MODIFICATION OF THE RADIOSURGERY-BASED ARTERIOVENOUS MALFORMATION GRADING SYSTEM

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OBJECTIVE: The radiosurgery-based arteriovenous malformation (AVM) grading scale was developed to predict patient outcomes after radiosurgery. The purpose of this study was to determine whether simplifying this grading system using location as a two-tiered variable detracted from the accuracy of the scale.

METHODS: Regression analysis modeling on 220 patients who underwent AVM radiosurgery between 1987 and 1992 at the University of Pittsburgh Medical Center using location as a two-tiered variable resulted in the following equation: AVM score = (0.1) (volume, mL) + (0.02) (age, yr) + (0.5) (location, hemispheric/corpus callosum/cerebellar = 0; basal ganglia/thalamus/brainstem = 1). Testing of the modified grading system was performed on 247 patients who underwent AVM radiosurgery between 1990 and 2001 at the Mayo Clinic. The mean modified AVM score was 1.62. The mean duration of patient follow-up was 70 months.

RESULTS: There was no difference between the original and modified radiosurgery-based AVM scale with regard to AVM obliteration without new neurological deficits ($F = 0.92$, $P = 0.53$) or decline in Modified Rankin Scale ($F = 0.83$, $P = 0.56$) after radiosurgery. The modified radiosurgery-based AVM scale correlated with the percentage of patients with AVM obliteration without new deficits (≤1.00, 89%; 1.01–1.50, 70%; 1.51–2.00, 64%; ≥2.00, 46%) ($r = -0.98$, $P < 0.01$) and a decline in Modified Rankin Scale (≤1.00, 0%; 1.01–1.50, 13%; 1.51–2.00, 20%; >2.00, 36%) ($r = 0.99$, $P < 0.01$).

CONCLUSION: Simplifying the radiosurgery-based AVM grading system using location as a two-tiered variable did not detract from the accuracy of the scale. This system has been validated by numerous centers performing both gamma knife- and linear accelerator-based procedures and should be used in future studies on AVM radiosurgery to stratify patients for more accurate comparative analyses.

KEY WORDS: Arteriovenous malformation, Grading scale, Radiosurgery

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The Spetzler-Martin grading system is widely accepted as an accurate method for predicting patient outcomes after surgical resection of arteriovenous malformations (AVM) (24). Comprised of three components (AVM size, location, and venous drainage), this system has been validated prospectively (7) and by numerous cerebrovascular centers of excellence (8, 22). Although some authors have suggested that Grade III AVMs represent a heterogeneous group and that further segregation of these patients is needed to better predict surgical morbidity (4, 9), the general consensus supports this grading scale as practical and reliable.

ABBREVIATIONS: AVM, arteriovenous malformation; **MRI**, magnetic resonance imaging; **MRS**, Modified Rankin Scale; **PAR**, Pittsburgh Arteriovenous Malformation Radiosurgery; **UPMC**, University of Pittsburgh Medical Center

Stereotactic radiosurgery is frequently used in patients with critically located cerebral AVMs for whom surgical resection is considered high risk. Although the Spetzler-Martin grading system is frequently used to describe obliteration rates or other results after AVM radiosurgery (6), factors critical to successful AVM radiosurgery are not inherent to this grading system, thus limiting its ability to more accurately predict patient outcomes after AVM radiosurgery. For example, an AVM 1 cm in diameter has an approximate volume of 0.6 ml, and the expected obliteration rate after radiosurgery using conventional dosimetric guidelines would be 90%. Conversely, an AVM 3 cm in diameter has an approximate volume of 14 ml, and the predicted obliteration rate would be 50%. Yet, both would be considered small (≤3 cm) in the Spetzler-Martin system. Retrospective case-control studies have shown that neurological morbidity is greater after AVM resection compared with radiosurgery, whereas recurrent bleeding is more frequent after AVM radiosurgery (14). This methodology is highly susceptible to patient selection bias; thus, the conclusions, although logical, do not provide solid evidence that one technique is superior to the other. Consequently, a valid instrument capable of accurately predicting outcomes after AVM radiosurgery is needed to compare the expected results of surgical resection and radiosurgery for individual patients with an AVM.

In 2002, the Mayo Clinic and the University of Pittsburgh Medical Center (UPMC) collaborated in developing a radiosurgery-based AVM grading system based on factors associated with successful single-session AVM radiosurgery (17). The radiosurgery-based AVM grading system has been shown in numerous studies to correlate with patient outcomes after AVM radiosurgery (1–3, 11–13, 16, 19, 20, 23, 26, 27). Although the system was developed at centers performing gamma knife surgery, it has also been demonstrated to work equally well for patients with AVMs who undergo linear accelerator-based radiosurgery (1, 2, 11, 26, 27). On the basis of the multivariate analysis of patients treated using angiography alone for dose planning, angiographic obliteration without new deficits was better predicted using a three-tiered ranking of location (5). The purpose of this study was to determine whether simplification of the radiosurgery-based AVM grading system using location as a two-tiered variable (basal ganglia/thalamus/brainstem versus other) detracts from the accuracy of the scale.

PATIENTS AND METHODS

Patients

Between January 1990 and December 2001, 308 patients underwent AVM radiosurgery at the Mayo Clinic in Rochester, MN. For this study, patients had to have received clinical and radiological follow-up for 2 or more years after radiosurgery, undergone AVM resection after radiosurgery, or died. Eighteen patients (6%) were lost to follow-up, and 42 patients (14%) had follow-up of less than 24 months. None of these patients had any functional decline. One patient refused research authorization. The remaining 247 patients (109 men and 138 women) were included in this study. The mean patient age was 38.7 years (range, 7.0–82.1 yr). Ninety patients (36%) had a history of AVM rupture. Fifty patients (20%) had AVMs located in the basal ganglia, thalamus, or brainstem. Fifty patients (20%) had undergone previous treatment, including AVM resection (n = 16), clot evacuation (n = 6), AVM embolization (n = 14), placement of a ventriculoperitoneal shunt (n = 8), aneurysm coiling (n = 4), aneurysm ligation (n = 3), and proton beam radiotherapy (n = 5).

Radiosurgery and Other Additional Surgery

Radiosurgery was performed using the Leksell gamma knife (Elekta Instruments, Norcross, GA). Dose planning was based on a combination of stereotactic magnetic resonance imaging (MRI) and biplanar angiography. Follow-up after radiosurgery consisted of clinical examination and MRI at 1, 2, and 3 years after radiosurgery. Follow-up angiography was typically performed 2 or more years after radiosurgery to determine the status of the AVM. Patients with a residual AVM on follow-up angiography were reevaluated for repeat radiosurgery or surgical resection on the basis of their age, their clinical condition, and the AVM response after the first radiosurgical procedure.

Radiosurgery was initially performed as a single procedure in 230 patients (93%) and a staged-volume procedure in 17 patients (7%) (21). The mean initial AVM volume was 7.4 mL (range, 0.1–53.3 mL). The mean AVM margin radiation dose was 18.9 Gy (range, 15–25 Gy). Forty-four patients (18%) underwent repeat radiosurgery, and two patients (1%) underwent three radiosurgical procedures. Ten patients (4%) underwent surgical resection of their AVM after radiosurgery failed to obliterate the nidus. Five patients (2%) had their obliterated AVM resected because of symptomatic cyst formation or persistent regions of increased signal on T2-weighted MRI (15). Two patients (1%) required placement of a ventriculoperitoneal shunt after an intraventricular hemorrhage caused hydrocephalus.

Modification of the Radiosurgery-based Arteriovenous Malformation Score

The radiosurgery-based grading system was developed to predict the chance of complete AVM obliteration without new deficits (excellent outcome) after a single radiosurgery procedure (17). On the basis of the multivariate analysis of patients undergoing AVM radiosurgery at UPMC between 1987 and 1992, patient outcomes were best predicted using a three-tiered ranking of location (frontal/temporal, lowest risk; parietal/occipital/corpus callosum/cerebellum, intermediate risk; basal ganglia/thalamus/brainstem, highest risk) (5). Calculation of the AVM score for individual patients is based on the following formula: AVM score = (0.1) (volume, mL) + (0.02) (age, yr) + (0.3) (location; frontal/temporal = 0, parietal/occipital/corpus callosum/cerebellar = 1, basal ganglia/thalamus/brainstem = 2).

In our original report, we noted that the patients in the Mayo series had better outcomes compared with the UPMC cohort relative to the radiosurgery-based AVM score. Although the patient groups were different with regard to age, presentation, AVM volume, and dose prescription, likely the most important distinction between the two patient groups was the imaging used for radiosurgical dose planning. The UPMC cohort had only biplanar angiography, whereas the Mayo Clinic cohort underwent both biplanar angiography and stereotactic MRI. In addition, unlike the UPMC group, outcomes after radiosurgery for the Mayo Clinic group were also predicted using location as a two-tiered variable (hemispheric/corpus callosum/cerebellum versus basal ganglia/thalamus/brainstem) compared with the more complicated three-tiered location variable model (Bruce E. Pollock, M.D., unpublished data, 2002). Multivariate regression analysis modeling of the UPMC group using location as a two-tiered variable (hemispheric/corpus callosum/cerebellum versus deep) yielded the following equation: AVM score = (0.1) (volume, mL) + (0.02) (age, yr) + (0.5) (location; hemispheric/corpus callosum/cerebellar = 0, basal ganglia/thalamus/brainstem = 1).

Follow-up and Statistical Analysis

Patient outcomes were determined at the time of the last follow-up examination (n = 229), AVM resection after radiosurgery (n = 10), or death (n = 8). The mean follow-up after the first radiosurgery was 70 months (range, 3–200 mo). Comparison of the patients' radiosurgery-based AVM scores with their modified radiosurgery-based AVM scores was performed with the Student *t* test. The *F* test was used to compare the fit of the equations for the original radiosurgery-based AVM score and the modified radiosurgery-based AVM score against two outcome measures (AVM obliteration without new neurological deficit and decline in Modified Rankin Scale [MRS] score). The correlation between the modified radiosurgery-based AVM score and these two outcome measures was expressed using the Pearson product-moment correlation coefficient. Confidence intervals were calculated by the modified Wald method.

RESULTS

Radiosurgical Outcomes

A total of 184 patients (75%) had AVM obliteration confirmed after radiosurgery by angiography (n = 155) or MRI (n = 29). Twenty-three patients (9%) had an intracranial hemorrhage after the initial radiosurgery. In these 23 patients, the intracranial hemorrhage caused no new deficits in six patients (2%), new deficits in nine patients (4%), and death in eight patients (3%). Twenty-four patients (10%) developed a radiation-related deficit after radiosurgery. Overall patient outcomes were classified as excellent (complete obliteration, no new deficit) in 167 patients (68%), good (complete obliteration, new minor deficit) in 9 patients (4%), fair (complete obliteration, new major deficit) in 8 patients (3%), unchanged (residual AVM, no new deficit) in 39 patients (16%), and poor (residual AVM, any new deficit) in 16 patients (7%). Eight patients died (3%).

Effect of Radiosurgery on MRS Score

The MRS scores of the patients before radiosurgery were as follows: 0 (n = 93, 38%), 1 (n = 138, 56%), 2 (n = 9, 4%), 3 (n = 4, 1%), and 4 (n = 3, 1%). Forty-one patients (17%) had a decline (median, −2) in their MRS score after radiosurgery. Changes in MRS scores were as follows: −1 (n = 13, 5%), −2 (n = 10, 4%), −3 (n = 6, 3%), −4 (n = 3, 1%), and −5 (n = 9, 4%).

Testing of the Modified Radiosurgery-based AVM Score

The mean radiosurgery-based AVM score of the 247 patients was 1.76 (range, 0.41–6.40), compared with a mean modified radiosurgery-based AVM score of 1.62 (range, 0.26–5.95) ($P < 0.001$). There was no difference between the two models with regard to AVM obliteration without new neurological deficits ($F = 0.92$, $P = 0.53$) or decline in MRS score ($F = 0.83$, $P = 0.56$) after radiosurgery. The modified radiosurgery-based AVM scale correlated with the percentage of patients with AVM obliteration without new deficits (≤1.00, 89%; 1.01–1.50, 70%; 1.51–2.00, 64%; ≥2.00, 46%) ($r = -0.98$, $P < 0.01$) (*Fig. 1*) and a decline in MRS score (≤1.00, 0%; 1.01–1.50, 13%; 1.51–2.00, 20%; >2.00, 36%) ($r = 0.99$, $P < 0.01$) (*Fig. 2*).

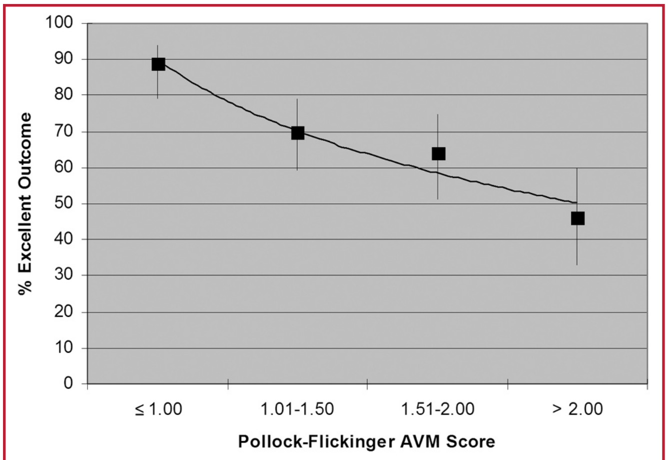

FIGURE 1. *Graph showing relationship between the radiosurgery-based arteriovenous malformation (AVM) score (Pollock-Flickinger AVM score) and the chance of AVM obliteration without new neurological deficit after radiosurgery* (r = −0.98, P < 0.01). Error bars *show 95% confidence intervals for each point.*

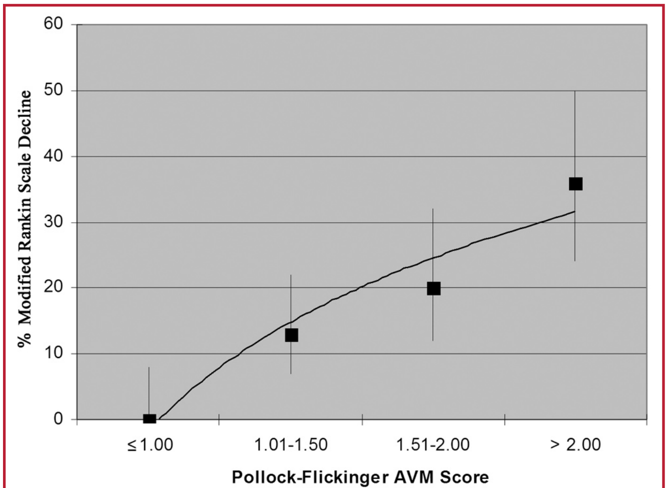

FIGURE 2. *Graph showing relationship between the radiosurgery-based AVM score (Pollock-Flickinger AVM score) and the chance of MRS decline after radiosurgery* (r = 0.99, P < 0.01). Error bars *show 95% confidence intervals for each point.*

DISCUSSION

Grading systems used by physicians to predict patient outcomes typically have three factors that have led to their acceptance. First, the system must be based on variables that are relevant to the disorder and can be measured accurately and reliably by independent observers. Second, the selected variables must clearly affect the outcome being measured. Third, the system cannot be overly cumbersome or complicated. Two commonly used grading systems in neurological surgery are the Glasgow Coma Scale and the Spetzler-Martin AVM grading scale (24, 25). Both of these grading scales have been used for more than 20 years and are used to classify patients with traumatic head injury and cerebral AVMs, respectively. These scales are clinically useful in guiding the management of individual patients, and they permit patient stratification during the analysis of outcomes for these patient groups. In addition, they provide a simple nomenclature for neurosurgeons to communicate effectively when describing patients to their colleagues. For example, when a resident calls his or her attending physician about a patient in the emergency department with a closed head injury and states that the patient has a Glasgow Coma Scale score of 4, the attending physician has a clear mental picture of the patient without hearing any more information. Likewise, if a neurologist consults a neurosurgeon regarding the risk of surgical resection of an unruptured AVM and relates that the radiology report describes it as a Spetzler-Martin Grade I AVM, the neurosurgeon can relate with relative confidence that the patient would likely benefit from surgical resection if the patient is healthy and has an extended life expectancy. Although these grading systems were developed on the basis of anecdotal experience without statistical confirmation of the variables used or the overall scores, both have been validated prospectively and by numerous independent investigators.

During the past 10 years, we developed and tested a grading system to predict outcomes after AVM radiosurgery. Initially conceived as the Pittsburgh Arteriovenous Malformation Radiosurgery (PAR) grading scale (18), the PAR grading scale was based on a multivariate analysis of factors that correlated with AVM obliteration without new neurological deficits after single-session AVM radiosurgery. However, calculation of a patient's PAR grade was rather complex, requiring five separate variables and a y-intercept value. Consequently, we used regression analysis modeling to simplify the grading scale on the same patient cohort as the PAR grading scale and developed the radiosurgery-based AVM grading system (17). This simpler system used only three factors (age, AVM volume, and AVM location) and was shown to predict outcomes for patients undergoing AVM radiosurgery at the Mayo Clinic between 1990 and 1997. The robustness of the grading scale was illustrated by the fact that the two groups were different with regard to age, presentation, AVM volume, and dose prescription. It is also significant that the grading system did not include any treatment-related factors, such as radiation dose, to use before the procedure to counsel individual patients on the chance of success after AVM radiosurgery. During the past 5 years, subset analyses by several centers have correlated the AVM score to outcomes for patients with deep AVMs (2, 19, 25), pediatric patients with AVMs (3, 27), and patients undergoing linear accelerator-based radiosurgery (1, 2, 11, 26, 27). Last, even though the AVM score was created to predict outcomes after a single radiosurgical procedure, it also correlates with outcomes after one or more radiosurgical procedures (20) and with the chance of neurological decline after AVM radiosurgery (12, 16).

In this study, we found that simplifying the radiosurgery-based AVM system using location as a two-tiered variable (deep versus other) did not affect the accuracy of the scale. As before, patients with AVM scores of 1 or less can be counseled that the chance of AVM obliteration without new neurological deficits is approximately 90% and the chance of any decline in daily activities is virtually zero. It is notable that two of the three patients with AVM scores of less than 1 and AVMs that failed to obliterate had AVMs that were diffuse rather than compact. Zipfel et al. (28), from the University of Florida, reviewed 268 patients and noted that patients with a diffuse AVM nidus were one-fourth as likely to achieve AVM obliteration compared with patients with compact AVMs. In particular, our system has been useful in discussing the option of radiosurgery for patients with unruptured AVMs. Lawton et al. (10), of the University of San Francisco Brain Arteriovenous Malformation Study group, found that 31 (34%) of 90 patients with unruptured Spetzler-Martin Grade I to III AVMs had a deterioration in MRS score at the last follow-up evaluation. They concluded that patients with unruptured AVMs usually have normal or nearly normal neurological function preoperatively and are at risk for functional deterioration when assessed by sensitive outcome measures such as the MRS. Our data support the concept that patients with unruptured AVMs who have low AVM scores may be preferentially managed using radiosurgery rather than resection. Radiosurgery continues to be the primary treatment option for patients with deeply located AVMs despite a lower chance of obliteration and a greater chance of morbidity compared with patients with hemispheric lesions. It remains unclear whether this grading system will be constructive when discussing the option of staged volume for patients with large AVMs (21, 23). Sirin et al. (23) reported 28 patients undergoing staged-volume AVM radiosurgery at the UPMC. Seven (33%) of 21 patients with follow-up beyond 36 months had AVM obliteration; 96% of patients in that series had AVM scores greater than 2. Our model would predict that less than half of patients with an AVM score of 2 or more will have obliteration without new neurological deficits.

CONCLUSION

Simplification of the radiosurgery-based AVM grading system using location as a two-tiered variable (deep versus other) did not affect the accuracy of the scale. This classification has been validated by numerous radiosurgery centers performing both gamma knife- and linear accelerator-based radiosurgery. Future research on AVM radiosurgery should use this system to stratify patients for more accurate comparative analyses.

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COMMENTS

Pollock and Flickinger expand on their prior work regarding a radiosurgery-based arteriovenous malformation (AVM) grading system. Their prior models involved more variables and thus were more cumbersome to use. In this article they simplified their model, which should make it easier for general neurosurgeons to use. I agree with the authors that the most commonly used Spetzler-Martin grading system was not really designed with consideration of radiosurgical treatments. Although I have some concerns regarding oversimplification of these mathematical models, the current model does indeed reliably predict both obliteration without new deficits and a decline in modified Rankin Scale score, both of which should provide neurosurgeons with data when AVM radiosurgical outcomes are discussed.

Steven D. Chang
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Pollock and Flickinger have developed a simplified AVM radiosurgery grading system, based on AVM volume, patient age, and AVM location (deep versus other) and found it to be highly reliable in predicting obliteration rates and adverse outcomes (hemorrhage, radiation injury, and others). It compared well with an older scheme, using a three-tiered location grade. I am intrigued by their new grading system and plan to test its accuracy on our AVM database at the University of Florida.

William A. Friedman
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Neurosurgeons like grading scales and scores. Whether for coma, subarachnoid hemorrhage, AVM resection, or other entities, they are useful if they are meaningful, easily remembered without going to the literature or a computer, and generalizable. Pollock and Flickinger have worked to develop a score for outcomes after AVM radiosurgery and in this work have tried to simplify it. It still requires some mathematics that will probably preclude its use at the bedside or "over the phone," but it is simple and particularly of value when one is evaluating and publishing results. In addition, it has been validated. I hope that future AVM reports include this score in data analysis.

Douglas Kondziolka
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In this article, Drs. Pollock and Flickinger simplify their previously described AVM grading system for stereotactic radiosurgery. The original system used a three-tiered ranking of location as follows: the lowest risk for AVMs in the frontal and temporal location; the intermediate risk for those in the parietal, occipital, cerebellum, and callosal regions; and the highest risk for those is in the brainstem, basal ganglia, and thalamus (1). In this article, Pollock and Flickinger validate a simplification of their original model. Here the simplification is based on use of a two-tiered location ranking in which AVMs located in the hemispheres, callosum, and cerebellum are lower risk and those located in the basal ganglia, thalamus, and brainstem are higher risk. In even simpler terms, the location variable of the new system might best be described as "deep" versus "superficial." Of note, the only term in this grading system that can truly be altered by the clinician is AVM volume. In the setting of AVM radiosurgery, altering the volume is most frequently accomplished by partial embolization of the nidus. The effect of prior embolization on radiosurgical obliteration and complication rates, however, is not at all clear.

The increased ease of use of this system and its continued validity in predicting radiosurgical outcomes will further extend the system's use within the neurosurgical community. This AVM grading system has become the radiosurgical equivalent of the Spetzler-Martin grading system (2).

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