HHS Public Access

Author manuscript

J Neurosurg. Author manuscript; available in PMC 2016 April 01.

Published in final edited form as:

J Neurosurg. 2015 April ; 122(4): 912–920. doi:10.3171/2014.12.JNS14938.

Current surgical results with low-grade arteriovenous malformations

Matthew B. Potts, MD[1], **Darryl Lau, MD**[1], **Adib A. Abla, MD**[1], **Helen Kim, PhD**[3], **William L. Young, MD**[2,3], and **Michael T. Lawton, MD**[1,3,*] **For the UCSF Brain AVM Study Project**

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

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

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

Abstract

OBJECTIVE—Surgical resection is an appealing therapy for brain arteriovenous malformations (AVM) because of its high cure rate, low complication rate, and immediacy, becoming the first-line therapy for many AVMs. To clarify safety, efficacy, and outcomes associated with AVM resection in the aftermath of ARUBA, we reviewed an experience with low-grade AVMs, the most favorable AVMs for surgery and the ones most likely to have been selected for treatment outside of ARUBA's randomization process.

METHODS—A prospective AVM registry was searched to identify patients with Spetzler-Martin grade I and II AVMs treated with surgical resection during a 16-year period.

RESULTS—Of the 232 surgical patients included, 117 (50%) presented with hemorrhage, 33% had Spetzler-Martin grade I, and 67% had grade II AVMs. Overall, 99 patients (43%) underwent preoperative embolization, with unruptured AVMs embolized more often than ruptured AVMs. AVM resection was accomplished in all patients and confirmed angiographically in 218 patients (94%). There were no deaths among patients with unruptured AVMs. Good outcomes (mRS 0–1) were found in 78% of patients with 97% improved or unchanged from their pre-operative mRS scores. Unruptured AVM patients had better functional outcomes (91% good outcome compared to 65% in the ruptured group, p=0.0008), while relative outcomes were equivalent (98% improved/unchanged in ruptured AVM patients versus 96% in unruptured AVM patients).

CONCLUSION—Surgery should be regarded as the "gold standard" therapy for the majority of low-grade AVMs, utilizing conservative embolization as a preoperative adjunct. High surgical cure rates and excellent functional outcomes in both ruptured and unruptured patients support a dominant surgical posture, with radiosurgery reserved for risky AVMs in deep, inaccessible, and

*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.

highly eloquent locations. Despite the technological advances in endovascular and radiosurgical therapy, surgery still offers the best cure rate, lowest risk profile, and greatest protection against hemorrhage for low-grade AVMs. ARUBA results are influenced by a low randomization rate, bias toward non-surgical therapies, a shortage of surgical expertise, a lower rate of complete AVM obliteration, a higher rate of delayed hemorrhage, and short study duration. Another randomized trial is needed to reestablish the role of surgery in unruptured AVM management.

INTRODUCTION

Surgical resection is an appealing therapy for brain arteriovenous malformations (AVM) because of its high cure rate, low complication rate, and immediacy, becoming the first-line therapy or "gold standard" for many AVMs.[4,25] Surgical results have improved over time with: (1) the creation of grading systems to select patients likely to experience optimal outcomes;[5,11,18,19,43] (2) the development of instruments such as bipolar forceps and AVM microclips to coagulate or occlude feeding arteries effectively; (3) the recognition of AVM subtypes that help decipher AVM anatomy;[5,9,17,35,36] and (4) the refinement of surgical approaches, strategies, and dissection techniques that facilitate safe AVM resection.[4,11,13,18,25,44] This impressive evolution of AVM surgery is at odds with the finding of the ARUBA Trial[23] (A Randomized trial of Unruptured Brain AVMs) that medical management alone was superior to interventional therapy for the prevention of death or stroke in patients with unruptured AVMs followed for 33 months. This finding is explained in part by the trial's 13% randomization rate, suggesting that many clinicians did not deem AVMs with low Spetzler-Martin grades (low treatment risk) to be in equipoise with medical management (high hemorrhage risk), or conversely, did not deem those with high grades (high treatment risk) to be in equipoise with medical management (low hemorrhage risk), and "selected treatment outside of the randomization process" (177 patients, or 79% of included patients).[23]

Another important explanation for the ARUBA finding is the trial's surprisingly nonsurgical management of patients in the interventional group.[23] Overall, 81% of patients were treated with embolization alone (32%), radiosurgery alone (33%), or combined embolization and radiosurgery (16%), and only 17 patients (18%) were treated surgically, with or without embolization. Therefore, the three-fold increase in death or stroke in the interventional arm reflects current nonsurgical therapies and should not be interpreted as an indictment of AVM surgery.[23] In the aftermath of ARUBA,[23] it is important to clarify the safety, efficacy, and outcomes associated with AVM resection. Therefore, we reviewed our experience in managing Spetzler-Martin grade I and II AVMs, the most favorable AVMs for surgery and the ones most likely to have been selected for treatment outside of ARUBA's randomization process.

METHODS

Data Collection

This study was approved by the Institutional Review Board 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 Spetzler-Martin grade I and II AVMs who were treated with surgical resection at our institution between 1997 and 2013. Operations were performed by the senior author (MTL). The database as well as medical records, pre- and post-treatment radiographic studies, and clinical follow-up evaluations were reviewed retrospectively.

Outcome Evaluation

The primary outcome measure was functional outcome at last follow-up based on the modified Rankin Scale score (mRS) dichotomized to "good" (mRS 0–1) or "poor" (mRS 2–6). Long-term functional outcomes were only evaluated in patients with more than 30 days of follow-up. Neurologic assessments were performed by a neurologist and/or a dedicated clinical research nurse, without involvement of treating neurosurgeons. The pretreatment functional status was obtained from pretreatment clinic visits or admission examinations, while follow-up information was obtained during post-treatment clinic visits, subsequent hospital admissions, or telephone interviews. The Social Security Death Index was searched for all patients with less than 30 days of follow-up to ensure that no early deaths were missed. Angiographic outcomes were determined by a neurointerventional radiologist.

Statistical Analysis

Statistical analysis was performed using JMP 11 (SAS, North Carolina, USA). Frequency distributions and summary statistics were calculated for all baseline characteristics and outcome measures. For all categorical variables (e.g., unruptured status), a cross-tabulation was generated and a Fisher's exact (for 2×2 contingency tables) or Pearson χ^2 test (for larger contingency tables) were used to compare distributions between groups of interest. Continuous variables were compared using a analysis of variance (ANOVA). Statistical significance was defined as $p<0.05$.

RESULTS

Patients and AVM Characteristics

Between 1997 and 2013, 332 patients with Spetzler-Martin grade I or II AVMs managed at our institution and 234 of these (70%) were managed surgically. Two of these patients who underwent concomitant surgical treatment for other pathologies (orbital squamous cell carcinoma resection in one and extracranial-to-intracranial bypass for moyamoya disease in the other) excluded from this cohort. Nine patients who had aneurysms clipped concomitantly were included. Baseline characteristics for the remaining 232 surgical patients are shown in Table 1. Overall, the mean age was 38 years with a slight female predominance (56%). The most common AVM location was the frontal lobe (34%). Half (117 patients) presented with AVM rupture and 53% presented with a mRS of 0 or 1. Spetzler-Martin grades were I in 33% and II in 67%. Patients presenting with AVM rupture differed from those presenting without ruputre in AVM location (p=0.0014), pre-operative mRS (p<0.0001), and supplementary AVM grade (p<0.0001).

Surgical Management

Overall, 99 patients (43%) underwent preoperative embolization, with unruptured AVMs embolized more often than ruptured AVMs (53% and 33%, respectively; p=0.005). Only 4 patients were treated previously, 2 with stereotactic radiosurgery and 2 with both remote embolization and radiosurgery.

AVM resection was accomplished with a single stage in all but 5 patients. These 5 patients had unexpected residual AVM noted on their postoperative angiogram and all were taken back to the operating room for complete resection. Post-operative angiograms were obtained in 218 patients (94%, Table 2). Of these, no residual was noted in 213 (98%). Repeat angiograms in the 5 patients with residual AVM confirmed complete AVM resection. Of the 14 patients with no postoperative angiography, 3 expired during their post-operative hospitalization. The remaining 11 patients refused postoperative angiography, but they had a mean follow-up time of 1.6 years (range 25 days to 6.2 years).

Significant intraoperative AVM rupture occurred in 1 patient. Post-operative hemorrhages due to surgical site bleeding occurred in 3 patients, all of which required evacuation of the hematoma. Two patients were noted to have postoperative infarcts, one involving a lenticulostriate artery and one a middle cerebral artery. Finally, 2 patients had wound infections requiring surgical debridement.

Of note, an 8 year-old patient who underwent complete resection of a left temporal grade II AVM with a negative post-operative angiogram was found to have recurrent AVM in that same location on a five-year follow-up angiogram. He underwent a repeat resection without complication and had no residual AVM noted on both the post-operative and a repeat 5-year follow-up angiogram.

Functional Outcomes

Four patients died within 30 days of their AVM resection, all in patients with ruptured AVMs. Three patients presented with devastating AVM hemorrhages (vermian, tonsillar, and temporal AVMs), underwent uncomplicated resection, had pre- and postoperative mRS scores of 5, and their families withdrew care. These deaths were attributed to severity of hemorrhage rather than surgery. One patient with a deep parietal AVM had an MCA stroke related to AVM resection and died from resulting medical complications (surgical mortality, 0.4%). There were no deaths among patients with unruptured AVMs.

Long-term follow-up was available in 207 patients (89%). Mean time to follow-up was 1.7 years (median 1.2 years, range 2 weeks to 12.8 years). Four additional patients were dead at late follow-up, all unrelated to their AVM surgery. One patient died from cancer 3 years postoperatively (mRS 1); one patient died from renal failure 4 months postoperatively (mRS 0); and two patients died of unknown causes 1.9 years (mRS 1) and 5.7 years (mRS 1) postoperatively. The mRS from the next-to-last clinical evaluation was used for the functional outcome analysis.

Overall, good outcomes (mRS 0–1) were found in 78% of patients with 97% improved or unchanged from their pre-operative mRS scores (Table 2). As expected, patients with unruptured AVMs had better functional outcomes, with 91% having a good outcome at time of last follow-up compared to 65% in the ruptured group (p=0.0008). Relative outcomes were slightly better in patients with ruptured AVMs, with 98% improved or unchanged, compared with 96% in patients with unruptured AVMs.

Univariate analysis of factors associated with good (mRS 0–1) versus poor (mRS ≥2) functional outcomes identified younger age (OR 0.98 for each increasing year; logistic regression, p=0.03), unruptured presentation (good outcomes in 88% of unruptured AVMs and 65% of ruptured AVMs; two-tailed Fisher's exact test, p=0.0001), and pre-operative mRS (good outcomes in 94% and 57% with pre-operative mRS scores of 0–1 and ≥2, respectively; χ^2 test, p<0.0001). Of note, AVM location, Spetzler-Martin and supplementary grades, pre-operative embolization, and time to follow-up were not significantly associated with functional outcome. The 3 variables above were fit into a logistic regression model that confirmed that young age (OR 0.98 for each increasing year, p=0.03) and low pre-operative mRS (OR 11.8 for mRS 0–1 versus mRS ≥2, p<0.0001) remained significantly associated with good outcomes. The odds ratio for hemorrhagic presentation in this model did not reach statistical significance (OR 0.97 for unruptured versus ruptured, p=0.95).

DISCUSSION

Surgical Results with Low-Grade AVMs

This study exemplifies a surgical posture towards low-grade AVMs that regards curative resection as the first-line or "gold standard" therapy for the majority of lesions, utilizing embolization as a preoperative adjunct and reserving radiosurgery for risky AVMs in deep, inaccessible locations, in eloquent areas that might be associated with postoperative neurological deficits, and/or with diffuse nidus morphology that might complicate microdissection. Patients were carefully selected to optimize outcomes, with a mean age of 38 years, supplementary grades of 3 or less in 69% of patients, and few (<4%) in deep locations or brainstem. Conservative embolization minimized additional treatment risk, with only 43% of patients undergoing embolization and no patients experiencing endovascular complications. Surgical cures were confirmed in all patients who underwent postoperative angiography. Overall, 6 patients (3%) were worse neurologically after surgery, with 161 patients (78%) in total and 91 patients (91%) with unruptured AVMs experiencing good outcomes (mRS 0–1). These surgical results are consistent with other reports in the literature (Table 3).[4,11–13,25,33,38,39,41,43,44] In a review of 1235 patients with low-grade AVMs, the average surgical morbidity and mortality rates were 2.2% and 0.3%, respectively, with an average cure rate of 98.5% and a post-operative or delayed hemorrhage rate of 0.3% (Table 3).

Endovascular and Radiosurgical Results with Low-Grade AVMs

The management of AVMs in other parts of the world is diverging from the surgical approach described above. In Europe, for example, treatment is often limited only to ruptured AVMs, beginning with aggressive embolization, frequently adding radiosurgery for incompletely embolized AVMs,[2,3,32,40] and rarely resorting to surgical resection. Onyx is an important endovascular advancement because its high viscosity allows for slow intranidal injection, its prolonged solidification promotes deep penetration to the venous side of the AVM,[24] and its nonadherence reduces catheter retention.[24,32] Onyx has improved the efficacy of endovascular therapy with better cure rates than NBCA glue, but cure rates are still low and curative attempts are associated with increased complications, occlusion of critical draining veins, and adverse imaging findings in as many as 40% of patients.[1,10,15,20,24,26,28–31,37,42,46–48] In a review of 1297 patients with mostly low-grade AVMs, the average endovascular morbidity and mortality rates were 6.2% and 1.6%, respectively, with an average cure rate of 29% and a post-operative or delayed hemorrhage rate of 8.0% (Table 4).[1,10,15,20,26,28–31,37,42,46–48] Therefore, aggressive endovascular therapy has higher procedural risks, significantly lower cure rates, and increased hemorrhage risks compared to surgery.

A similar comparison can be made with radiosurgery for low-grade AVMs. Although these lesions are ideal for radiosurgery because of their lower target volumes and higher obliteration rates, the 2 to 3 year latency period between treatment and obliteration opens a time window for AVM hemorrhage and associated complications. Radiation-induced complications are low, but in a review of 1051 patients with low-grade AVMs, 7.2% of patients hemorrhaged after treatment, resulting in morbidity and mortality rates of 6.5% and 1.2%, respectively (Table 5).[6–8,14,16,21,27,34,49] The 75.2% radiosurgical cure rate was substantially better than the endovascular cure rate, but still less than surgery. Therefore, despite the technological advances in endovascular and radiosurgical therapy, surgery still offers the best cure rate, lowest risk profile, and greatest protection against hemorrhage for low-grade AVMs. Surgery cannot compete with the minimally invasive appeal of these other modalities, but this issue remains secondary to functional outcome.

The results of our analysis are consistent with other systematic meta-analyses of AVM therapy not limited to low-grade AVMs. In a recent meta-analysis of 13,698 patients by van Beijnum et al.,[45] the complication rates and case fatality rates were: 6.6 and 0.96 % for embolization; 5.1 and 0.5 % for radiosurgery; and 7.4 and 1.1 % for surgery, with the increased surgical risks reflecting the inclusion of intermediate and high-grade AVMs. However, obliteration rates were 13%, 38%, and 96% for embolization, radiosurgery, and surgery, respectively.[45] Estimates of hemorrhage risk after surgery were 1.7, 1.7, and 0.2 % for embolization, radiosurgery, and surgery, respectively.[45]

Critique of ARUBA

How do we interpret the ARUBA findings in the context of our study? First, based on the surgical experience described above, a significant number of neurosurgical investigators in ARUBA did not consider low-grade AVMs to be in equipoise with medical management and “selected treatment outside of the randomization process” (177 patients, or close to the number of included patients).[23] Conversely, intermediate (31.8%) and high-grade AVMs (10.3%) that are generally considered to have a more benign natural history and high risk for any treatment were included in the trial, diminishing the interventional results.[23]

As a participating site in the ARUBA trial, we screened 473 patients, identified 87 who were eligible, and enrolled only 4. Of the 74 ARUBA-eligible patients with sufficient follow-up for analysis, 61 were treated (including 36 low-grade AVMs) and 13 were observed. Most treated patients underwent surgical resection with or without preoperative embolization (43/61, 70.5%). Stroke and death, the primary end-points by ARUBA definitions, were observed in 10 patients, including 1 in the observation group (8%), 5 in the surgical group (11%), and 4 in the radiosurgical group (27%). There was no significant difference in stroke/death rates (HR 1.34, 95% C.I. 0.12–14.53, p=0.807) or clinical impairment (Fisher's exact p=0.68) between observed and treated patients. Therefore, our results in ARUBA-eligible patients were better than those reported in ARUBA, leading to an entirely different conclusion about AVM intervention. This difference was due to utilizing surgery as the primary therapy, selecting surgical patients judiciously with established outcome predictors, and developing surgical expertise through high AVM case volume.

Second, ARUBA was unusually biased towards non-surgical therapy, with 81% of patients treated with endovascular embolization alone (32%), radiosurgery alone (33%), or combined embolization-radiosurgery (16%).[23] The 18% of ARUBA patients treated surgically contrasts sharply with the 71% of ARUBA-eligible patients treated surgically at our site. Data on cure rates were not published with ARUBA,[23] but the number of incompletely obliterated AVMs was likely significant and resulted in ongoing ruptures. Therefore, the event rates observed in Kaplan-Meier estimates of "as-treated" patients reflected the procedural morbidity of endovascular therapy plus the delayed morbidity of latency hemorrhage associated with radiosurgery.[23] The outcome of such a group could never exceed that of an observational group whose only morbidity was the natural history risk.

Third, the shortage of surgical expertise in the ARUBA trial is apparent. Two-thirds of patients in the interventional group had low-grade, surgical AVMs and yet only 18% underwent surgery, which is well below expectation for the gold standard therapy.[23] The rates of stroke and death in this trial do not match reported surgical outcomes (Table 3). Therefore, the overall management of AVMs in ARUBA reflects a non-surgical posture consistent with the fact that of the 38 of 65 total ARUBA sites were in Europe, Australia, and Brazil.[22] Centers were required to manage 10 AVM patients per year, but there were no minimum requirements for neurosurgeons. AVM resection is among the most challenging neurosurgical cases, and the best AVM surgeons typically perform three times ARUBA's minimum requirement annually. In a review of AVM outcome data from the National Inpatient Sample, we found that mortality rates were lowest and discharges to home were highest amongst neurosurgeons with the highest case volume, defined as the top quartile with 30 or more AVM resections per year. Had the ARUBA trial been embraced by the neurosurgical community, the application of surgical therapy would have been higher, the interventional outcomes would have been better, and the benefits of intervention would have been obvious. Had ARUBA been more surgical with complete resections and no delayed hemorrhage in nearly all patients as described above, the event rates observed in Kaplan-Meier estimates of "as-treated" patients would have plateaued and the benefits of intervention would have been realized in much less than 10 years. Although this time interval is reasonable in a population of young patients (mean age 45 years) with long life expectancy, the trial was stopped long before reaching this cross-over point (median follow-up duration, 33 months).[23]

Another Randomized Trial: BARBADOS

The ARUBA trial has had significant impact because it was a randomized, controlled trial. Our results with low-grade AVMs were derived from a larger cohort of patients than ARUBA (232 versus 223) and more than twice the number of treated patients (232 versus 98), but the impact of our results is limited by study design. Although the UCSF AVM database is prospectively maintained by statisticians with input from multiple disciplines, including functional outcomes from dedicated clinical research nurses and neurologists (not treating neurosurgeons), and angiographic outcomes from neurointerventional radiologists, this case series is influenced by referral biases, institutional biases, and selection biases. Patients are selected according to established outcome predictors embodied in the Spetzler-Martin and Supplementary grading systems. Furthermore, our site is a high-volume center with dedicated experts who have collaborated as a team for decades, which might set a high surgical benchmark but lower the generalizability of our results. As important as these surgical results are in ARUBA's aftermath, another trial is needed to re-establish the role of surgery in AVM management, this time conducted and embraced by the neurosurgical community.

We propose BARBADOS: **B**eyond **A**RUBA – **R**andomized trial, **B**est neurosurgeons, **A**VMs unruptured, **D**on't embolize, **O**nly low grades, and **S**urgical cures. The elements of the trial are obvious from the name, and efforts are ongoing to organize, fund, and initiate it. There is now urgency among neurosurgeons to respond to ARUBA, which we expect to increase the acceptance of such a trial. In the meantime, the management of ruptured AVMs should remain unaffected by ARUBA and surgery should remain a dominant therapy because of its ability to evacuate hematomas, relieve intracranial pressure, and work through hematoma cavities.

CONCLUSION

Surgery should be regarded as the first-line or "gold standard" therapy for the majority of low-grade AVMs, utilizing conservative embolization as a preoperative adjunct. High surgical cure rates and excellent functional outcomes in both ruptured and unruptured patients support a dominant surgical posture, with radiosurgery reserved for risky AVMs in deep, inaccessible, and highly eloquent locations. In the aftermath of ARUBA, additional randomized trials are needed to validate the role of surgical resection.

Acknowledgments

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

References

1. Abud DG, Riva R, Nakiri GS, et al. Treatment of brain arteriovenous malformations by double arterial catheterization with simultaneous injection of onyx: retrospective series of 17 patients. AJNR Am J Neuroradiol. 2011; 32:152–158. [PubMed: 20966066]
2. Blackburn SL, Ashley WW Jr, Rich KM, et al. Combined endovascular embolization and stereotactic radiosurgery in the treatment of large arteriovenous malformations. J Neurosurg. 2011; 114:1758–1767. [PubMed: 21332288]

3. Dalyai R, Theofanis T, Starke RM, et al. Stereotactic radiosurgery with neoadjuvant embolization of larger arteriovenous malformations: an institutional experience. Biomed Res Int. 2014; 2014:306518. [PubMed: 24579080]

4. Davidson AS, Morgan MK. How safe is arteriovenous malformation surgery? A prospective, observational study of surgery as first-line treatment for brain arteriovenous malformations. Neurosurgery. 2010; 66:498–504. discussion 504–495. [PubMed: 20173544]

5. Davies JM, Kim H, Young WL, et al. Classification schemes for arteriovenous malformations. Neurosurg Clin N Am. 2012; 23:43–53. [PubMed: 22107857]

6. Ding D, Yen CP, Xu Z, et al. Radiosurgery for low-grade intracranial arteriovenous malformations. J Neurosurg. 2014

7. Fokas E, Henzel M, Wittig A, et al. Stereotactic radiosurgery of cerebral arteriovenous malformations: long-term follow-up in 164 patients of a single institution. J Neurol. 2013; 260:2156–2162. [PubMed: 23712798]

8. Friedman WA, Bova FJ, Bollampally S, et al. Analysis of factors predictive of success or complications in arteriovenous malformation radiosurgery. Neurosurgery. 2003; 52:296–308. [PubMed: 12535357]

9. Gabarrós Canals A, Rodriguez-Hernandez A, Young WL, et al. Temporal lobe arteriovenous malformations: anatomical subtypes, surgical strategy, and outcomes. J Neurosurg. 2013; 119:616–628. [PubMed: 23848823]

10. Gao K, Yang XJ, Mu SQ, et al. Embolization of brain arteriovenous malformations with ethylene vinyl alcohol copolymer: technical aspects. Chin Med J (Engl). 2009; 122:1851–1856. [PubMed: 19781359]

11. Hamilton MG, Spetzler RF. The prospective application of a grading system for arteriovenous malformations. Neurosurgery. 1994; 34:2–6. discussion 6–7. [PubMed: 8121564]

12. Hartmann A, Stapf C, Hofmeister C, et al. Determinants of neurological outcome after surgery for brain arteriovenous malformation. Stroke. 2000; 31:2361–2364. [PubMed: 11022064]

13. Heros RC, Korosue K, Diebold PM. Surgical excision of cerebral arteriovenous malformations: late results. Neurosurgery. 1990; 26:570–577. discussion 577–578. [PubMed: 2330077]

14. Kano H, Lunsford LD, Flickinger JC, et al. Stereotactic radiosurgery for arteriovenous malformations, Part 1: management of Spetzler-Martin Grade I and II arteriovenous malformations. J Neurosurg. 2012; 116:11–20. [PubMed: 22077452]

15. Katsaridis V, Papagiannaki C, Aimar E. Curative embolization of cerebral arteriovenous malformations (AVMs) with Onyx in 101 patients. Neuroradiology. 2008; 50:589–597. [PubMed: 18408923]

16. Koltz MT, Polifka AJ, Saltos A, et al. Long-term outcome of Gamma Knife stereotactic radiosurgery for arteriovenous malformations graded by the Spetzler-Martin classification. J Neurosurg. 2013; 118:74–83. [PubMed: 23082882]

17. Lawton MT. Seven AVMs: Tenets and Techniques for Resection: Thieme. 2014

18. Lawton MT. Spetzler-Martin Grade III arteriovenous malformations: surgical results and a modification of the grading scale. Neurosurgery. 2003; 52:740–748. discussion 748–749. [PubMed: 12657169]

19. Lawton MT, Kim H, McCulloch CE, et al. A supplementary grading scale for selecting patients with brain arteriovenous malformations for surgery. Neurosurgery. 2010; 66:702–713. discussion 713. [PubMed: 20190666]

20. Maimon S, Strauss I, Frolov V, et al. Brain arteriovenous malformation treatment using a combination of Onyx and a new detachable tip microcatheter, SONIC: short-term results. AJNR Am J Neuroradiol. 2010; 31:947–954. [PubMed: 20190210]

21. Meder JF, Oppenheim C, Blustajn J, et al. Cerebral arteriovenous malformations: the value of radiologic parameters in predicting response to radiosurgery. AJNR Am J Neuroradiol. 1997; 18:1473–1483. [PubMed: 9296188]

22. Mohr JP, Moskowitz AJ, Stapf C, et al. The ARUBA trial: current status, future hopes. Stroke. 2010; 41:e537–540. [PubMed: 20634478]

23. Mohr JP, Parides MK, Stapf C, et al. Medical management with or without interventional therapy for unruptured brain arteriovenous malformations (ARUBA): a multicentre, non-blinded, randomised trial. Lancet. 2014; 383:614–621. [PubMed: 24268105]
24. Moret, J. Neurosurgical Face-off. Arteriovenous Malformations (AVMs) vs. Surgeon in AANS Annual Meeting; San Francisco, CA. 2014;
25. Morgan MK, Rochford AM, Tsahtsarlis A, et al. Surgical risks associated with the management of Grade I and II brain arteriovenous malformations. Neurosurgery. 2004; 54:832–837. discussion 837–839. [PubMed: 15046648]
26. Mounayer C, Hammami N, Piotin M, et al. Nidal embolization of brain arteriovenous malformations using Onyx in 94 patients. AJNR Am J Neuroradiol. 2007; 28:518–523. [PubMed: 17353327]
27. Nataf F, Schlienger M, Bayram M, et al. Microsurgery or radiosurgery for cerebral arteriovenous malformations? A study of two paired series. Neurosurgery. 2007; 61:39–50. [PubMed: 17621017]
28. Panagiotopoulos V, Gizewski E, Asgari S, et al. Embolization of intracranial arteriovenous malformations with ethylene-vinyl alcohol copolymer (Onyx). AJNR Am J Neuroradiol. 2009; 30:99–106. [PubMed: 18842759]
29. Perez-Higueras A, Lopez RR, Tapia DQ. Endovascular Treatment of Cerebral AVM: Our Experience with Onyx. Interv Neuroradiol. 2005; 11:141–157. [PubMed: 20584469]
30. Pierot L, Cognard C, Herbreteau D, et al. Endovascular treatment of brain arteriovenous malformations using a liquid embolic agent: results of a prospective, multicentre study (BRAVO). Eur Radiol. 2013; 23:2838–2845. [PubMed: 23652849]
31. Pierot L, Januel AC, Herbreteau D, et al. Endovascular treatment of brain arteriovenous malformations using onyx: results of a prospective, multicenter study. J Neuroradiol. 2009; 36:147–152. [PubMed: 19223075]
32. Pierot L, Kadziolka K, Litre F, et al. Combined treatment of brain AVMs with use of Onyx embolization followed by radiosurgery. AJNR Am J Neuroradiol. 2013; 34:1395–1400. [PubMed: 23391837]
33. Pikus HJ, Beach ML, Harbaugh RE. Microsurgical treatment of arteriovenous malformations: analysis and comparison with stereotactic radiosurgery. J Neurosurg. 1998; 88:641–646. [PubMed: 9525708]
34. Pollock BE, Lunsford LD, Kondziolka D, et al. Patient outcomes after stereotactic radiosurgery for “operable” arteriovenous malformations. Neurosurgery. 1994; 35:1–7. discussion 7–8. [PubMed: 7936129]
35. Potts MB, Young WL, Lawton MT. Deep arteriovenous malformations in the basal ganglia, thalamus, and insula: microsurgical management, techniques, and results. Neurosurgery. 2013; 73:417–429. [PubMed: 23728451]
36. Rodriguez-Hernandez A, Kim H, Pourmohamad T, et al. Cerebellar arteriovenous malformations: anatomic subtypes, surgical results, and increased predictive accuracy of the supplementary grading system. Neurosurgery. 2012; 71:1111–1124. [PubMed: 22986595]
37. Saatci I, Geyik S, Yavuz K, et al. Endovascular treatment of brain arteriovenous malformations with prolonged intranidal Onyx injection technique: long-term results in 350 consecutive patients with completed endovascular treatment course. J Neurosurg. 2011; 115:78–88. [PubMed: 21476804]
38. Schaller C, Schramm J. Microsurgical results for small arteriovenous malformations accessible for radiosurgical or embolization treatment. Neurosurgery. 1997; 40:664–672. discussion 672–664. [PubMed: 9092839]
39. Schaller C, Schramm J, Haun D. Significance of factors contributing to surgical complications and to late outcome after elective surgery of cerebral arteriovenous malformations. J Neurol Neurosurg Psychiatry. 1998; 65:547–554. [PubMed: 9771782]
40. Schwyzer L, Yen CP, Evans A, et al. Long-term results of gamma knife surgery for partially embolized arteriovenous malformations. Neurosurgery. 2012; 71:1139–1147. discussion 1147–1138. [PubMed: 22986603]
41. Sisti MB, Kader A, Stein BM. Microsurgery for 67 intracranial arteriovenous malformations less than 3 cm in diameter. J Neurosurg. 1993; 79:653–660. [PubMed: 8410243]

42. Song D, Leng B, Gu Y, et al. Clinical Analysis of 50 Cases of BAVM Embolization with Onyx, a Novel Liquid Embolic Agent. Interv Neuroradiol. 2005; 11:179–184. [PubMed: 20584473]
43. Spetzler RF, Martin NA. A proposed grading system for arteriovenous malformations. J Neurosurg. 1986; 65:476–483. [PubMed: 3760956]
44. Sundt TM Jr, Piepgras DG, Stevens LN. Surgery for supratentorial arteriovenous malformations. Clin Neurosurg. 1991; 37:49–115. [PubMed: 2009702]
45. van Beijnum J, van der Worp HB, Buis DR, et al. Treatment of brain arteriovenous malformations: a systematic review and meta-analysis. JAMA. 2011; 306:2011–2019. [PubMed: 22068993]
46. van Rooij WJ, Sluzewski M, Beute GN. Brain AVM embolization with onyx. AJNR Am J Neuroradiol. 2007; 28:172–177. [PubMed: 17213451]
47. Weber W, Kis B, Siekmann R, et al. Endovascular treatment of intracranial arteriovenous malformations with onyx: technical aspects. AJNR Am J Neuroradiol. 2007; 28:371–377. [PubMed: 17297015]
48. Xu F, Ni W, Liao Y, et al. Onyx embolization for the treatment of brain arteriovenous malformations. Acta Neurochir (Wien). 2011; 153:869–878. [PubMed: 21046174]
49. Yamamoto M, Jimbo M, Hara M, et al. Gamma knife radiosurgery for arteriovenous malformations: long-term follow-up results focusing on complications occurring more than 5 years after irradiation. Neurosurgery. 1996; 38:906–914. [PubMed: 8727815]

Table 1

Baseline characteristics of patients with low-grade AVMs

Variable	Unruptured AVM	Ruptured AVM	p Value*	Total
Total no. of patients	112	120		232
Mean age at surgery ± SD (yrs)	39.4 ± 15.3	36.9 ± 18.4	0.16	38.1 ± 17
Females (%)	70 (63)	61 (51)	0.16	131 (56)
Presentation (%)			Not tested	
Hemorrhage	0	120 (100)		120 (52)
Seizure	37 (33)	0		37 (16)
Headache	40 (36)	0		40 (17)
Other	35 (31)	0		35 (15)
AVM location (%)			**0.0014**	
Frontal	49 (44)	29 (24)		78 (34)
Parietooccipital	27 (24)	31 (26)		58 (25)
Temporal	22 (20)	22 (18)		44 (19)
Cerebellar	7 (6)	28 (33)		35 (15)
Ventricular	2 (2)	6 (5)		8 (3)
Deep	3 (3)	4 (3)		7 (3)
Brainstem	1 (1)	0		1 (<1)
Mixed†	1 (1)	0		1 (<1)
AVM side (%)			0.07	
Rt	59 (53)	57 (48)		116 (50)
Lt	52 (46)	55 (46)		107 (46)
Midline	1 (1)	8 (7)		9 (4)
Preop mRS score (%)			**<0.0001**	
0	48 (43)	14 (12)		62 (27)
1	45 (40)	16 (13)		61 (26)
2	15 (13)	20 (17)		35 (15)
3	4 (4)	26 (22)		30 (13)
4	0	22 (18)		22 (9)
5	0	22 (18)		22 (9)
Spetzler-Martin Grade (%)			0.56	
I	37 (33)	39 (33)		76 (33)
II	75 (67)	81 (68)		156 (67)
Supplementary AVM Grade (%)			**<0.0001**	
1	0	22 (18)		22 (9)
2	11 (10)	35 (29)		46 (20)
3	37 (33)	55 (46)		92 (40)
4	59 (53)	8 (7)		67 (29)

Variable	Unruptured AVM	Ruptured AVM	p Value*	Total
5	5 (4)	0		5 (2)
Prior treatments (%)	61(54)	42 (35)		103 (44)
Preop embolization	59 (53)	40 (33)	**0.005**	99 (43)
Remote embolization	0	2 (2)	0.5	2 (1)
Radiosurgery	3 (3)	1 (1)	0.1	4 (2)

*Comparing unruptured and ruptured AVMs, an ANOVA was used for continuous variables, Fisher's exact test for 2 × 2 contingency tables, and Pearson chi-square test for larger contingency tables. Bold values are statistically significant.

†Refers to an AVM involving both the temporal and parietooccipital regions.

Table 2

Surgical results with low-grade AVMs

Variable	Unruptured AVM	Ruptured AVM	p Value	Total
Total	112	120		232
Angiography outcome (%)			0.46	
Complete	106 (95)	112 (93)		218 94)
Residual	0 (0)	0 (0)		0 (0)
No study	6 (5)	8 (7)		14 (6)
Patients w/>30-day follow-up (%)	100 (89)	107 (89)	Not tested	207 (89)
Mean duration of follow-up ± SD (yrs)	1.8 ± 2.1	1.6 ± 1.4	Not tested	1.7 ± 1.8
Median duration of last follow-up in yrs (range)	1.2 (0.1–12.8)	1.3 (0.1–6.3)	Not tested	1.2 (0.1–12.8)
Functional outcome (mRS score)*			0.0008	
0–1	91 (91)	70 (65)		161 (78)
2	6 (6)	25 (23)		31 (15)
3	3 (3)	5 (5)		8 (4)
4	0 (0)	2 (2)		2 (1)
5	0 (0)	4 (4)		4 (2)
6	0 (0)	1 (1)		1 (0)
Improved/unchanged	96 (96)	105 (98)	0.43	201 (97)
Worse	4 (4)	2 (2)		6 (3)

*Only available in 207 patients.

Table 3

Summary of surgical results with low-grade AVMs

Authors & Year	No. of Patients	Morbidity (%)	Mortality (%)	Cure Rate (%)	Hemorrhage (%)
Spetzler & Martin, 1986	44	2.3	0	NA	NA
Heros et al., 1990	47	2.2	2.2	100	0
Sundt et al., 1991	84	2.2	0	100	0
Sisti et al., 1993	67	1.5	0	94	0
Hamilton & Spetzler, 1994	40	0.0	0	100	NA
Schaller & Schramm, 1997	50	3.2	0	NA	2
Schaller et al., 1998	81	0.0	0	NA	NA
Pikus et al., 1998	26	3.8	0	100	0
Hartmann et al., 2000	48	6.6	0	NA	NA
Morgan et al., 2004	220	0.9	0.5	100	0
Davidson & Morgan, 2010	296	0.7	0	97	NA
Lawton, 2014	232	2.4	0.5	98	0
Total	1235	2.2 (mean)	0.3 (mean)	98.5 (mean)	0.3 (mean)

NA = not available

Table 4

Summary of endovascular results with Onyx for mostly low-grade AVMs

Authors & Year	No. of Patients	Morbidity (%)	Mortality (%)	Cure Rate (%)	Hemorrhage (%)
Pérez-Higueras et al., 2005	45	15.5	2.0	22	8.9
Song et al., 2005	50	10.0	0.0	20	6.0
Van Rooij et al., 2007	44	4.6	2.3	16	6.8
Weber et al., 2007	93	5.4	0.0	20	NA
Mounayer et al., 2007	94	4.3	3.2	28	8.5
Katsaridis et al., 2008	101	8.0	3.0	28	5.9
Pierot et al., 2009	50	8.0	2.0	8	8.0
Panagiotopoulos et al., 2009	82	7.3	2.4	20	12.2
Gao et al., 2009	115	2.6	0.9	26	2.6
Maimon et al., 2010	43	2.3	0.0	37	13.9
Xu et al., 2011	86	3.5	1.2	19	7.0
Saatci et al., 2011	350	4.3	1.4	51	4.0
Abud et al., 2011	17	5.9	0.0	94	11.7
Pierot et al., 2013	127	5.1	4.3	24	8.5
Total	1297	6.2 (mean)	1.6 (mean)	29.5 (mean)	8.0 (mean)

NA = not available

Table 5

Summary of radiosurgical results with low-grade AVMs

Authors & Year	No. of Patients	Morbidity (%)	Mortality (%)	Cure Rate (%)	Hemorrhage (%)
Pollock et al., 1994	65	5.0	3.0	86.0	7.7
Yamamoto et al., 1996	19	NA	0.0	63.2	2.5
Meder et al., 1997	57	NA	NA	65.0	NA
Friedman et al., 2003	107	NA	NA	66.4	10.4
Nataf et al., 2007	27	NA	0.0	77.8	10.0
Kano et al., 2012	217	3.2	2.8	93.0	6.0
Fokas et al., 2013	24	NA	NA	61.0	6.0
Koltz et al., 2013	33	12.1	0.0	88.0	9.1
Ding et al., 2014	502	5.6	NA	76.1	5.6
Total	1051	6.5 (mean)	1.2 (mean)	75.2 (mean)	7.2 (mean)

NA = not available