson B, Lindquist C, Steiner L: Prediction of obliteration after gamma knife surgery for cerebral arteriovenous malformations. **Neurosurgery** 40:425–431, 1997
17. Kihlström L, Guo WY, Karlsson B, et al: Magnetic resonance imaging of obliterated arteriovenous malformations up to 23 years after radiosurgery. **J Neurosurg** 86:589–593, 1997
18. Kjellberg RN, Hanamura T, Davis KR, et al: Bragg-peak proton-beam therapy for arteriovenous malformations of the brain. **N Engl J Med** 309:269–274, 1983
19. Lax I, Karlsson B: Prediction of complications in gamma knife radiosurgery of arteriovenous malformation. **Acta Oncol** 35:49–55, 1996
20. Lunsford LD, Kondziolka D, Flickinger JC, et al: Stereotactic radiosurgery for arteriovenous malformations of the brain. **J Neurosurg** 75:512–524, 1991
21. Maesawa S, Flickinger JC, Kondziolka D, et al: Repeated radiosurgery for incompletely obliterated arteriovenous malformations. **J Neurosurg** 92:961–970, 2000
22. Meder JF, Oppenheim C, Blustajn J, et al: Cerebral arteriovenous malformations: the value of radiologic parameters in predicting response to radiosurgery. **AJNR** 18:1473–1483, 1997
23. Miyawaki L, Dowd C, Wara W, et al: Five year results of LINAC radiosurgery for arteriovenous malformations: outcome for large AVMs. **Int J Radiat Oncol Biol Phys** 44:1089–1096, 1999
24. Morgan MK, Drummond KJ, Grinnell V, et al: Surgery for cerebral arteriovenous malformation: risks related to lenticulostriate arterial supply. **J Neurosurg** 86:801–805, 1997
25. Pik JHT, Morgan MK: Microsurgery for small arteriovenous malformations of the brain: results in 110 consecutive patients. **Neurosurgery** 47:571–577, 2000
26. Pikus HJ, Beach ML, Harbaugh RE: Microsurgical treatment of arteriovenous malformations: analysis and comparison with stereotactic radiosurgery. **J Neurosurg** 88:641–646, 1998
27. Pollock BE: Radiosurgery and microsurgery for AVMs. **J Neurosurg** 89:691–693, 1998 (Letter)
28. Pollock BE, Flickinger JC, Lunsford LD, et al: Factors associated with successful arteriovenous malformation radiosurgery. **Neurosurgery** 42:1239–1247, 1998
29. Pollock BE, Flickinger JC, Lunsford LD, et al: Hemorrhage risk after stereotactic radiosurgery of cerebral arteriovenous malformations. **Neurosurgery** 38:652–661, 1996
30. Pollock BE, Kondziolka D, Lunsford LD, et al: Repeat stereotactic radiosurgery of arteriovenous malformations: factors associated with incomplete obliteration. **Neurosurgery** 38:318–324, 1996
31. Pollock BE, Lunsford LD, Kondziolka D, et al: Patient outcomes after stereotactic radiosurgery for “operable” arteriovenous malformations. **Neurosurgery** 35:1–8, 1994
32. Pollock BE, Lunsford LD, Kondziolka D, et al: Patient outcomes after stereotactic radiosurgery for “operable” arteriovenous malformations. **Neurosurgery** 36:434–435, 1995 (Letter)
33. Porter PJ, Shin AY, Detsky AS, et al: Surgery versus stereotactic radiosurgery for small, operable cerebral arteriovenous malformations: a clinical and cost comparison. **Neurosurgery** 41:757–766, 1997
34. Robinson JR Jr, Brown AP, Spetzler RF: Patient outcomes after stereotactic radiosurgery for “operable” arteriovenous malformations. **Neurosurgery** 36:433–434, 1995 (Letter)
35. Schaller C, Schramm J: Microsurgical results for small arteriovenous malformations accessible for radiosurgical or embolization treatment. **Neurosurgery** 40:664–674, 1997
36. Schlienger M, Atlan D, Lefkopoulou D, et al: Linac radiosurgery for cerebral arteriovenous malformations: results in 169 patients. **Int J Radiat Oncol Biol Phys** 46:1135–1142, 2000
37. Schwartz M, Sixel K, Young C, et al: Prediction of obliteration of arteriovenous malformations after radiosurgery: the obliteration prediction index. **Can J Neurol Sci** 24:106–109, 1997
38. Sisti MB, Kader A, Stein BM: Microsurgery for 67 intracranial arteriovenous malformations less than 3 cm in diameter. **J Neurosurg** 79:653–660, 1993
39. Spetzler RF, Martin NA: A proposed grading system for arteriovenous malformations. **J Neurosurg** 65:476–483, 1986
40. Steiner L, Lindquist C, Adler JR, et al: Clinical outcome of radiosurgery for cerebral arteriovenous malformations. **J Neurosurg** 77:1–8, 1992
41. Voges J, Treuer H, Lehrke R, et al: Risk analysis of LINAC radiosurgery in patients with arteriovenous malformation (AVM). **Acta Neurochir Suppl** 68:118–123, 1997
42. Yamamoto M, Jimbo M, Hara M, et al: Gamma knife radiosurgery for arteriovenous malformations: long-term follow-up results focusing on complications occurring more than 5 years after irradiation. **Neurosurgery** 38:906–914, 1996
43. Yamamoto Y, Coffey RJ, Nichols DA, et al: Interim report on the radiosurgical treatment of cerebral arteriovenous malformations. The influence of size, dose, time, and technical factors on obliteration rate. **J Neurosurg** 83:832–837, 1995

Manuscript received December 19, 2000.

Accepted in final form September 26, 2001.

Address reprint requests to: Bruce E. Pollock, M.D., Department of Neurological Surgery, Mayo Clinic, 200 First Street SW, Rochester, Minnesota 55905. email: pollock.bruce@mayo.edu.