Outcomes of Multimodality Therapy in Pediatric Patients With Ruptured and Unruptured Brain Arteriovenous Malformations

BACKGROUND: Brain arteriovenous malformations (BAVMs) are a frequent cause of pediatric hemorrhagic stroke, which frequently results in significant morbidity and mortality.

OBJECTIVE: To analyze the results of multimodality treatment for a consecutive series of pediatric patients with ruptured and unruptured BAVMs at a single institution.

METHODS: Forty patients, 18 years of age were retrospectively reviewed. Results were divided by hemorrhage status, ie, ruptured or unruptured, and the intended curative treatment modality, ie, surgical resection or stereotactic radiosurgery.

RESULTS: Twenty-seven patients (68%) presented with hemorrhage, and 13 patients (32%) presented without hemorrhage. Among ruptured patients, 19 (70%) underwent surgery and 8 (30%) underwent stereotactic radiosurgery. In surviving patients, 23 of 26 (88%) had a modified Rankin Scale (mRS) score of 0 to 2 at the last follow-up, and 24 of 26 (92%) obtained radiographic cure. For unruptured BAVMs, all 6 patients with grade I to III BAVM obtained radiographic cure and had an mRS score of 0 to 1 at the last follow-up, whereas 1 of 5 patients (20%) with grade IV and V BAVM had BAVM obliteration and a mean mRS score of 1.8 at the last follow-up. In a total of 93.6 years of follow-up from date of presentation to last clinical follow-up, there was 1 hemorrhage (1.1%/y). Of 30 patients with radiographic obliteration, 2 patients had radiographic recurrence (7% incidence).

CONCLUSION: The majority of ruptured patients had an mRS score of 0 to 2 at the last follow-up and obtained radiographic cure. Unruptured patients with grade I to III BAVMs had superior outcomes compared with those with grade IV and V AVMs. Treatment of grade I to III BAVMs appears safe, and additional study is needed to determine optimal strategies for the management of unruptured grade IV and V BAVMs.

KEY WORDS: Brain arteriovenous malformations, Clinical outcome, Microsurgical resection, Stereotactic radiosurgery, Pediatrics

ABBREVIATIONS: ARUBA, A Randomized Trial of Unruptured Brain Arteriovenous Malformations; BAVM, brain arteriovenous malformation; RBAS, radiosurgery-based brain arteriovenous malformation grading system; mRS, modified Rankin Scale; SAIVM, Scottish Audit of Intracranial Vascular Malformations; SRS, stereotactic radiosurgery; WFNS, World Federation of Neurosurgical Societies

Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal’s Web site (www.neurosurgery-online.com).
these reasons, early, aggressive treatment for pediatric ruptured BAVMs is usually appropriate, especially in patients with risk factors for early rebleeding.7

The management of unruptured pediatric BAVMs is less defined in the literature; however, this age group was not included in A Randomized Trial of Unruptured Brain AVMS (ARUBA).8 Two recent retrospective studies have shown that excellent clinical outcomes and high obliteration rates can be obtained in ARUBA-eligible patients, especially in Spetzler-Martin grade I to II BAVMs treated with surgical resection.9,10 Stereotactic radiosurgery (SRS) may represent another acceptable treatment modality for pediatric BAVMs, especially in patients with excessive surgical risk.11

Treatment modalities for pediatric BAVMs include surgical resection, SRS, endovascular embolization, or combination, multimodality therapy. The purpose of this study was to review treatment outcomes with the multimodal management of ruptured and unruptured pediatric BAVMs.

METHODS

This retrospective study was approved by the University of Washington Institutional Review Board Human Subjects Division. At our institution, 46 consecutive patients <18 years of age with BAVMs were treated from 2005 to 2012, which represented 17% of patients treated during this time frame. Patients with age <5 years, vein of Galen malformations, dural arteriovenous fistulas, and spinal vascular malformations were excluded. Six patients with treatment before 2005 or treatment at other institutions before referral to our institution were also excluded because of the limited availability of clinical data, leaving 40 patients for statistical analysis. Analysis of diagnosis and treatment coding data was used to develop the patient list, and the database was developed from a retrospective review of electronic medical records. Data were obtained for clinical presentation, BAVM anatomical characteristics, treatment modalities, complications, and radiographic and clinical outcomes. The Spetzler-Martin grading scale was used to grade and analyze BAVMs.12 Deep location was defined as any involvement of the brainstem, basal ganglia, insula, or thalamus.

Treatment

The BAVM management strategy at our institution has been previously described.10 A multidisciplinary team of dual-trained cerebrovascular neurosurgeons (L.J.K., L.N.S.), interventional neuroradiologists (D.K.H., B.V.G.), and a radiation oncologist (J.K.R.) were involved in management decisions. Overall, surgical resection was typically offered for pediatric patients with Spetzler-Martin grade I and II BAVMs and Spetzler-Martin grade III BAVMs with lobar location. SRS with a Gamma Knife (Elekta, Stockholm, Sweden) was generally reserved for patients with excessive surgical risk, including Spetzler-Martin grade IV and V BAVMs and BAVMs with a deep location, as well as for residual or recurrent BAVMs after surgical resection. Endovascular embolization with Onyx (ev3 Neurovascular, Irvine, California) was performed primarily as adjunctive therapy for volume reduction or elimination of high-risk features before surgical resection or SRS. Coil embolization was also performed as indicated for associated aneurysms.

Clinical and Radiographic Outcomes

The World Federation of Neurosurgical Societies (WFNS) subarachnoid hemorrhage grading scale was used to grade pretreatment clinical status at presentation in patients who presented with ruptured BAVMs. The modified Rankin Scale (mRS) was used to grade pretreatment clinical status in unruptured BAVMs and posttreatment clinical outcome in both ruptured and unruptured cohorts. The WFNS and mRS scores were obtained retrospectively from a review of electronic medical records. Complications were defined as posttreatment hemorrhage, return to operating room, any posttreatment neurological deficit, supportive therapy for adverse radiation effects, and posttreatment mortality. The last time point of clinical follow-up was used to determine follow-up length after treatment. Radiographic obliteration was defined as no evidence of residual BAVM on posttreatment imaging, including computed tomographic angiography, magnetic resonance angiography (MRA), or diagnostic cerebral angiography. Radiographic response after SRS was defined as decreased BAVM nidus size on follow-up imaging.

Statistical Analysis

Statistical analysis was completed with IBM SPSS Statistics 19. Statistical significance was defined as a value of $P < .05$, and adjustments were not made for multiple comparisons. Significance of association was tested with the independent-samples $t$ test and the Fisher exact test as appropriate. The Mann-Whitney test was used to test significance of association with Spetzler-Martin comparisons. One patient with Wyburn-Mason syndrome and a diffuse grade V unruptured BAVM treated with palliative embolization was excluded from statistical comparisons regarding BAVM morphology and treatment. Results for clinical presentation, management strategies, clinical outcome, and radiographic outcome were categorized by hemorrhage status, ie, ruptured or unruptured BAVMs.

RESULTS

Our institution treated 46 pediatric patients with BAVMs from 2005 to 2012. To define our institution’s management strategy, 6 patients were excluded from analysis because treatment was initiated before 2005 or at outside institutions and records from the initial presentation were unavailable. Patient and BAVM characteristics are detailed in Table 1. Treatment modalities are listed in Table 2. Overall obliteration rate, mean last follow-up mRS score, and complication rate by Spetzler-Martin grade, rupture status, and treatment modality are listed in Table 3. In the sections that follow, results are divided by hemorrhage status, ie, ruptured or unruptured, as well as by the intended curative treatment modality, ie, surgical resection or SRS. Unruptured BAVMs on average had higher Spetzler-Martin grades ($P = .08$), likely because of their larger nidus size (4.1 cm [SD, 1.8 cm] vs 2.4 cm [SD, 1.2 cm]; $P = .004$; Table 1). On average, more ruptured patients were treated with surgical resection compared with unruptured patients, but this difference did not reach statistical significance (19 of 27 [70%] vs 6 of 12 [50%]; $P = .29$). After exclusion of 1 patient with Wyburn-Mason syndrome and a diffuse grade V unruptured BAVM who underwent treatment with palliative embolization and shunt placement, treatment modalities by location and intended curative modality were as
follows: 22 of 31 (71%) lobar BAVMs were treated with surgical resection; 4 of 5 (80%) deep BAVMs were treated with SRS; and 2 of 3 (67%) cerebellar BAVMs were treated with surgical resection. Surgery without and with embolization was the intended curative modality for 8 of 8 (100%) grade I, 5 of 7 (71%) grade II, 8 of 14 (57%) grade III, 3 of 8 (38%) grade IV, and 0 of 2 grade V BAVMs. For grade III BAVMs, 8 of 10 (80%) with a lobar location underwent surgical resection, whereas 0 of 4 with a deep location or deep component underwent surgery.

Ruptured BAVMs

Twenty-seven of 40 patients (68%) had a history of BAVM hemorrhage and were treated during the study period. Patient and BAVM characteristics are detailed in Table 1. The mean WFNS score at presentation was 3.5. The mean maximum size was 2.4 cm (SD, 1.1 cm; range, 0.9-4.6 cm). Spetzler-Martin grades were as follows: I, 26%; II, 19%; III, 37%; and IV, 15%. Treatment modalities are listed in Table 2 and detailed below. Overall results are listed in Table 3.

Surgical Resection

Surgical resection without and with preoperative embolization was used as the intended curative modality in 19 patients (70%). Three patients underwent emergent decompression on presentation. Treatment was initiated during the initial hospitalization at a mean of 4.0 days, and 16 of 19 patients (84%) underwent surgical resection during their initial hospitalization. Three patients (16%) underwent resection after initial discharge (mean time to resection, 20 days; range 5-48 days). By Spetzler-Martin grade, surgical resection was performed in 7 of 7 (100%) grade I, 4 of 5 (80%) grade II, 5 of 10 (50%) grade III, and 2 of 4 (50%) grade IV patients. Spetzler-Martin data were not available for 1 patient who underwent emergent decompression. Sixteen of 19 patients (84%) with ruptured lobar BAVMs underwent surgery. One grade III patient underwent SRS postoperatively for known deep residual BAVM seen during resection. One grade IV patient underwent SRS after recurrent BAVM was identified 1.5 years after surgical cure (detailed below in Recurrent BAVMs and Illustrative Cases).

The mean WFNS score was 4.0 (SD, 0.94; range 2-5). There were 3 complications (16% patients). The mortality occurred in a grade IV patient who presented with WFNS 5 and underwent emergent decompression on presentation, and the family later withdrew care. Two patients returned to the operating room for bone flap removal secondary to postoperative cerebral edema. In surviving patients, the mean follow-up was 1.6 years (SD, 1.5 years; range, 0.04-5.7), and the last follow-up mRS scores were as follows: 0, 6 patients (33%); 1, 5 (28%); 2, 4 patients (22%); 3, 1 patient (6%); and 4, 2 patients (11%). There were no statistically significant differences in impaired functional outcome, defined as last follow-up mRS score >1 and >2 based on presentation WFNS score ($P = .49$ and $P = .15$), respectively. Eighteen of 19 patients (95%) obtained immediate radiographic cure, and all patients had radiographic cure at the last follow-up. There were no recurrent hemorrhages in 29.3 patient-years of follow-up.

**TABLE 1. Patient and Brain Arteriovenous Malformation Characteristics**

<table>
<thead>
<tr>
<th></th>
<th>Ruptured BAVMs</th>
<th>Unruptured BAVMs</th>
<th>$P$ Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients, n (%)</td>
<td>27 (68)</td>
<td>13 (33)</td>
<td></td>
</tr>
<tr>
<td>Age (SD), y</td>
<td>11.3 (3.6)</td>
<td>11.9 (3.3)</td>
<td>.57</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>10 (37)</td>
<td>4 (31)</td>
<td>&gt;.99</td>
</tr>
<tr>
<td>Presentation WFNS (ruptured), n (%)</td>
<td>3 (11)</td>
<td>2 (7)</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>7 (26)</td>
<td>8 (30)</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td></td>
<td>7 (26)</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Presentation mRS (unruptured), n (%)</td>
<td>5 (39)</td>
<td>6 (46)</td>
<td>.99</td>
</tr>
<tr>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td></td>
<td>1 (8)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td></td>
<td>1 (8)</td>
<td></td>
</tr>
<tr>
<td>Spetzler-Martin grade, n (%)</td>
<td>7 (26)</td>
<td>1 (8)</td>
<td>.08</td>
</tr>
<tr>
<td>I</td>
<td>7 (26)</td>
<td>1 (8)</td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>5 (19)</td>
<td>2 (15)</td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>10 (37)</td>
<td>4 (31)</td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>4 (15)</td>
<td>4 (31)</td>
<td></td>
</tr>
<tr>
<td>V</td>
<td></td>
<td>2 (15)</td>
<td></td>
</tr>
<tr>
<td>AVM morphology(d)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean maximum diameter (SD), cm</td>
<td>2.4 (1.1)</td>
<td>4.1 (1.8)</td>
<td>.004</td>
</tr>
<tr>
<td>Eloquent location, n (%)</td>
<td>16 (59)</td>
<td>6 (54)</td>
<td>.73</td>
</tr>
<tr>
<td>Deep venous drainage, n (%)</td>
<td>12 (44)</td>
<td>9 (75)</td>
<td>.16</td>
</tr>
</tbody>
</table>

*AVM, arteriovenous malformation; BAVM, brain arteriovenous malformation; mRS, modified Rankin Scale.
\(a\)Detailed BAVM data were available for 26 of 27 ruptured BAVMs. Significance was determined by the Fisher exact test unless otherwise noted.
\(b\)Significance was determined by the Mann-Whitney test.
\(c\)Significance was determined by log-transformed \(t\) test.

**TABLE 2. Treatment Modalities**

<table>
<thead>
<tr>
<th></th>
<th>Ruptured BAVMs, n (%)</th>
<th>Unruptured BAVMs, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgery alone</td>
<td>8 (30)</td>
<td>1 (8)</td>
</tr>
<tr>
<td>Preoperative embolization and surgery</td>
<td>9 (33)</td>
<td>4 (31)</td>
</tr>
<tr>
<td>Radiosurgery alone</td>
<td>6 (22)</td>
<td>5 (39)</td>
</tr>
<tr>
<td>Preoperative embolization and radiosurgery</td>
<td>2 (7)</td>
<td>1 (8)</td>
</tr>
<tr>
<td>Embolization alone</td>
<td>---</td>
<td>1 (8)</td>
</tr>
<tr>
<td>Surgery and radiosurgery</td>
<td>1 (4)</td>
<td>---</td>
</tr>
<tr>
<td>All modalities</td>
<td>1 (4)</td>
<td>1 (8)</td>
</tr>
</tbody>
</table>

*BAVM, brain arteriovenous malformation.
Stereotactic Radiosurgery

SRS without and with pretreatment embolization was used as the intended curative modality in 8 patients (30%). The mean time to SRS treatment in the 6 patients who did not undergo embolization was 3.8 months (range, 1.1-7.4 months). Embolization for high-risk features and source of hemorrhage was used at a mean time to treatment of 3.7 days in 2 patients. By Spetzler-Martin grade, SRS was used to treat 1 of 5 (20%) grade II, 5 of 10 (50%) grade III, and 2 of 4 (50%) grade IV patients. Two of 3 patients (67%) undergoing SRS with lobar BAVMs (1 grade III, 1 grade IV) had a dominant temporal lobe BAVM location. Two patients underwent volume-staged SRS. One patient underwent embolization of an intranidal aneurysm seen on follow-up imaging after volume-staged SRS.

The mean WFNS score was 2.4 (SD, 1.3; range, 1-4). There were 3 complications (38%); all were transient neurological deficits secondary to post-SRS cerebral edema that occurred at a mean time of 6.3 months after SRS and resolved on follow-up. The mean follow-up length was 2.7 years (SD, 1.3 years; range, 0.93-5.3 years), and the last follow-up mRS scores were 0 in 2 patients (25%), 1 in 3 patients (38%), and 2 in 3 patients (38%). Six of 8 patients (75%) achieved a radiographic cure with a mean time to cure of 2.2 years (SD, 0.94 years; range, 0.87-3.4 years).

The 2 patients awaiting radiographic obliteration were <3 years removed from SRS and had evidence of response on last follow-up imaging. In 10 total SRS treatments, the mean margin dose was 18.2 Gy (SD, 2.3 Gy; range, 16-22 Gy). In the 8 patients, the mean BAVM volume treated was 6.4 mL (SD, 6.1 mL; range, 0.12-17.2 mL).

The modified radiosurgery-based BAVM grading system (RBAS) was calculated (0.1 \cdot \text{volume in mL}^{0.2} \cdot \text{age in years}^{0.5} \cdot \text{location [1 point for basal ganglia/thalamus/brainstem]}).^{13} The mean modified RBAS score was 1.1 (SD, 0.58; range, 0.38-2.02). Mean modified RBAS scores were significantly higher in patients without radiographic cure (2.0 vs 0.85; \(P = .009\)). Mean modified RBAS scores were higher but not statistically different for patients with and without complications (1.4 vs .0.94, respectively; \(P = .30\)). There were no recurrent hemorrhages before or after SRS with 21.5 patient-years of follow-up.

Summary of Ruptured BAVMs

On the basis of the intended curative treatment modality, mean WFNS scores on presentation were significantly higher in surgical patients compared with SRS patients (mean, 4.0 vs 2.4; \(P = .001\)); however, mean mRS scores in all patients at the last follow-up were not statistically significant (1.6 vs 1.1, respectively;
Spetzler-Martin grades were significantly higher in patients undergoing SRS as the intended curative modality ($P = .48$). There were no significant differences in incidence of eloquence ($P = .42$) or mean maximum diameter ($P = .65$) between the SRS and surgery cohorts; however, more SRS patients had evidence of deep venous drainage (88% vs 28%; $P = .009$; Table 4). There was a trend for longer follow-up in SRS patients (2.7 vs 1.5 years, respectively; $P = .07$). There were no recurrent hemorrhages in patients awaiting treatment or after treatment in 57.9 years of follow-up after presentation. Regardless of treatment modality, the majority of surviving patients (23 of 26, 88%) had mRS scores of 0 to 2 at the last follow-up and obtained radiographic obliteration of the BAVM (24 of 26, 92%).

### Unruptured BAVMs

Thirteen of 40 patients (32%) did not have a history of BAVM hemorrhage and were treated during the study period. Patient and BAVM characteristics are detailed in Table 1. Eleven patients (85%) have an mRS score of 0 to 1. Presenting symptoms included seizure (5 patients, 39%), neurological deficit (4, 31%), headache (3, 23%), and incidental findings (5, 39%). The mean maximum size was 4.4 cm (SD, 1.9 cm; range, 1.1-7.8 cm). Spetzler-Martin grades were as follows: I, 1 patient (8%); II, 2 patients (15%); III, 4 patients (31%); IV, 4 patients (31%); and V, 2 patients (15%). Treatment modalities are listed in Table 2 and detailed below. Overall results are listed in Table 3. One patient with Wyburn-Mason syndrome and a grade V BAVM presented with an mRS score of 3 with hemiparesis was treated with palliative embolization alone.

#### Surgical Resection

Surgical resection without and with preoperative embolization was used as the intended curative modality in 6 patients (50%). Five patients (83%) had Spetzler-Martin grades I, II, and III BAVMs (1, 1, and 3 patients, respectively); 1 patient had a grade IV BAVM. All BAVMs had a lobar location. Complications occurred in 2 patients (33%): transient lower-extremity weakness in a patient with grade III BAVM after surgical resection and persistent hemiparesis in the patient with grade IV BAVM from an ischemic stroke during embolization resulting in mRS 3 functional status. All grade I to III patients presented with mRS scores of 0 to 1, had mRS scores of 0 to 1 at the last follow-up, and obtained radiographic cure. The grade IV patient had a recurrent nidus adjacent to the resection cavity seen on angiography 4.5 years after she represented with seizure; after SRS, the patient had a persistent early draining vein with a small nidus at the 3-year follow-up (detailed below in Recurrent BAVMs and Illustrative Cases). Mean follow-up after the last treatment was 1.4 years (SD, 1.0 years; range, 0.18-2.9 years).

### Stereotactic Radiosurgery

SRS without and with pretreatment embolization was used as the intended curative modality in 6 patients (50%). One patient with an incidental grade II lobar BAVM presented an mRS score of 0, achieved radiographic obliteration at 2.0 years, and had an mRS score of 0 at the last follow-up. One patient with a grade III BAVM was lost to follow-up after SRS. The remaining 4 patients were in grade IV (3 patients) and grade V (1 patient), and 3 patients (75%) presented with seizures or neurological deficits. The grade IV patients presented with mRS scores of 0 to 1, had radiographic response on the last imaging without cure, and had mRS scores of 0 to 1 at the last follow-up (mean, 2.1 years; SD, 0.1 year). Two grade IV patients required prolonged courses of steroids for headaches secondary to cerebral edema 4 and 6 months after SRS, and another developed posttreatment seizures. The grade V

### Table 4. Comparison of Brain Arteriovenous Malformation Morphology Between Stereotactic Radiosurgery and Surgery for Ruptured and Unruptured Brain Arteriovenous Malformations

<table>
<thead>
<tr>
<th></th>
<th>Ruptured BAVMs</th>
<th>Unruptured BAVMs</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>SRS</td>
<td>Surgery</td>
</tr>
<tr>
<td>Patients, n (%)</td>
<td>8 (30)</td>
<td>19 (70)</td>
</tr>
<tr>
<td>Spetzler-Martin grade, n (%)</td>
<td>I</td>
<td>0 (0)</td>
</tr>
<tr>
<td></td>
<td>II</td>
<td>1 (13)</td>
</tr>
<tr>
<td></td>
<td>III</td>
<td>5 (63)</td>
</tr>
<tr>
<td></td>
<td>IV</td>
<td>2 (25)</td>
</tr>
<tr>
<td></td>
<td>V</td>
<td>0 (0)</td>
</tr>
<tr>
<td>AVM morphology</td>
<td>Mean maximum diameter (SD), cm$^d$</td>
<td>2.7 (1.5)</td>
</tr>
<tr>
<td></td>
<td>Eloquent location, n (%)</td>
<td>6 (75)</td>
</tr>
<tr>
<td></td>
<td>Deep venous drainage, n (%)</td>
<td>7 (88)</td>
</tr>
</tbody>
</table>

$^a$AVM, arteriovenous malformation; BAVM, brain arteriovenous malformation; SRS, stereotactic radiosurgery.  
$^b$Detailed BAVM data were available for 26 of 27 ruptured BAVMs. Significance was determined by the Fisher exact test unless otherwise noted.  
$^c$Significance was determined by the Mann-Whitney test.  
$^d$Significance was determined by log-transformed t test.
patient underwent 3 stages of embolization before volume-staged SRS, developed transient weakness 2.1 years after SRS, and then sustained BAVM hemorrhage from an untreated venous varix 1.4 years later, resulting in poor neurological condition (mRS score, 5). This patient later underwent subsequent endovascular embolization for the varix and nidus with coils and Onyx. The mean modified RBAS score was 2.67 (SD, 2.3; range, 0.26-6.46). In 8 total SRS treatments, the mean margin dose was 17.5 Gy (SD, 1.7 Gy; range, 15-20 Gy). In the 6 patients, the mean BAVM volume treated was 24.8 mL (SD, 23.1 mL; range, 0.695-63.1 mL).

Summary of Unruptured BAVMs

In 11 patients who completed treatment, there were no significant differences between surgical resection (6 patients) and SRS (5 patients) in maximum BAVM diameter (3.7 cm vs 4.5 cm, respectively; \( P = .47 \)), presentation mRS score (0.5 vs 0.8; \( P = .49 \)), last follow-up mRS score (0.7 vs 1.2; \( P = .62 \)), and mean length of follow-up (1.4 vs 1.8 years; \( P = .42 \)). In all unruptured patients, there was a trend for a higher Spetzler-Martin grade in patients undergoing SRS as the intended curative modality (\( P = .13 \); Table 4). Mean maximum diameter (\( P = .72 \)) and incidence of deep venous drainage (\( P > .99 \)) were similar between the SRS and surgery cohorts (Table 4). On average, more SRS patients had BAVMs in eloquent locations (83% vs 17%; \( P = .08 \); Table 4). All 6 grade I to III patients with follow-up achieved radiographic cure and had mRS scores of 0 to 1 at the last follow-up. One of 5 grade IV and V patients (20%) achieved radiographic cure during follow-up, and 4 of 5 patients (80%) sustained a complication from treatment. The mean mRS score at the last follow-up was 1.8. Three complications brought about transient neurological deficits, resulting in mRS scores of 0 and 1; however, 1 patient had posttreatment hemorrhage, resulting in an mRS score of 5. The other complication resulted in an mRS score of 3 after ischemic stroke from embolization. In 35.7 patient-years of follow-up from time of presentation to last clinical follow-up, there was 1 hemorrhage.

Recurrent BAVMs and Illustrative Cases

In this series, there were 2 cases of recurrence, which are detailed below.

Case 1

The patient was an 8-year-old girl who presented with seizure and headaches and disabling vertigo and was found to have an unruptured grade IV right frontoparietal BAVM involving motor and sensory cortex (Figure 1A). The patient’s family was counseled preoperatively about the lifelong risk of hemorrhage and that, given her young age, she would be more likely to recover from any neurological deficits after treatment. She underwent 4 sessions of preoperative endovascular embolization with Onyx for volume reduction before surgery (approximately 70%); however, session 3 was complicated by left-sided hemiparesis. She underwent surgical resection. The craniotomy was fashioned to include exposure of the superior sagittal sinus and to allow visualization of the major draining vein. The BAVM was dissected circumferentially. Mini–aneurysm clips were used to occlude small feeding arteries and arterialized veins that proved difficult to cauterize. An intraoperative angiogram was performed because the BAVM remained turgid, which identified branches of the callosomarginal artery feeding the BAVM. These vessels were initially preserved because they appeared to be arterialized veins. After cauterization and occlusion with permanent aneurysm clips, the draining vein occluded, and the BAVM was excised. Postoperative and 6-month angiography demonstrated no evidence of residual BAVM (Figure 1B). She continued to have complex partial seizures during follow-up, which stopped with medical therapy. The patient then had a generalized tonic-clonic seizure 4.5 years after resection, and another angiogram was performed, which demonstrated recurrent BAVM at the resection margin (Figure 1C). She underwent Gamma Knife radiosurgery for the recurrence. At the 3-year follow-up, the patient had persistent mild left hemiparesis that did not limit daily activities, and angiography demonstrated an early draining vein with small residual nidus (Figure 1D). Despite the hemiparesis, the patient was able to participate in athletics.

Case 2

The patient was an 8-year-old boy who presented with aphasia and right-sided hemiparesis caused by an intraparenchymal hemorrhage involving the left frontal lobe, insula, and basal ganglia from a diffuse grade IV BAVM (Figure 2A). He underwent 1 session of embolization with Onyx to occlude the apparent extravasation point, followed by surgical resection the next day (Figures 2B and 2C). Early surgical resection was performed because the hematoma created a path to the BAVM, making it more accessible. Postoperative and 6-month angiography demonstrated no residual BAVM (Figure 2D). Routine follow-up angiography 1.5 years later demonstrated a recurrent nidus fed by the lenticulostriate arteries, left anterior temporal artery, and recurrent artery of Huebner (Figure 2E). He underwent SRS for the recurrent nidus. Radiographic obliteration occurred after 2 years, and no recurrent BAVM was identified 1 year after obliteration (Figure 2F). At the last follow-up 5 years after presentation, the patient’s hemiparesis had resolved, but he required special education coursework.

Case 3

This 17-year-old male patient presented with severe right-sided headaches and disabling vertigo and was found to have an unruptured grade III right medial frontal BAVM fed by 2 branches of the anterior cerebral artery and an enlarged lenticulostriate artery supplying the apex from the sylvian fissure (Figures 3A and 3B). The patient’s family was offered treatment because of the severe symptoms he experienced. He underwent 3 sessions of preoperative endovascular embolization via anterior cerebral artery branch supply with Onyx for volume reduction (approximately 60%-70% achieved). He underwent a right frontotemporal/bifrontal craniotomy for resection, which was planned with
neuronavigation. The primary venous drainage along the medial frontal cortex to the superior sagittal sinus was identified early. The dissection began with opening the sylvian fissure to identify the enlarged lenticulostriate artery. A temporary clip was placed on the artery, and motor and sensory evoked potentials were monitored for 10 minutes without evidence of change; this clip was replaced with a permanent clip (See Video, Supplemental Digital Content, http://links.lww.com/NEU/A789, which demonstrates clip placement on the enlarged lenticulostriate artery and resection of the BAVM; 00:40). The dissection was then directed along the anterior interhemispheric fissure. Feeding arteries were cauterized and divided with care to preserve the en passage cortical branches. At this point, the BAVM became soft and a smaller anterior draining vein was cauterized while the major draining vein was preserved. Dissection continued along the superior and lateral aspects of BAVM to separate it from the frontal lobe (01:13) and then toward the apex and roof of lateral ventricle with careful division of the small vessels entering and exiting (01:52). The apical bleeding was less than expected, presumably because of occlusion of the lenticulostriate feeder. The dissection was carried posteriorly, and pial vessels were divided (02:00). The draining vein remained patent, and the callosomarginal and pericallosal arteries were subsequently cauterized and divided. This completed the disconnection of arterial supply; the draining vein was observed to be occluded (02:14), and the BAVM was removed. Intraoperative angiography confirmed complete obliteration. Postoperatively, the patient experienced left-sided hemiparesis and required inpatient rehabilitation. At the 2-year follow-up, he made a complete neurological recovery, his headaches had resolved, he had completed high school, and angiography confirmed complete obliteration.

Case 4

The patient was an 8-year-old girl with a history of spontaneous left temporal lobe intraparenchymal hemorrhage at 5 years of age.
with a negative workup at that time (Figure 4A). She presented after routine surveillance MRA and subsequent angiogram demonstrated a grade III left posterolateral temporal lobe BAVM (Figures 4B and 4C). Treatment was offered because of her young age and history of hemorrhage. Microsurgical resection and SRS were discussed with the parents, and functional magnetic resonance imaging was recommended to localize the language cortex before the final treatment recommendations. The functional study revealed left-sided speech dominance with areas of activation surrounding the AVM anteriorly, superiorly, and posteriorly. Therefore, the patient was referred to radiation oncology and underwent Gamma Knife radiosurgery. The BAVM (target volume, 5.9 mL) was covered by 18 Gy to the 50% isodose with the use of 11 isocenters. She tolerated the treatment well with transient headaches 6 months later. At 2 years after treatment, magnetic resonance imaging/MRA revealed no residual BAVM, and angiography at 3.3 years after treatment confirmed obliteration (Figure 4D). At the last follow-up, she continued to experience occasional headaches; however, she had no neurological deficits and performed well in school.

**DISCUSSION**

This retrospective review of a consecutive series of pediatric BAVMs treated with either surgical resection or SRS as the intended curative modality has shown excellent clinical and radiographic outcomes with ruptured BAVMs and unruptured grade I to III BAVMs. Of patients with ruptured BAVMs, 88% had mRS scores of 0 to 2 at the last follow-up, and all patients with adequate radiographic follow-up obtained obliteration (2 patients without radiographic cure after SRS were <3 years removed from treatment). For unruptured BAVMs, all 6 patients with grade I to III BAVMs obtained radiographic cure and had mRS scores of 0 to 1 at the last clinical follow-up, whereas 1 of 5 patients (20%)
with grade IV and V had obliteration and 80% sustained a complication from treatment; however, 1 of 4 complications resulted in a worse clinical condition. In a total of 93.6 years of follow-up from date of presentation to the last clinical follow-up, there was 1 hemorrhage (1.1%/y), which occurred in a grade V patient after multiple rounds of embolization and SRS. Of 30 patients with radiographic obliteration, 2 patients (7% incidence) had recurrence treated with SRS, with 1 obtaining cure with retreatment.

In this series, surgery without and with preoperative embolization in surviving patients, regardless of rupture status, resulted in a 92% (23 of 25 patients) rate of immediate radiographic cure overall with a 95% (20 of 21 patients) rate in Spetzler-Martin grade I to III BAVMs. Eighty-four percent (21 of 25) of grade I to III patients with lobar BAVMs underwent surgery. SRS was used as intended curative modality for 14 of 40 patients (35%), including 2 (29%) grade II patients, 6 (43%) grade III patients, 5 (64%) grade IV patients, and 1 (50%) grade V patient; 54% of patients (7 of 13) with any follow-up obtained radiographic cure. Of the remaining 6 patients, 5 had a documented radiographic response but inadequate radiographic follow-up (<3 years after SRS).

**Treatment Options for Pediatric BAVMs**

Surgical resection, SRS, and multimodality therapy are the major treatment options for pediatric BAVMs. Several groups have reported their outcomes in retrospective series with variable rates of morbidity and radiographic obliteration, and controversy exists as to which methods are preferred in this subgroup of patients.

In the surgical literature, low rates of neurological morbidity and high rates radiographic obliteration have been reported. Sanchez-Mejia et al. found that pediatric patients have superior outcomes compared with adults with more improvement in final mRS scores and lower mRS score overall with similar rates of surgical cure (97% vs 98%). Similarly, Gross et al. had good functional outcomes (mRS score, 0-2) in 94% of patients with low rates of hemorrhage (0.3%) and recurrence (0.9%) and found that immediate postoperative angiography improved obliteration rates from 86% to 100%. Like adult patients, pediatric patients with grade I to III BAVMs have been shown to have superior clinical and radiographic outcomes, especially compared with patients with grade IV and V BAVMs.

With radiosurgery, reported cure rates and neurological morbidity are variable and depend on treatment parameters and patient and BAVM characteristics. Rates of obliteration range from 34% to 81%. Kano et al. reported 45% obliteration at 3 years and found that 70% patients with >4 years of follow-up obtained radiographic cure. In that study, higher margin dose was associated with higher rates of obliteration, larger target volume was associated with higher rates of posttreatment hemorrhage, and higher rates of adverse radiation effects occurred with higher Pollock-Flickinger scores. The authors also concluded that SRS might be a relatively safe option for patients with high risks with surgery. Potts et al. recommended a margin dose of ≥18 Gy to maximize radiographic cure and to minimize hemorrhage and subsequent neurological deficit because lower doses led to cure in 16% of patients and higher rates of posttreatment hemorrhage.

Multimodality therapy has also been advocated to improve clinical and radiographic outcomes. Hoh et al. reported 95% good or excellent outcomes and 93% complete obliteration with
higher rates of surgical resection for grade I to III BAVMs and higher rates of radiosurgery for grades IV to V. Darsaut et al\textsuperscript{26} reported significantly lower rates of neurological complications (5\% vs 28\%), higher rates of follow-up mRS scores of 0 to 1 (72\% vs 35\%), and higher rates of obliteration (87\% vs 26\%) in grade I to III compared with grade IV and V BAVMs, respectively. In ruptured patients alone, Blauwblomme et al\textsuperscript{7} recommended a treatment approach based on BAVM radiographic characteristics and suggested that immediate surgery or curative embolization be used for BAVMs with risk factors for rehemorrhage such as associated aneurysms and deep venous drainage and that SRS may be suited for patients without these features.

Unruptured BAVMs

Although little debate exists about the need to treat ruptured BAVMs, the indications for and utility of treatment for unruptured BAVMs are less certain. The ARUBA trial found that conservative medical management was superior to “interventional therapy” (ie, embolization, surgical resection, or radiosurgery) in the prevention of death or symptomatic stroke at a mean follow-up of 33 months.\textsuperscript{8} In contrast, 2 recently published single-institution studies of ARUBA-eligible patients at high-volume centers demonstrated that treatment can lead to favorable clinical outcomes with high rates of radiographic cure.\textsuperscript{9,10} Importantly, the Scottish Audit of Intracranial Vascular Malformations (SAIVM) supported ARUBA findings, but SAIVM also found that cumulative rates of death or handicap with follow-up \(>12\) years may favor treatment.\textsuperscript{27} The sum of these findings indicates that clinical outcomes may be institution specific and dependent on local expertise and that long-term follow-up is critical to assess the effectiveness of therapy.

Pediatric patients were not included in the ARUBA, ARUBA-eligible, and SAIVM studies; however, the lifelong cumulative risk of rupture and subsequent morbidity from BAVM hemorrhage are...
the key factors that appear to justify treatment in appropriately selected pediatric patients. For example, ApSimon et al\textsuperscript{3} reported the incidence of first BAVM hemorrhage of 4.6% in the first decade of life compared with 21.1% in the fourth decade and 40% in the seventh decade. This study also found a 4.6% risk of mortality with the initial hemorrhage and that BAVM treatment lowered the risk of mortality from 24.6% to 3.9%.\textsuperscript{3} Similarly, Kim et al\textsuperscript{3} found a 30% increase in risk of BAVM hemorrhage for every 10-year increase in age. Together, these studies support the notion that pediatric patients have a greater lifetime risk of BAVM-associated morbidity.

There is limited literature on the ideal management of unruptured pediatric BAVMs because results are frequently reported within a series of ruptured and unruptured patients, which limits the generalizability of the results to unruptured BAVMs. Ding et al\textsuperscript{28} recently reported the first treatment analysis of unruptured pediatric BAVMs. In that study, 51 patients were treated with SRS with a 58.8% rate of radiographic cure and a 5.9% incidence of neurological deterioration, indicating that radiosurgery may offer a favorable risk-to-benefit profile.\textsuperscript{28} Although that study was limited to patients treated with SRS and did not comment on surgically treated patients, it established the need for pediatric literature focused on the management on unruptured BAVMs as a separate clinical entity.

**Recurrent BAVMs in Pediatric Patients**

Rates of recurrence are reported to be higher for pediatric patients than for adults even after complete obliteration, with rates as high as 13% to 14%.\textsuperscript{19,20} Therefore, close radiographic follow-up and intraoperative angiography have been advocated, particularly for BAVMs with diffuse nidi.\textsuperscript{19-21} Recurrence more commonly occurs in BAVMs with a diffuse nidus.\textsuperscript{19} Early evidence of recurrent BAVM may be residual BAVM not identified because of angiographically unfilled regions, which may create unseen compartments.\textsuperscript{29} BAVM formation may be an active process, and immature blood vessels in the resection cavity may predispose patients to BAVM formation.\textsuperscript{30} High astrocyte vascular endothelial growth factor expression in BAVM specimens has also been associated with recurrence.\textsuperscript{31} Together, immature vessels and differences in cellular milieu help explain recurrence in the pediatric population. This series identified 2 cases (7% incidence), but incidence of recurrence is variable and depends on length of follow-up, with some centers reporting rates as high as 13%.\textsuperscript{19} Thus, follow-up angiography is necessary even after radiographic cure. Our center routinely obtains angiographic follow-up at 1 and 5 years after treatment in pediatric patients.

**Limitations**

This study is a retrospective review of our institution’s experience with the management of ruptured and unruptured BAVMs. BAVMs, especially in the pediatric population, are rare entities, which produces a relatively low number of patients, which limits the statistical power. This fact is further heightened by the need to divide clinical and radiographic outcomes by rupture status and intended curative modality of treatment. The database was retrospectively collected, including clinical and radiographic outcomes, which may bias results and limit generalizability. There is no comparison cohort of untreated patients because patients seen during this period but not treated were not included in this study, which limits the natural history analysis of unruptured BAVMs. All patients were treated, and the decision to treat and the modality of treatment was biased toward the expertise of the treating clinician and multidisciplinary team, which also limits the generalizability of the results. Follow-up was limited overall, which may have influenced the assessment of clinical outcome, radiographic obliteration after SRS, recurrence rates after obliteration, posttreatment hemorrhage, and other complications. The mRS was used to assess clinical outcome, and it has not been validated in the pediatric population. The WFNS score was used to assess admission, which has not been validated for BAVM or pediatric patients. Six patients treated at other institutions or before 2005 were excluded from this study, which may also bias the reported outcomes. For SRS, MRA and computed tomographic angiography were used in addition to angiography to determine radiographic obliteration at the discretion of the treating physician, which may have biased the reported rates of cure.

**Treatment Philosophy**

The treatment of pediatric patients with BAVMs is dependent on rupture status, the clinical condition of the patient, and discussion with the patients’ families. At our institution, patients with acutely ruptured BAVMs are immediately stabilized and assessed, and this begins with first determining whether emergent decompression for cerebral herniation is necessary. Neurologically stable patients are admitted to the pediatric intensive care unit and undergo cerebral angiography once stabilized. Angiography is used to delineate BAVM anatomy, to identify high-risk features such as associated aneurysms and deep arterial supply that may be amenable to endovascular embolization, and to determine whether surgical resection or SRS should be offered as the intended curative modality. In general, patients with grade I, grade II, and lobar grade III BAVMs are prepared for early surgical resection during the initial hospitalization, whereas BAVMs with deep location and grade IV and V BAVMs are reserved for SRS after discharge. In this series, Spetzler-Martin grade was significantly higher for patients undergoing SRS for ruptured BAVMs.

For unruptured BAVMs, the decision to treat and the type of treatment offered are also dependent on patient and BAVM characteristics, and these decisions are made on a case-by-case basis. Treatment is offered to eliminate the lifelong risk of hemorrhage and to prevent future morbidity. Similar to ruptured BAVMs, surgical resection is generally offered for accessible grade I to III BAVMs, whereas SRS is reserved for grade I to III BAVMs in critical locations, for symptomatic grade IV and V BAVMs, and for...
families who request treatment but elect to forgo surgery. SRS is also offered as adjunctive therapy for residual or recurrent BAVMs after surgery. Endovascular embolization is primarily an adjunct to surgery or SRS. In this series, on average, more SRS patients had BAVMs in eloquent locations.

CONCLUSION

In this study, most patients with ruptured BAVMs had mRS scores of 0 to 2 at the last follow-up and obtained radiographic cure. In addition, unruptured grade I to III BAVMs were treated safely with excellent cure rates, especially in patients undergoing surgical resection. As a result of patient-specific BAVM management in a multidisciplinary team, this study suggests that good clinical and radiographic outcomes can be obtained with both surgery and SRS in selected patients. Unruptured grade IV and V BAVMs had more frequent treatment complications with lower rates of radiographic response and cure. Therefore, treatment of high-grade BAVMs requires careful discussion with the family about the goals and risks of therapy and long-term follow-up. In this setting, as with their adult counterparts, future studies are needed to determine which unruptured grade IV and V patients will have the best outcomes with therapy.

Disclosure

Dr Kim is a consultant for Aesculap, Inc and Covidien, Inc and a shareholder of Spire Surgical Inc. Dr Ghodke is a consultant for Covidien, Inc and Viket Medical Inc. Dr Sekhar is a consultant for Viket Medical Inc, and a shareholder in Spi Surgical Inc. The other authors have no personal, financial, or institutional interest in any of the drugs, materials, or devices described in this article.

REFERENCES


Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal’s Web site (www.neurosurgery-online.com).