Title

Deep Arteriovenous Malformations in the Basal Ganglia, Thalamus, and Insula: Multimodality Management, Patient Selection, and Results

Journal
World Neurosurgery, 82(3-4)

ISSN
1878-8750

Authors
Potts, Matthew B
Jahangiri, Arman
Jen, Maxwell
et al.

Publication Date
2014-09-01

DOI
10.1016/j.wneu.2014.03.033

Peer reviewed

World Neurosurg. Author manuscript; available in PMC 2015 September 01.

Published in final edited form as:
World Neurosurg. 2014 ; 82(0): 386–394. doi:10.1016/j.wneu.2014.03.033.

Deep Arteriovenous Malformations in the Basal Ganglia, Thalamus, and Insula: Multimodality Management, Patient Selection, and Results

Matthew B. Potts, MD[1], **Arman Jahangiri, BS**[1], **Maxwell Jen, MD**[1], **Penny K. Sneed, MD**[2], **Michael W. McDermott, MD**[1], **Nalin Gupta, MD, PhD**[1,3], **Steven W. Hetts, MD**[4], **William L. Young, MD**[5,6], and **Michael T. Lawton, MD**[1,6,*] **for the UCSF Brain AVM Study Project**

[1]Department of Neurological Surgery, University of California, San Francisco, San Francisco, CA, USA

[2]Department of Radiation Oncology, University of California, San Francisco, San Francisco, CA, USA

[3]Department of Pediatrics, University of California, San Francisco, San Francisco, CA, USA

[4]Department of Radiology, University of California, San Francisco, San Francisco, CA, USA

[5]Department of Anesthesia and Perioperative Care, University of California, San Francisco, San Francisco, CA, USA

[6]Center for Cerebrovascular Research, University of California, San Francisco, San Francisco, CA, USA

Abstract

Objective—To describe a single institution's experience treating arteriovenous malformations (AVMs) of the basal ganglia, thalamus, and insula in a multimodal fasion.

Methods—We conducted a retrospective review of all deep AVMs treated at our institution between 1997–2011 with attention to patient selection, treatment strategies, and radiographic and functional outcomes.

Results—97 patients underwent initial treatment at our institution. 64% presented with hemorrhage. 29% were located in the basal ganglia, 41% in the thalamus, and 30% in the insula. 80% were Spetzler-Martin grade III-IV. Initial treatment was microsurgical resection in 42%, stereotactic radiosurgery (SRS) in 45%, and observation in 12%. Radiographic cure was achieved in 54% after initial surgical or SRS treatment (71% and 23%, respectively) and in 63% after subsequent treatments, with good functional outcomes in 78% (median follow-up 2.2 years). Multivariate logistic regression analysis revealed treatment group and age as factors associated with radiographic cure, while Spetzler-Martin score and time to follow-up were significantly

*Corresponding author: Michael T. Lawton, MD, Department of Neurological Surgery, University of California, San Francisco, 505 Parnassus Ave, M780, Box 0112, San Francisco, CA 94143-0112, Phone: (415) 353-3998, Fax: (415) 353-3596, lawtonm@neurosurg.ucsf.edu.

Disclosures: The authors have no personal or financial interests in the drugs, materials, or devices described in this article.

associated with improved/unchanged functional status at time of last follow-up. Post-treatment hemorrhage occurred in 11% (7% of surgical and 18% of SRS patients).

Conclusions—Modern treatment of deep AVMs includes a multidisciplinary approach utilizing microsurgery, SRS, embolization, and observation. Supplementary grading adds meaningfully to traditional Spetzler-Martin grading to guide patient selection. Surgical resection is more likely to result in obliteration compared to SRS, and is associated with satisfactory results in highly selected patients.

Keywords

Arteriovenous malformations; basal ganglia; radiosurgery; thalamus; surgery; therapeutic embolization

Introduction

Arteriovenous malformations (AVMs) of the basal ganglia, thalamus, and insula pose significant treatment challenges. Such deep AVMs are known to have aggressive natural histories, with annual hemorrhage rates ranging from 10–34% (2,20) and mortality rates up to 62.5% (17). The difficulties associated with microsurgical resection of deep AVMs have prompted some to consider them inoperable (12). However, radiosurgical treatment of deep AVMs is associated with significant complications and hemorrhage during the latency period (2,6,7,14,20) as well as lower obliteration rates compared to other locations (7,17). More recent surgical experiences with deep AVMs have shown improving results, with superior obliteration rates and lower mortality compared to radiosurgical series (4,12).

At our institution, the treatment of brain AVMs is performed by a multidisciplinary team that includes neurosurgeons, neurologists, interventional neuroradiologists, and radiation oncologists. The Spetzler-Martin and Supplementary AVM grading systems are important considerations in deciding to treat a deep AVM with surgical resection, stereotactic radiosurgery (SRS), or observation. In general, known surgical risks associated with higher grade AVMs (Spetzler-Martin and Supplementary grades IV and V) favor SRS or observation. Conversely, superior obliteration rates and lower post-treatment hemorrhage rates in surgically-managed AVMs make lower grade AVMs more appealing for surgical resection. It is not clear, however, if such generalizations can be applied to deep-seated AVMs or if the challenges associated with deep location and a more aggressive natural history warrant different treatment strategies. In an attempt to further elucidate these issues, we present here a series of 97 patients with deep AVMs treated in a multidisciplinary fashion.

Methods

Data Collection

This study was approved by the Institutional Review Board of the University of California, San Francisco, and conducted in compliance with Health Insurance Portability and Accountability Act regulations. The prospective registry of the UCSF Brain Arteriovenous Malformation Study Project was searched to identify patients with basal ganglia, thalamic, and insular AVMs who were treated at our institution between 1997 and 2011. Patients were excluded if they had received prior treatments at an outside institution or before the study period. Patients were categorized based on their initial treatment (surgical resection, SRS, or observation) during the defined study period. We conducted a retrospective review of this database as well as medical records, pre- and post-treatment radiographic studies, and clinical follow-up evaluations. Recorded pre-treatment characteristics included age at initial treatment, clinical presentation, functional status, and AVM characteristics such as location, Spetzler-Martin grade and Supplemental grade. The Spetzler-Martin AVM grading scale (19) incorporates AVM size (<3cm, 3–6cm, or >6cm), venous drainage pattern (deep versus superficial), and eloquence of the AVM location (eloquent versus noneloquent). The Supplemental AVM grading scale (9) incorporates patient age (<20y, 20–40y, or >40y), hemorrhage on presentation (ruptured versus unruptured), and AVM compactness (compact versus diffuse).

Patient Selection

Patients with AVMs of the basal ganglia, thalamus, and insula are reviewed by our institution's multidisciplinary cerebrovascular team, which includes neurosurgeons, neurologists, interventional neuroradiologists, and radiation oncologists. In general, surgical preference is given to small AVMs with compact niduses, superficial venous drainage, and hemorrhagic presentation. Patients with poorer functional status at presentation are also often selected for surgical resection. Conversely, SRS is favored for larger AVMs, non-hemorrhagic presentations, and good functional status. Observation is typically reserved for deep AVMs deemed too large for safe surgical resection or SRS. Patient preference and medical comorbidities are also considered when deciding treatment recommendations.

Surgical Resection

Microsurgical resection was performed by the senior author (MTL). As reported previously (16), the surgical approaches used to resect basal ganglia, thalamic, and insular AVMs fall into three broad categories: transsylvian, transcallosal, and transcortical. Transsylvian approaches require a wide splitting of the Sylvian fissure to expose the insula. From there, AVMs at the surface of the insula can be resected while deeper AVMs of the insula and basal ganglia can be reached through a transinsular corridor. Transsylvian variations include the anterior and posterior transinsular (15) and the supracarotid-infrafrontal (21) approaches. Transcallosal approaches require interhemispheric dissection to expose the corpus callosum (8,18). Variations include the anterior ipsilateral transcallosal for lesions of the superior thalamus, anterior contralateral transcallosal for lesions of the thalamus and caudate nucleus, transcallosal-transchoroidal for medial thalamic lesions, and posterior transcallosal for more posterior lesions of the superior thalamus. Finally, transcortical approaches take advantage of hematoma or encephalomacia surrounding an AVM that provides a direct, non-anatomical corridor to the AVM. The choice of surgical approach was based on AVM location, arterial supply, and presence of surrounding hematoma or encephalomalacia.

Stereotactic Radiosurgery

SRS was performed for all cases using the model B, C, 4C, or Perfexion Leksell Gamma Knife (Electa Instruments, Atlanta, GA). After administration of local anesthetic, a Leksell head frame was placed and patients underwent pre-SRS imaging, which included a stereotactic angiogram and gadolinium-enhanced magnetic resonance imaging (MRI). Results of these studies were superimposed to aid in target delineation, which was performed by the attending radiation oncologist and neurosurgeon. The treatment plan was created by a physicist using GammaPlan treatment planning software (Electa, Stockholm, Sweden) and approved by the attending radiation oncologist and neurosurgeon. Volume-staged SRS was considered if the treatment volume exceeded 8–10cm^3, treating approximately 8–10cm^3 per stage spaced 3–6mos apart. After treatment, patients were discharged home.

Outcome Evaluation

Two main outcome measures were examined: radiographic response to treatment and functional outcome. Radiographic response was determined based on post-treatment angiograms. For surgical resection, post-treatment angiograms were typically obtained during the early post-operative period (most often on post-operative day 1–3). Conversely, for SRS, post-treatment angiograms are typically obtained 3–5 years after treatment. Radiographic response was graded as complete obliteration or partial/no response. Functional neurologic outcome was assessed using the Rankin Scale (RS). Neurologic assessments were performed by a neurologist, neurosurgeon, or associated nurse clinician. The pre-treatment RS was obtained from routine pre-treatment clinic visits or admission physicals. Follow-up information was obtained during routine post-treatment clinic visits, subsequent hospital admissions, or telephone interviews. Good outcomes were defined as a final RS score of 1–2 while poor outcomes were defined as a final RS greater than 2. Functional improvement was defined as a decrease in the RS score from the preoperative exam to the final follow-up exam. Deterioration was likewise defined as an increase in the RS score.

Statistical Analysis

Statistical analysis was performed using JMP 10.0 (SAS, North Carolina, USA). Frequency distributions and summary statistics were calculated for all baseline characteristics and outcome measures. For all categorical variables (e.g., Spetzler-Martin grade), a cross-tabulation was generated and a Pearson χ^2 test was used to compare distributions among the three initial treatment groups (surgical resection, stereotactic radiosurgery, and observation). Continuous variables (e.g., age) were compared with a t-test. Univariate analyses of factors associated with radiographic outcome (obliterated versus not obliterated) and functional outcome (improved/unchanged versus worsened RS) were also performed. Factors that were significantly associated with these dichotomous outcomes on univariate analysis were then incorporated into multivariate analyses using nominal logistic regression models. Statistical significance was defined as $p<0.05$.

Results

Patient and AVM Characteristics

Between 1997 and 2011, 108 patients with basal ganglia, thalamic, and insular AVMs were treated at our institution. Of those, nine had undergone prior treatments (surgery or SRS) for their AVM while two patients underwent endovascular embolization in preparation for surgical resection at other institutions. These patients were excluded, leaving 97 patients for inclusion in this analysis. Of note, four patients in this analysis had been followed with observation at outside institutions prior to being referred to our institution for further management. Mean age of the included 97 patients was 32 years with a relatively equal gender distribution (47% female, 53% male). The majority (64%) presented with hemorrhage while seizure accounted for 11% and focal deficit and headache each accounted for 8% of presentations. Overall, 29% of AVMs were located in the basal ganglia, 41% in the thalamus, and 30% in the insula. Fifty-eight percent were located on the left, 39% on the right, and 3% had bilateral thalamic AVMs. The majority of AVMs were Spetzler-Martin grade III or IV (44% and 36%, respectively), while 12% were grade II and 7% were grade V. There were no Spetzler-Martin grade I AVMs in this series. Supplementary AVM grades were more evenly distributed, with 20% grade I, 32% grade II, 22% grade III, 24% grade IV, and only 2% grade V. Initial treatment for this population during the study period included surgical resection in 42%, SRS in 45%, and observation in 13%.

Table 1 describes the baseline characteristics of each initial treatment group. Notable differences between treatment groups included age (p=0.049), presentation (p=0.035), and AVM location (p<0.0001). More patients managed with surgery presented with hemorrhage (75%) compared to the cohorts treated with SRS (64%) or observation (25%). In the surgical group, the majority of AVMs were located within the insula (59%) compared to only 7% in the SRS group and 17% of those managed with observation. In addition, pre-treatment functional neurologic status based on the RS also differed among treatment groups (p=0.017) with patients treated surgically having overall poorer RS grades than the SRS or observation groups.

Table 2 describes the AVM characteristics for each treatment group based on the Spetzler-Martin and Supplementary AVM grading scales. As expected, there were several significant differences among treatment groups based on the variables comprising these two scales. Size, venous drainage pattern, and the overall Spetzler-Martin grade were all significantly different (p=0.001, p=0.0004, and p<0.0001, respectively). The majority of AVMs in the surgical group were small (<3cm, 66%) compared to the SRS (48%) and observation (17%) groups. In addition, there were no large (>6cm) AVMs treated with initial surgery while both the SRS and observation groups contained large AVMs (7% and 33%, respectively). Eloquence was not a significant factor among treatment groups since the vast majority (98%) of deep AVMs in this study were considered eloquent. Within the Supplementary AVM grading scale, unruptured presentation and compactness were also significantly different among treatment groups (p=0.0132 and p=0.0376, respectively). AVMs treated surgically were less likely to be diffuse (only 10%) compared to those in the SRS and observation groups (18% and 45%, respectively). Interestingly, both age and overall Supplementary AVM grade were not significantly different among treatment groups. However, the supplemented Spetzler-Martin grade (Spetzler-Martin + Supplementary AVM grades) was different among groups (p<0.0001), with the lowest overall grades in the surgical group and the highest overall grades in the observation group (Table 2).

AVM Management

As described in Tables 1 and 2, the initial AVM treatment was surgical resection in 42%, SRS in 45%, and observation in 13%. Pre-treatment embolization was used more often prior to surgical resection than SRS (51% versus 9%, respectively, p<0.0001). In all cases of pre-treatment embolization, AVM feeding arteries were embolized to reduce blood flow to the AVM. The majority of patients undergoing pre-treatment embolization were treated with a single round, although one SRS and three surgical resection patients underwent two rounds of embolization while an additional surgical resection patient underwent three rounds. Pre-treatment embolization was performed between one and 11 days preoperatively for all but one patient in the surgical group. This additional patient suffered a stroke during pre-treatment embolization so their surgical resection was postponed six months to allow them time for recovery. For SRS patients, pre-treatment embolization was initiated between one and 81 days prior to SRS. Table 3 lists the surgical approaches employed based on AVM location. Overall, transsylvian approaches were used in 68%, transcallosal in 15%, and transcortical in 17%.

For the 44 patients who initially underwent SRS, mean target volume was 7.4cm^3 (median 4.6cm^3, range 0.12–28.1cm^3). Mean modified Pollock radiosurgery-based AVM grade (13) was 1.85 (median 1.62, range 0.7–4.52). Twelve patients underwent staged treatments (2 stages in 10 and 3 stages in 2 patients). The median prescription dose administered was 17Gy (range 15–20Gy) with the vast majority treated to the 50% isodose line.

No patient in the observation group underwent any treatments directed at the AVM nidus. One patient had a feeding artery aneurysm that was embolized while a second patient underwent embolization of an associated aneurysm.

Radiographic Outcomes

All patients in the surgery group underwent a post-operative angiogram. Per protocol, the majority of post-operative angiograms were obtained within three days of surgical resection. Longer intervals to post-operative angiography were required in patients not medically stable for angiography. For purposes of analyzing radiographic response to SRS, we only included post-treatment imaging performed after a latency period of ~3 years, which was available in 50% of the SRS patients. In this group, the mean time post-treatment imaging was 4 years (median 3.8 years, range 2.9–6 years) with angiography for 21 patients and an MRI for one. Of note, there were no post-SRS imaging studies performed within 3 years of treatment that showed complete obliteration of an AVM. Table 3 details the radiographic results based on initial treatment group (surgery or SRS). Among patients in the surgical and SRS groups, radiographic obliteration was achieved after initial treatment in 54%. Among these patients, 16 had repeat imaging after subsequent treatments (discussed below), bringing the overall obliteration rate to 63%. No AVM obliteration was observed on follow-up imaging in the observation group.

Univariate analysis identified several variables that were significantly associated with obliteration after the first treatment. Obliteration rates were higher in the surgical group (71%) compared to the SRS (23%) and observation (0%) groups (p<0.0002). Insular lesions were more likely to be completely obliterated (79%) than lesions in the basal ganglia or thalamus (54 and 31%, respectively, p=0.0021). AVMs with superficial venous drainage were more likely to be completely obliterated than those with deep drainage (92% versus 44%, p=0.0008). And finally, older patients were more likely to achieve complete obliterations compared to younger patients based on the Supplementary AVM age grade (48% age <20 years, 36% age 20–40 years, and 83% age >40, p=0.0066). A nominal logistic regression model comprising the variables identified in univariate analysis found treatment group (surgery versus SRS: OR 4.6, CI 1.04–23.8, p=0.044) and age (≤60 versus >60 years: OR 0.4, CI 0.17–0.86, p=0.018) as independent variables associated with radiographic outcome after AVM treatment.

Subsequent Treatments

Of the 38 patients in the surgical and SRS groups with radiographic documentation of residual AVM after their initial treatment, 24 underwent subsequent treatment at our institution (Figure 1). Four of these patients underwent a third round of treatment, while one patient ultimately underwent four separate treatments. Subsequent treatments were performed in eight patients from the surgical group and 16 patients from the SRS group. SRS was used in all eight surgical patients (mean target volume of $1.7cm^3$, median prescription dose of 18.25Gy, range 17–20Gy, treated to 50% isodose line in all but one patient). Follow-up imaging obtained approximately one-year post-SRS treatment was available in four of these patients and showed residual AVM in all. There was no longer-term imaging available for these patients. Salvage SRS was also used in 13 of the initial SRS treatment patients (mean target volume of $3.2cm^3$, median prescription dose of 18Gy, range 15–20Gy, ten treated to 50% isodose line, one patient staged). Follow-up imaging was available in 11 of these patients with three achieving complete obliteration. Surgery was used in the remaining three patients initially treated with SRS as well as an additional four patients who failed salvage SRS treatment. Surgery was deemed safe in these patients based on the presence of new hemorrhage or significant reduction of the AVM volume after prior SRS treatments. Complete resection was achieved in four of these patients. One of the patients with a subtotal resection went on to receive another round of salvage radiosurgery, but still had residual AVM at time of last imaging. Post-treatment hemorrhage led to subsequent treatment in three patients while the remaining patients were treated for residual AVM found on routine post-treatment imaging.

Functional Outcomes and Post-Treatment Hemorrhage

Median follow-up for the total population was 2.2 years (mean 3.2 years, ranging from immediately post-treatment to 14 years). Functional outcome status was available in 94 patients (97%) with 79% having good outcomes (RS 1–2) at time of last follow-up. Among the 92 patients who had both pre- and post-treatment RS scores available, 82% had either improved or remained unchanged at time of last follow-up compared to their pre-treatment functional status. Figure 2 compares the pre-treatment and post-treatment (time of last follow-up) RS distributions for the overall population as well as by initial treatment group. Of note, length of follow-up significantly differed among treatment groups (p<0.0001) with a median of 0.6 years in the surgical resection group (mean 1.3, range immediately post-op to 10 years), 4.1 years in the SRS group (mean 4.7, range immediately post-treatment to 14 years), and 3.2 years in the observation group (mean 4.3, range immediately after diagnostic angiogram to 13 years). Univariate analysis identified several factors associated with improved/unchanged functional status (versus worsened functional status) at time of last follow-up, including treatment group (surgery 95%, SRS 71%, observation 70%, p=0.006), pre-treatment RS (77% RS 1–2, 93% RS 3–5, p=0.047), Spetzler-Martin score (100% grade II, 79% grade III, 85% grade IV, and 43% grade V, p=0.015), and time to last follow-up (88% with follow-up ≤5 years and 58% with follow-up >5 years, p=0.006).Subsequent multivariate analysis of the total population incorporating significant factors identified by univariate analysis confirmed that a good functional outcome was associated with the Spetzler-Martin score (SMG 2–4 versus 5: OR 14.7, CI 1.8–178.6, p=0.01) and time to last follow-up (OR 0.03 for each increasing year, CI 0.002–0.4, p=0.008).

Post-treatment hemorrhage was recorded in 11 patients (11%); three patients (7%) in the surgical group and eight patients (18%) in the SRS group. In two patients treated with staged surgical resection, hemorrhage occurred after the first of two stages. In both instances, a gross total resection of the residual AVM was achieved during the second stage. An additional patient from the surgical resection group who had undergone a subtotal resection followed by SRS suffered a hemorrhage approximately nine months after their initial resection (and six months after SRS). This patient then underwent a second surgical resection during which a gross total resection was achieved. The remaining eight hemorrhages occurred in the initial SRS treatment group, with a median time to hemorrhage after initial SRS of 1.4 years (mean 2.5 years, range 3.2 months to seven years). One of these patients had failed their initial SRS treatment and undergone subsequent salvage SRS three years prior to hemorrhage. Two of these patients from the initial SRS group underwent subsequent surgical gross total resection. One patient from the initial SRS treatment group ultimately suffered three additional post-treatment hemorrhages. This patient had a Spetzler-Martin grade V bilateral thalamic AVM that was deemed inoperable. Given that her initial hemorrhages occurred during the post-SRS latency period, the decision was made to continue observation. This patient expired after the 4^{th} hemorrhage. Of note, there were no hemorrhages recorded in the observation group. Overall, the annual post-treatment hemorrhage rate after SRS was 3.9% (8 hemorrhages over 207.2 years).

There were seven recorded deaths among this population, ranging from 1.5–7 years after the initial treatment. Three deaths were directly attributable to a post-treatment hemorrhage while an additional death occurred within six months of a post-treatment hemorrhage. The cause of death is not known in the remaining three patients.

Discussion

This study demonstrates the application of a multidisciplinary approach to the treatment of basal ganglia, thalamic, and insular AVMs. As expected, most Spetzler-Martin and Supplementary grading scale variables significantly differed among initial treatment groups. Surgical resection was most often applied to smaller, compact AVMs in the insula with superficial drainage and hermorrhagic presentation. Conversely, observation was reserved mostly for larger AVMs of the basal ganglia and thalamus without hemorrhagic presentation. SRS was most often used for intermediate grade AVMs of the basal ganglia and thalamus. However, there was significant overlap between treatment groups, making such generalizations inexact. The Spetzler-Martin grading system does little more than distinguish the size of deep AVMs because they are typically eloquent and drain deeply. The Supplementary grading system adds an important anatomical component, namely nidal compactness or diffuseness, which is critical in the central core of the cerebral hemisphere. Furthermore, the Supplementary grade sizes up the patient, concisely quantitating their natural history risk, neurological condition, and recoverability with scores for hemorrhagic presentation and age. In general, older patients with unruptured AVMs and intact neurological exams are managed with observation or with SRS, whereas younger patients with ruptured AVMs and presenting deficits are selected for microsurgical resection. While the Spetzler-Martin and Supplementary AVM grading scales encompass universal AVM variables with known associations to surgical outcomes, there are other patient variables such as medical comorbidities and patient preferences that must also be considered when deciding upon treatment strategies. Unfortunately we were unable to analyze such factors in this study.

Overall, in our practice, we found surgical resection to have the greatest efficacy in terms of AVM obliteration. When choosing surgical resection, the potential risks of surgery are weighed against the natural history of an AVM. Rupture is the most devastating event that can occur in an untreated or incompletely treated AVM and deep-seated AVMs are reported to have rupture rates as high as 34% (2,20). In our series, there were no instances of hemorrhage after complete resection or obliteration of an AVM. Successful surgical resection thus immediately eliminates the risk of hemorrhage. The three instances of hemorrhage within the surgical treatment group occurred in patients who had residual AVM after their first operation. In the SRS group, eight patients suffered post-treatment hemorrhages – all with residual AVM. Prior series of deep AVMs treated with radiosurgery have reported annual post-treatment hemorrhage rates ranging from 1.3–9.5%, depending on size, location, prior history of hemorrhage, and time since radiosurgical treatment (1,5,10,14,17). It is important to note that the post-radiosurgical hemorrhage rates in our series and prior series are lower than the natural history of deep-seated AVMs.

Our overall obliteration rate in the SRS treatment after initial treatment was just 23% and increased to 45% after subsequent treatments (including seven patients who underwent subsequent surgical resection). This obliteration rate is below that of several prior series of radiosurgery for deep-seated AVMs. Three year obliteration rates have been reported from 57–68% (5,10), with overall obliteration rates as high as 81% (1,5,7,10,11,14). There are several variables that can account for such differences. In general, we tend to favor surgery versus radiosurgery, which leaves higher grade AVMs in the SRS treatment group. Examination of our treatment parameters also shows that our prescription doses tend to be lower than that of other reported series. In this series, the median marginal prescription dose was 17Gy while other large series have reported median marginal doses from 18–25Gy (5,7,11,14). Both size and marginal dose are known to be associated with AVM obliteration (3,5,7,10).

Although we show that surgical management is associated with superior obliteration rates, we do not see a similar effect with functional outcomes. In fact, functional outcome is more associated with the Spetzler-Martin grading scale and time to last follow-up. This finding suggests that our management strategy does in fact provide comparable functional outcomes for all patients and that surgical resection, radiosurgery, and observation all have their place in the treatment of deep-seated AVMs.

An important aspect of this study is our management of initial treatment failures. In general, incomplete surgical resection is managed with subsequent SRS. Partial or no response to initial SRS is most often treated with salvage SRS if the same risk factors precluding surgical resection are still present. If initial SRS resulted in sufficient reduction in AVM size, however, surgical resection can be considered. In addition, post-SRS hemorrhage often facilitates surgery by creating a route of access through the hematoma or separating the nidus from eloquent brain. Hemorrhage also diminishes the patient’s neurological condition such that surgical risks compare more favorably to natural history risks. These factors make surgical resection a viable and successful option, and are reflected in a Supplementary score that is lowered by post-SRS hemorrhage

This study has several limitations. While the timing of radiographic outcomes was fairly uniform within treatment groups (immediate post-operative period for surgical resection and 3–5 years post-treatment for SRS and observation), time to follow-up functional status was significantly variable, with shorter follow-up time for patients in the initial surgical resection group compared to SRS or observation. This makes it difficult to compare functional outcomes among treatment groups or to adequately analyze factors associated with functional outcome. Indeed, time to last follow-up was associated with functional outcomes. However, it is understandable that surgical patients, who were more likely to obtain cure of their AVMs, would not undergo as extensive long-term follow-up as patients treated with SRS or those followed with observation. In addition, we only had three-year radiographic follow-up in 50% of the SRS patients (compared to post-surgical radiographic follow-up in 100% of surgical patients). As a tertiary care center, patients often receive follow-up imaging and care at other institutions and we were not able to obtain more records. Finally, while we report 8 deaths within this population, it is not clear if all of these deaths were necessarily related to complications of AVM treatment. However, five of these deaths occurred in close enough proximity to AVM treatment or post-treatment hemorrhage that it can safely be assumed they were related.

Conclusion

This large series of deep AVMs demonstrates the importance of a multidisciplinary treatment approach. Supplementary grading, with its consideration of age, bleeding status, and compactness, added meaningfully to traditional Spetzler-Martin grading and guided treatment decisions. Treatment modality was significantly associated with radiographic obliteration, with surgical resection more likely to result in obliteration compared to SRS and observation. Overall functional status was improved or unchanged in this deep AVM population. This experience demonstrates that within the context of a multidisciplinary team, highly selected patients with deep AVMs can be treated microsurgically with satisfactory results.

Acknowledgments

This research is funded in part by the National Institutes of Health, R01 NS034949 (WLY) and P01 NS044155 (Center for Cerebrovascular Research).

Abbreviations

AVM	arteriovenous malformation
RS	Rankin scale
SRS	stereotactic radiosurgery

References

1. Andrade-Souza YM, Zadeh G, Scora D, Tsao MN, Schwartz ML. Radiosurgery for basal ganglia, internal capsule, and thalamus arteriovenous malformation: clinical outcome. Neurosurgery. 2005; 56(1):56–63. discussion 63–4, [PubMed: 15617586]
2. Fleetwood IG, Marcellus ML, Levy RP, Marks MP, Steinberg GK. Deep arteriovenous malformations of the basal ganglia and thalamus: natural history. J Neurosurg. 2003; 98(4):747–750. [PubMed: 12691399]
3. Flickinger JC, Kondziolka D, Maitz AH, Lunsford LD. An analysis of the dose-response for arteriovenous malformation radiosurgery and other factors affecting obliteration. Radiother Oncol. 2002; 63(3):347–354. [PubMed: 12142099]
4. Gross BA, Duckworth EAM, Getch CC, Bendok BR, Batjer HH. Challenging traditional beliefs: microsurgery for arteriovenous malformations of the basal ganglia and thalamus. Neurosurgery. 2008; 63(3):393–410. discussion 410–1, [PubMed: 18812951]
5. Hideyuki, Kano; Kondziolka, Douglas; Flickinger, John C.; Yang, Huai-che; Flannery, Thomas J.; Niranjan, Ajay; Novotny, Josef, Jr; Lunsford, L Dade. Stereotactic radiosurgery for arteriovenous malformations, Part 4: management of basal ganglia and thalamus arteriovenous malformations. J Neurosurg. 2012; 116:33–43. [PubMed: 22077451]
6. Kano H, Kondziolka D, Flickinger JC, Yang H-C, Flannery TJ, Awan NR, Niranjan A, Novotny J, Lunsford LD. Stereotactic radiosurgery for arteriovenous malformations, Part 3: outcome predictors and risks after repeat radiosurgery. J Neurosurg. 2012; 116(1):21–32. [PubMed: 22077445]
7. Kiran NAS, Kale SS, Kasliwal MK, Vaishya S, Gupta A, Singh Sharma M, Shankar Sharma B, Kumar Mahapatra A. Gamma knife radiosurgery for arteriovenous malformations of basal ganglia, thalamus and brainstem--a retrospective study comparing the results with that for AVMs at other intracranial locations. Acta Neurochir (Wien). 2009; 151(12):1575–1582. [PubMed: 19415175]
8. Lawton MT, Golfinos JG, Spetzler RF. The contralateral transcallosal approach: experience with 32 patients. Neurosurgery. 1996; 39(4):729–734. discussion 734–5, [PubMed: 8880765]
9. Lawton MT, Kim H, McCulloch CE, Mikhak B, Young WL. A supplementary grading scale for selecting patients with brain arteriovenous malformations for surgery. Neurosurgery. 2010; 66(4):702–713. discussion 713, [PubMed: 20190666]
10. Nagy G, Major O, Rowe JG, Radatz MWR, Hodgson TJ, Coley SC, Kemeny AA. Stereotactic Radiosurgery for Arteriovenous Malformations Located in Deep Critical Regions. Neurosurgery. 2011
11. Nicolato A, Foroni R, Crocco A, Zampieri PG, Alessandrini F, Bricolo A, Gerosa MA. Gamma Knife Radiosurgery in the Management of Arteriovenous Malformations of the Basal Ganglia Region of the Brain. Minim Invasive Neurosurg. 2002; 45(4):211–223. [PubMed: 12494356]
12. Perret G, Nishioka H. Report on the cooperative study of intracranial aneurysms and subarachnoid hemorrhage. Section VI. Arteriovenous malformations. An analysis of 545 cases of cranio-cerebral arteriovenous malformations and fistulae reported to the cooperative study. J Neurosurg. 1966; 25(4):467–490. [PubMed: 5925721]

13. Pollock BE, Flickinger JC. Modification of the Radiosurgery-Based Arteriovenous Malformation Grading System. Neurosurgery. 2008; 63(2):239–243. [PubMed: 18797353]

14. Pollock BE, Gorman DA, Brown PD. Radiosurgery for arteriovenous malformations of the basal ganglia, thalamus, and brainstem. J Neurosurg. 2004; 100(2):210–214. [PubMed: 15086226]

15. Potts MB, Chang EF, Young WL, Lawton MT. UCSF Brain AVM Study Project. Transsylvian-transinsular approaches to the insula and basal ganglia: operative techniques and results with vascular lesions. Neurosurgery. 2012; 70(4):824–834. discussion 834, [PubMed: 21937930]

16. Potts MB, Young WL, Lawton MT. For the UCSF Brain AVM Study Project. Deep Arteriovenous Malformations In the Basal Ganglia, Thalamus, and Insula: Microsurgical Management, Techniques, and Results. Neurosurgery. 2013

17. Sasaki T, Kurita H, Saito I, Kawamoto S, Nemoto S, Terahara A, Kirino T, Takakura K. Arteriovenous malformations in the basal ganglia and thalamus: management and results in 101 cases. J Neurosurg. 1998; 88(2):285–292. [PubMed: 9452237]

18. Shucart WA, Stein BM. Transcallosal approach to the anterior ventricular system. Neurosurgery. 1978; 3(3):339–343. [PubMed: 740132]

19. Spetzler RF, Martin NA. A proposed grading system for arteriovenous malformations. J Neurosurg. 1986; 65(4):476–483. [PubMed: 3760956]

20. Stapf C, Mohr JP, Pile-Spellman J, Solomon RA, Sacco RL, Connolly ES. Epidemiology and natural history of arteriovenous malformations. Neurosurg Focus. 2001; 11(5):e1. [PubMed: 16466233]

21. Waldron JS, Lawton MT. The supracarotid-infrafrontal approach: surgical technique and clinical application to cavernous malformations in the anteroinferior Basal Ganglia. Neurosurgery. 2009; 64(3 Suppl):86–95. discussion 95, [PubMed: 19050656]

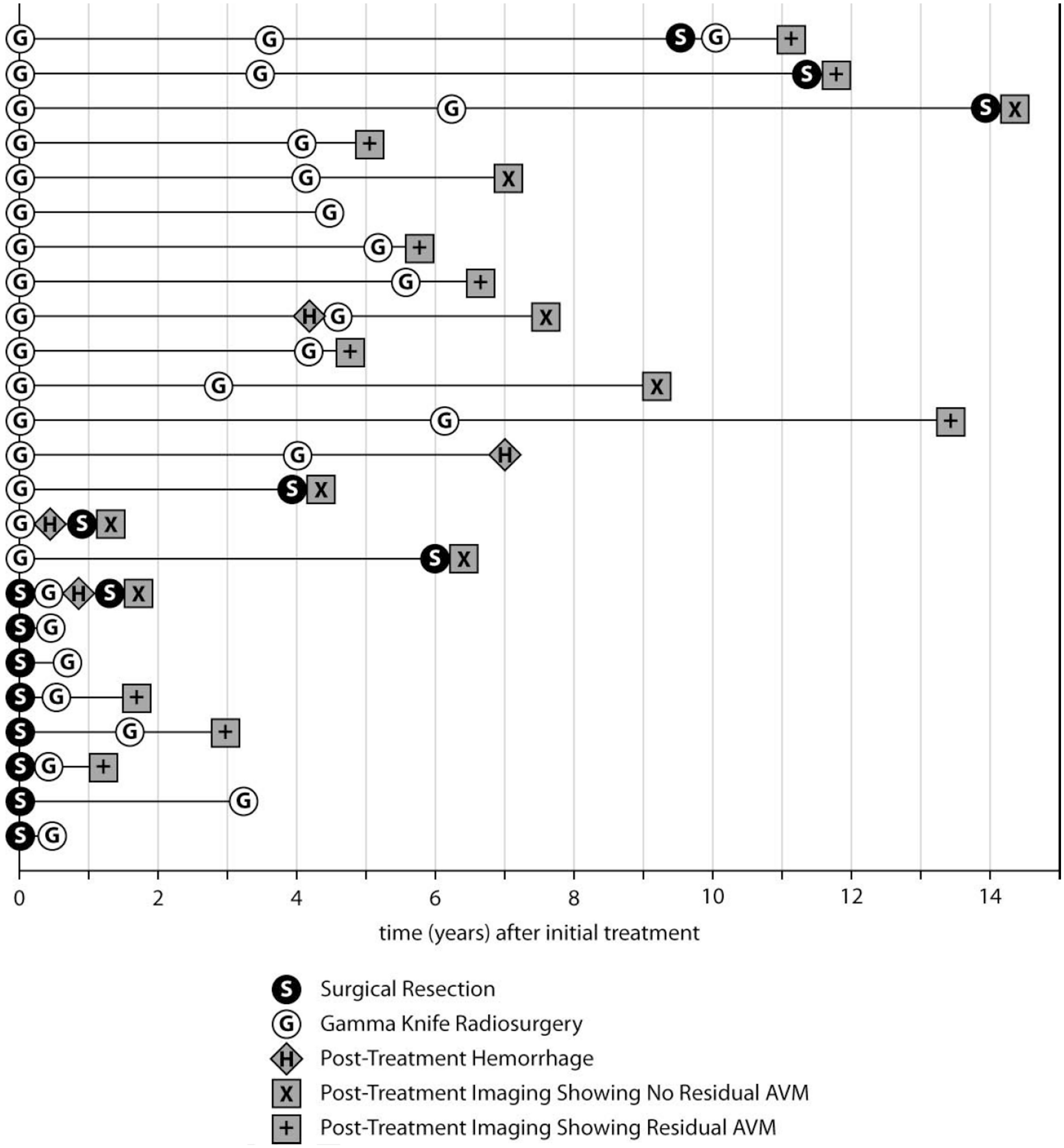

Figure 1. Treatment Course for Patients Undergoing Multiple Treatments

Twenty-four patients (16 from the SRS and 8 from the surgical resection treatment groups) underwent subsequent treatments after failure of their initial treatment. Each line represents one patient with the initial treatment shown at time 0. Post-treatment imaging results are shown only for those patients with imaging after their final treatment (i.e., prior imaging results have been excluded for clarity). Thirteen SRS patients were treated with salvage SRS while three underwent subsequent surgical resection. Residual AVM in all of the patients from the initial surgery group were treated with SRS.

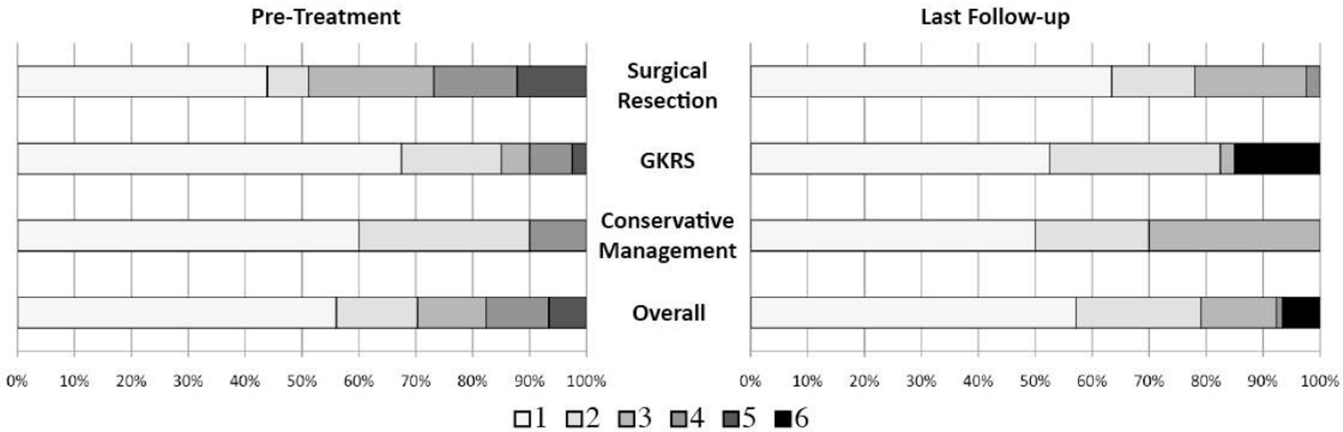

Figure 2. Pre-Treatment and Follow-up Functional Status Based on the Rankin Scale*

Pre-treatment and follow-up RS scores for each treatment group and the overall population.* Mean follow-up time for the overall population was 3.2y (median 2.2y) with mean follow-up times for the conservative treatment, SRS, and surgery groups of 4.1y, 4.8y, and 1.3y, respectively.

*based on the ninety-two patients with both pre-treatment and follow-up RS scores.

Table 1

Patient and AVM Characteristics Based on Initial Treatment

	Surgical Resection	SRS	Conservative	All	p-value
Total	41 (42%)	44 (45%)	12 (12%)	97	
Mean age (yrs ± SD)	29.9 ± 17	30.6 ± 18.7	44.2 ± 20.2	32 ± 18.6	**0.049**
Gender					0.2
Female	17 (41%)	25 (57%)	4 (33%)	46 (47%)	
Male	24 (59%)	19 (43%)	8 (67%)	51 (53%)	
Presentation					**0.035**
Hemorrhage	31 (75%)	28 (64%)	3 (25%)	62 (64%)	
Focal Deficit	1 (2%)	6 (14%)	1 (8%)	8 (8%)	
Seizure	4 (10%)	5 (11%)	2 (17%)	11 (11%)	
Headache	3 (7%)	3 7%)	2 (17%)	8 (8%)	
Incidental	2 (5%)	1 (2%)	2 (17%)	5 (5%)	
Enlarging Head Circ.	0	1 (2%)	0	1 (1%)	
Unknown	0	0	2 (17%)	2 (2%)	
Location					**<0.0001**
Basal Ganglia	8 (20%)	15 (34%)	5 (42%)	28 (29%)	
Thalamus	9 (22%)	26 (59%)	5 (42%)	40 (41%)	
Insula	24 (59%)	3 (7%)	2 (17%)	29 (30%)	
Side					0.41
Left	21 (51%)	29 (66%)	6 (50%)	56 (58%)	
Right	19 (46%)	13 (30%)	6 (50%)	38 (39%)	
Bilateral	1 (2%)	2 (5%)	0	3 (3%)	
Pre-Treatment RS*					**0.017**
1	18 (44%)	29 (69%)	7 (63%)	54 (58%)	
2	3 (7%)	7 (17%)	3 (27%)	13 (14%)	
3	9 (22%)	2 (5%)	0	11 (12%)	
4	6 (15%)	3 (7%)	1 (9%)	10 (11%)	
5	5 (12%)	1 (2%)	0	6 (6%)	

SRS = stereotactic radiosurgery

SD = standard deviation

Circ. = circumference

* Pre-treatment RS values were not available for 3 patients (2 in the SRS group and 1 in the conservative management group). The denominator for percentage calculations was therefore adjusted accordingly.

Table 2

Spetzler-Martin and Supplementary Arteriovenous Malformation Grading

	Surgical Resection (n=41)	SRS (n=44)	Conservative (n=12)	All (n=97)	p-value
Spetzler-Martin Grade					
AVM Size (cm)					**0.001**
<3	27 (66%)	21 (48%)	2 (17%)	50 (52%)	
3–6	14 (34%)	20 (45%)	6 (50%)	40 (41%)	
>6	0	3 (7%)	4 (33%)	7 (7%)	
Venous Drainage					**0.0004**
Superficial	13 (32%)	1 (2%)	1 (8%)	15 (15%)	
Deep	28 (68%)	43 (98%)	11 (92%)	82 (85%)	
Eloquence					0.76
No	1 (2%)	1 (2%)	0	2 (2%)	
Yes	40 (98%)	43 (97%)	12 (100%)	95 (98%)	
Spetzler-Martin Grade					**<0.0001**
I	0	0	0	0	
II	9 (22%)	2 (5%)	1 (8%)	12 (12%)	
III	23 (56%)	19 (43%)	1 (8%)	43 (44%)	
IV	9 (22%)	20 (45%)	6 (50%)	35 (36%)	
V	0	3 (7%)	4 (33%)	7 (7%)	
Supplementary Grade					
Age at Treatment (yrs)					0.14
<20	14 (34%)	14 (32%)	3 (25%)	31 (32%)	
20–40	13 (32%)	17 (39%)	1 (8%)	31 (32%)	
>40	14 (34%)	13 (30%)	8 (67%)	35 (36%)	
Hemorrhagic Presentation					**0.006**
Ruptured	31 (76%)	28 (64%)	3 (25%)	62 (64%)	
Unruptured	10 (24%)	16 (36%)	9 (75%)	35 (36%)	
Compactness*					**0.038**
Compact	37 (90%)	36 (82%)	6 (55%)	79 (82%)	

	Surgical Resection (n=41)	SRS (n=44)	Conservative (n=12)	All (n=97)	p-value
Diffuse	4 (10%)	8 (18%)	5 (45%)	17 (17%)	
Supplementary Grade*					0.059
I	11 (27%)	8 (18%)	0	19 (20%)	
II	14 (34%)	16 (36%)	1 (9%)	31 (32%)	
III	8 (20%)	10 (23%)	3 (27%)	21 (22%)	
IV	7 (17%)	9 (20%)	4 (63%)	23 (24%)	
V	1 (2%)	1 (2%)	0	2 (2%)	
Supplemented Spetzler-Martin Grade					
Combined Grade*					**<0.0001**
II	0	0	0	0	
III	0	0	0	0	
IV	13 (32%)	5 (11%)	0	18 (19%)	
V	9 (22%)	10 (23%)	0	19 (20%)	
VI	12 (29%)	17 (39%)	2 (18%)	31 (32%)	
VII	6 (15%)	4 (9%)	0	10 (10%)	
VIII	1 (2%)	6 (14%)	8 (73%)	15 (16%)	
IX	0	1 (2%)	1 (9%)	2 (2%)	
X	0	1 (2%)	0	1 (1%)	

Table 3

Summary of microsurgical approaches used based on AVM location

Microsurgical Approach	Basal Ganglia	Thalamus	Insula	Total
Transsylvian	5 (12%)	0	23 (56%)	28 (68%)
Transinsular – Anterior	2 (5%)	0	9 (22%)	11 (27%)
Transinsular – Posterior	2 (5%)	0	14 (34%)	16 (39%)
Supracarotid-Infrafrontal	1 (2%)	0	0	1 (2%)
Transcallosal				6 (15%)
Contralateral	2 (5%)	0	0	2 (5%)
Transchoroidal	0	3 (7%)	0	3 (7%)
Posterior	0	1 (2%)	0	1 (2%)
Transcortical	1 (2%)	5 (12%)	1 (2%)	7 (17%)
Transfrontal	1 (2%)	0	0	1 (2%)
Transtemporal	0	3 (7%)	1 (2%)	4 (10%)
Transparietal	0	2 (5%)	0	2 (5%)

Percentages expressed as total number of surgical patients (n=41)

Table 4

Radiographic Outcomes*

	Surgical Resection	Radiosurgery‡	All
Number of Patients	41 (100%)	22 (50%)	63
After initial treatment*			
No Residual AVM	29 (71%)	5 (23%)	34 (54%)
Residual AVM	12 (29%)	17 (77%)	29 (46%)
Mean Time to Imaging	3 days	4 years	---
After all treatments§			
No Residual AVM	30 (73%)	10 (45%)	40 (63%)
Residual AVM	11 (27%)	12 (55%)	23 (37%)

*Includes one patient with a post-SRS MRI instead of angiogram

†Includes only post-SRS images obtained ~3 or more years after treatment (range 2.9 – 6 years post-SRS). Of note, all imaging studies performed on SRS patients prior to 3 years post-treatment showed residual AVM.

‡(%) indicates the percentage of patients in each initial treatment group with radiographic follow-up.

§Includes the last recorded imaging result for each patient, including those who underwent subsequent treatments.