Microsurgery Versus Stereotactic Radiosurgery for Brain Arteriovenous Malformations: A Matched Cohort Study

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Received, August 22, 2017.
Accepted, April 5, 2018.
Published Online, May 12, 2018.

BACKGROUND: Microsurgery (MS) and stereotactic radiosurgery (SRS) remain the preferred interventions for the curative treatment of brain arteriovenous malformations (AVM), but their relative efficacy remains incompletely defined.

OBJECTIVE: To compare the outcomes of MS to SRS for AVMs through a retrospective, matched cohort study.

METHODS: We evaluated institutional databases of AVM patients who underwent MS and SRS. MS-treated patients were matched, in a 1:1 ratio based on patient and AVM characteristics, to SRS-treated patients. Statistical analyses were performed to compare outcomes data between the 2 cohorts. The primary outcome was defined as AVM obliteration without a new permanent neurological deficit.

RESULTS: The matched MS and SRS cohorts were each comprised of 59 patients. Both radiological (85 vs 11 mo; $P < .001$) and clinical (92 vs 12 mo; $P < .001$) follow-up were significantly longer for the SRS cohort. The primary outcome was achieved in 69% of each cohort. The MS cohort had a significantly higher obliteration rate (98% vs 72%; $P = .001$), but also had a significantly higher rate of new permanent deficit (31% vs 10%; $P = .011$). The posttreatment hemorrhage rate was significantly higher for the SRS cohort (10% for SRS vs 0% for MS; $P = .027$). In subgroup analyses of ruptured and unruptured AVMs, no significant differences between the primary outcomes were observed.

CONCLUSION: For patients with comparable AVMs, MS and SRS afford similar rates of deficit-free obliteration. Nidal obliteration is more frequently achieved with MS, but this intervention also incurs a greater risk of new permanent neurological deficit.

KEY WORDS: Gamma knife, Intracranial arteriovenous malformation, Intracranial hemorrhages, Microsurgery, Radiosurgery, Stroke, Vascular malformations

Neurosurgery 84:696–708, 2019 DOI:10.1093/neuros/nyy174 www.neurosurgery-online.com

The interventions used in the contemporary management of brain arteriovenous malformations (AVM) include microsurgery (MS), stereotactic radiosurgery (SRS), and embolization.[1-10] At many cerebrovascular centers, MS and SRS are the modalities of choice for the definitive treatment of an AVM, while nidal embolization is primarily reserved for preoperative devascularization, pre-SRS volume reduction, or occlusion of high-risk arterial feeders.[2,8,11-18] Since MS is preferentially employed for superficially located, noneloquent AVMs, and SRS is preferentially employed for deep-seated, eloquent lesions, a rigorous comparison of the 2 interventions is lacking.[19-27] Previously published series that juxtaposed MS- and SRS-treated AVMs did not account for differences in baseline patient and AVM factors.[28-31] Therefore, the aim of this retrospective, matched cohort study is to directly compare the outcomes of MS to SRS for comparable AVMs.

ABBREVIATIONS: ARUBA, A Randomized Trial of Unruptured Brain AVMs; **AVM,** arteriovenous malformations; **CT,** computed tomography; **MRI,** magnetic resonance imaging; **MS,** Microsurgery; **OR,** odds ratio; **RBAS,** modified radiosurgery-based AVM score; **RIC,** radiation-induced changes; **SM,** Spetzler–Martin; **SRS,** stereotactic radiosurgery; **VRAS,** Virginia Radiosurgery AVM Scale

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METHODS

Study Design

We retrospectively reviewed institutional review board approved databases of consecutive AVM patients who underwent MS and SRS at our institution from 2001 to 2013. Patient consent was not required by the committee due to the retrospective nature of the review and deidentification of data presented. The inclusion criteria for MS cohort and SRS cohort-eligible patients were as follows: (1) age $\geq$ 18 yr; (2) sufficient data regarding baseline patient, AVM, and treatment factors; (3) AVM treatment with either MS or single-session SRS; (4) available posttreatment radiological and clinical outcomes data; and (5) for SRS cohort-eligible patients, a minimum follow-up duration of 2 yr.

SRS Procedure

All SRS procedures were performed using the Gamma Knife (Elekta AB, Stockholm, Sweden). Our institution's technique has been previously described in detail.[32] All patients underwent pre-SRS catheter angiography and stereotactic thin-slice (slice width $\leq$ 1mm) magnetic resonance imaging (MRI) or computed tomography (CT). Dose planning was performed using the Kula software (Kula Software LLC, Gaithersburg, Maryland) until June 1994, and then the Gamma Plan software (Elekta AB) thereafter.

MS Procedure

All patients underwent preoperative catheter angiography to evaluate the AVM's angioarchitecture and either MRI or CT for surgical planning. The specific surgical approach and use of electrophysiological neuromonitoring or neuronavigation were dependent on AVM location and the preferences of four treating neurosurgeons. The operating microscope and standard microsurgical techniques were used to perform the AVM resection. Postoperatively, patients were monitored in our neurological intensive care unit. A brain CT was routinely performed within 12 h of surgery to evaluate for postoperative hemorrhage.

Baseline Data

Baseline data comprised patient, AVM, and treatment variables. Patient variables included age and gender, AVM variables included prior hemorrhage, maximum diameter, venous drainage pattern, location, and presence of AVM-associated arterial aneurysm, Spetzler–Martin (SM) grade, and prior embolization.[33] The treatment variable was modality of intervention. The supplemented grade was determined for each MS- and SRS-treated patient.[34] The AVM nidus volume, as calculated during SRS treatment planning, Virginia Radiosurgery AVM Scale (VRAS), and modified radiosurgery-based AVM score (RBAS) were calculated for each SRS-treated patient.[32,35] SRS treatment parameters included margin dose, isodose line, and number of isocenters.

Follow-up

MS-treated patients typically underwent a postoperative angiogram during the same hospitalization as the surgery and had clinical follow-up at postoperative intervals of 2 wk, and 3 mo, and 1 yr, and then annually thereafter. SRS-treated patients underwent MRI every 6 mo for the first 2 yr after SRS, and then annually thereafter. Confirmatory catheter angiography was recommended to patients who were determined to have AVM obliteration on MRI. SRS-treated patients with obliterated nidi were recommended to undergo MRI every 2 to 5 yr to monitor for delayed, long-term complications. Additional neuroimaging was obtained for patients with new or worsening neurological symptoms.

Obliteration was defined as the absence of flow voids on MRI or a lack of abnormal arteriovenous shunting on catheter angiography. For SRS-treated patients, radiation-induced changes (RIC) were defined as perinidal T2-weighted hyperintensities on MRI and classified as radiological, symptomatic, or permanent; and cyst formation was defined as the development of a cystic cavity within or adjacent to the region of the original AVM nidus. The primary outcome of this study was defined as AVM obliteration without a new permanent neurological deficit. The secondary outcomes were obliteration, and development of a new deficit, and posttreatment hemorrhage.

Statistical Analysis

The MS cohort was matched manually, in a 1:1 ratio without replacement using the nearest neighbor method based on age, sex, prior hemorrhage, deep venous drainage, AVM nidus location, maximum AVM diameter, AVM-associated aneurysms, and SM grade, to the SRS cohort-eligible patients. All statistical analyses were performed using Stata (version 14.2, College Station, Texas). The aforementioned patient and AVM variables were compared between cohorts. Continuous variables were compared using Student's t or Mann–Whitney U-tests, as appropriate. Categorical variables were compared using Pearson's chi-square or Fisher's exact tests, as appropriate. We performed univariate logistic regression analyses to assess the relationships between intervention and the primary and secondary outcomes. The findings from the logistic regression analyses were adjusted for variables with $P < .20$ in the comparison between the 2 cohorts. Subgroup analyses were performed for ruptured and unruptured AVMs. Statistical significance was defined as $P < .05$, and all tests were 2-tailed. Missing data were not imputed.

RESULTS

Characteristics of the MS and SRS Cohorts

The MS and SRS databases comprised 68 and 1400 patients, respectively. After the application of inclusion and exclusion criteria, the cohorts comprised 59 and 763 patients, respectively. Nine MS-treated patients were excluded due to lack of follow-up. The matching process yielded a total of 118 AVM patients, comprised of 59 in each of the MS and SRS cohorts. Table 1 compares the patient, AVM, and treatment characteristics of the matched MS and SRS cohorts. There were no significant differences between the baseline characteristics of the 2 cohorts. The mean ages of the MS and SRS cohorts were 38.6 and 34.6 yr, respectively ($P = .135$). The mean maximum AVM diameters of the MS and SRS cohorts were 2.3 and 2.4 cm, respectively ($P = .452$). The SM grades were I–II for 69% and III–IV for 31% of each cohort. The incidences of prior AVM embolization for the MS and SRS cohorts were 41% and 27%, respectively ($P = .120$). The SRS cohort had significantly longer radiological (85 vs 11 mo; $P < .001$) and clinical (92 vs 12 mo; $P < .001$) follow-up.

We performed subgroup analyses for the MS and SRS outcomes of ruptured and unruptured AVMs Table 2 compares the patient, nidal, and treatment characteristics of the ruptured AVMs in the MS and SRS cohorts. There were no significant

TABLE 1. Comparison of the Patient, AVM, and Treatment Characteristics of the Matched Microsurgery and Stereotactic Radiosurgery Cohorts

	Microsurgery (n = 59)	Stereotactic radiosurgery (n = 59)	*P*-value
Age, yr (SD)	38.6 (16.6)	34.6 (12.4)	.135[a]
Male gender, n (%)	29 (49.2)	28 (47.5)	.854[a]
Prior AVM hemorrhage, n (%)	44 (74.6)	40 (67.8)	.416[a]
Maximum AVM diameter, n (%)			1.000[a]
< 3 cm	44 (74.6)	44 (74.6)	
3-6 cm	15 (25.4)	15 (25.4)	
Mean, cm (SD)	2.3 (1.2)	2.4 (1.1)	.452[a]
AVM volume, mL (SD)	–	5.3 (5.1)	–
Deep venous drainage, n (%)	35 (59.3)	33 (55.9)	.709[a]
AVM location, n (%)			.486[a]
Supratentorial	49 (83.0)	46 (78.0)	
Infratentorial	10 (17.0)	13 (22.0)	
Eloquent AVM location, n (%)	26 (44.1)	25 (42.4)	.853
AVM-associated aneurysms, n (%)			.651[a]
Intranidal	11 (18.6)	7 (11.9)	
Prenidal	9 (15.3)	7 (11.9)	
SM grade, n (%)			1.000[a]
I	10 (17.0)	10 (17.0)	
II	31 (52.5)	31 (52.5)	
III	12 (20.3)	12 (20.3)	
IV	6 (10.2)	6 (10.2)	
Supplemented SM grade, n (%)			–
I	10 (17.0)	8 (13.6)	
II	14 (23.7)	19 (32.2)	
III	26 (44.1)	24 (40.7)	
IV	9 (15.3)	8 (13.6)	
Prior AVM embolization, n (%)	24 (40.7)	16 (27.1)	.120
SRS margin dose, Gy (SD)	–	21.0 (4.2)	–
Isodose line, % (SD)	–	55.2 (13.1)	–
Isocenters, n (SD)	–	2.8 (2.1)	–
VRAS, n (%)			–
0	–	1 (1.7)	
1	–	13 (22.0)	
2	–	17 (28.8)	
3	–	19 (32.2)	
4	–	9 (15.3)	
RBAS, n (%)			–
≤ 1.00	–	19 (32.2)	
1.01-1.50	–	26 (44.1)	
1.51-2.00	–	10 (17.0)	
> 2.00	–	4 (6.8)	
Radiological follow-up, mo (SD)	11.2 (19.8)	85.0 (56.1)	**< .001**
Clinical follow-up, mo (SD)	12.2 (22.4)	92.1 (58.3)	**< .001**

SM = Spetzler–Martin; SRS = stereotactic radiosurgery; VRAS = Virginia Radiosurgery AVM Scale; RBAS = modified radiosurgery-based AVM score; n = number; SD = standard deviation. Bold values indicates statistical significance at a *P*-value of <0.05.
[a]Matched covariates.

differences between the baseline characteristics of MS- and SRS-treated ruptured AVMs. Ruptured AVMs in the SRS cohort had significantly longer radiological (11 vs 83 mo; $P < .001$) and clinical (13 vs 90 mo; $P < .001$) follow-up durations. Table 3 compares the patient, nidal, and treatment characteristics of the unruptured AVMs in the MS and SRS cohorts. Deep venous drainage was significantly more common in MS-treated unruptured AVMs (87% vs 47%; $P = .017$). Unruptured AVMs in the SRS cohort had significantly longer radiological (13 vs 90 mo; $P < .001$) and clinical (97 vs 9 mo; $P < .001$) follow-up.

TABLE 2. Comparison of the Patient, Nidal, and Treatment Characteristics of the Ruptured AVMs in the Microsurgery and Stereotactic Radiosurgery Cohorts

	Microsurgery (n = 44)	Stereotactic radiosurgery (n = 40)	*P*-value
Age, yr (SD)	38.6 (17.5)	32.7 (13.1)	.088
Male gender, n (%)	23 (52.3)	19 (47.5)	.662
Maximum AVM diameter, n (%)			.584
< 3 cm	33 (75.0)	32 (80.0)	
3-6 cm	11 (25.0)	8 (20.0)	
Mean, cm (SD)	2.2 (1.2)	2.2 (1.0)	.833
AVM volume, mL (SD)	–	4.0 (3.1)	–
Deep venous drainage, n (%)	22 (50.0)	24 (60.0)	.358
AVM location, n (%)			.449
Supratentorial	34 (77.3)	28 (70.0)	
Infratentorial	10 (22.7)	12 (30.0)	
Eloquent AVM location, n (%)	18 (40.9)	16 (40.0)	.932
AVM-associated aneurysms, n (%)			.530
Intranidal	8 (18.2)	5 (12.5)	
Prenidal	7 (15.9)	3 (7.5)	
SM grade, n (%)			1.000
I	8 (18.2)	8 (20.0)	
II	23 (52.3)	20 (50.0)	
III	9 (20.5)	8 (20.0)	
IV	4 (9.1)	4 (10.0)	
Supplemented SM grade, n (%)			–
I	10 (22.7)	8 (20.0)	
II	12 (27.3)	19 (47.5)	
III	22 (50.0)	13 (32.5)	
IV	0 (0)	0 (0)	
Prior AVM embolization, n (%)	15 (34.1)	10 (25.0)	.363
SRS margin dose, Gy (SD)	–	22.0 (3.7)	–
Isodose line, % (SD)	–	56.6 (13.1)	–
Isocenters, n (SD)	–	2.75 (2.3)	–
VRAS, n (%)			–
0	–	0 (0.0)	
1	–	8 (20.0)	
2	–	12 (30.0)	
3	–	11 (27.5)	
4	–	9 (22.5)	
RBAS, n (%)			–
≤ 1.00	–	16 (40.0)	
1.01-1.50	–	17 (42.5)	
1.51-2.00	–	7 (17.5)	
> 2.00	–	0 (0.0)	
Radiological follow-up, mo (SD)	10.6 (19.8)	82.6 (56.9)	**< .001**
Clinical follow-up, mo (SD)	13.4 (24.8)	89.7 (60.5)	**< .001**

SM = Spetzler–Martin; SRS = stereotactic radiosurgery; VRAS = Virginia Radiosurgery AVM Scale; RBAS = modified radiosurgery-based AVM score; n = number; SD = standard deviation. Bold values indicates statistical significance at a *P*-value of <0.05.

Outcomes of the MS vs SRS Cohorts

Table 4 compares the primary and secondary outcomes between the SRS vs MS cohorts. The primary outcome was achieved in 41 patients (69%) in each cohort ($P = 1.000$). After adjusting for age and prior AVM embolization, a significant difference was not found in the rate of primary outcome between the 2 cohorts.

The AVM obliteration rate was significantly higher in the MS cohort (98% vs 72%; $P = .003$). This difference remained significant, in favor of MS, after adjusting for the covariates (odds ratio

TABLE 3. Comparison of the Patient, Nidal, and Treatment Characteristics of the Unruptured AVMs of the Microsurgery and Stereotactic Radiosurgery Cohorts

	Microsurgery (n = 15)	Stereotactic radiosurgery (n = 19)	*P*-value
Age, yr (SD)	38.7 (14.1)	38.5 (9.9)	.950
Male gender, n (%)	6 (40.0)	9 (47.4)	.667
Maximum AVM diameter, n (%)			.715
< 3cm	11 (73.3)	12 (63.2)	
3-6cm	4 (26.7)	7 (36.8)	
Mean, cm (SD)	2.5 (1.2)	2.8 (1.2)	.571
AVM volume, mL (SD)	–	7.8 (7.2)	–
Deep venous drainage, n (%)	13 (86.7)	9 (47.4)	**.017**
AVM location, n (%)			1.000
Supratentorial	15 (100.0)	18 (94.7)	
Infratentorial	0 (0.0)	1 (5.3)	
Eloquent AVM location, n (%)	8 (53.3)	9 (47.4)	.730
AVM-associated aneurysms, n (%)			.880
Intranidal	3 (20.0)	2 (10.5)	
Prenidal	2 (13.3)	4 (21.1)	
SM grade, n (%)			1.000
I	2 (13.3)	2 (10.5)	
II	8 (53.3)	11 (57.9)	
III	3 (20.0)	4 (21.1)	
IV	2 (13.3)	2 (10.5)	
Supplemented SM grade, n (%)			–
I	0 (0)	0 (0)	
II	2 (13.3)	0 (0)	
III	4 (26.7)	11 (57.9)	
IV	9 (60.0)	8 (42.1)	
Prior AVM embolization, n (%)	9 (60.0)	6 (31.6)	.097
SRS margin dose, Gy (SD)	–	18.7 (4.5)	–
Isodose line, % (SD)	–	52.2 (13.0)	–
Isocenters, n (SD)	–	3.1 (1.9)	–
VRAS, n (%)			–
0	–	1 (5.3)	
1	–	5 (26.3)	
2	–	5 (26.3)	
3	–	8 (42.1)	
4	–	0 (0.0)	
RBAS, n (%)			–
≤1.00	–	3 (15.8)	
1.01-1.50	–	9 (47.4)	
1.51-2.00	–	3 (15.8)	
>2.00	–	4 (21.1)	
Radiological follow-up, mo (SD)	12.8 (20.6)	90.0 (55.6)	**< .001**
Clinical follow-up, mo (SD)	8.7 (13.2)	97.0 (54.8)	**< .001**

SM = Spetzler–Martin; SRS = stereotactic radiosurgery; VRAS = Virginia Radiosurgery AVM Scale; RBAS = modified radiosurgery-based AVM score; n = number; SD = standard deviation. Bold values indicates statistical significance at a *P*-value of <0.05.

[OR] = 39.536; $P = .001$). AVM obliteration was confirmed by catheter angiography in 81% (35/43 patients) and 97% (56/58 patients) of the SRS and MS cohorts, respectively. The rate of new neurological deficit was also significantly higher in the MS (31% vs 10%; $P = .009$). This difference remained significant, in favor of MS, after adjusting for the covariates (OR = 3.758; $P = .011$).

The posttreatment hemorrhage rates were significantly higher for the SRS cohort compared to the MS cohort (10% vs 0%; $P = .027$). In the SRS cohort, RIC was radiologically evident

TABLE 4. Comparisons of the Primary and Secondary Outcomes Between the Matched Stereotactic Radiosurgery and Microsurgery Cohorts, Including the Subgroup Analyses of Ruptured and Unruptured AVMs

	Stereotactic radiosurgery	Microsurgery	Unadjusted OR [95% CI]	*P*-value	Adjusted OR [95% CI]	*P*-value
Overall						
Primary outcome						
Obliteration without new deficit, n (%)	41/59 (69.5)	41/59 (69.5)	1.000 [0.457–2.190]	1.000	1.192 [0.518–2.744] [a]	.679[a]
Secondary outcome						
Obliteration, n (%)	43/59 (72.3)	58/59 (98.3)	21.581 [2.755–169.061]	**.003**	39.536 [4.498–347.475][a]	**.001** [a]
New deficit, n (%)	6/59 (10.2)	18/59 (30.5)	3.878 [1.413–10.646]	**.009**	3.758 [1.347–10.489][a]	**.011**[a]
Hemorrhage, n (%)	6/59 (10.2)	0/59 (0)	NA[e]	**.027**[f]	NA[e]	NA[e]
Ruptured AVMs						
Primary outcome						
Obliteration without new deficit, n (%)	33/40 (82.5)	33/44 (75.0)	0.636 [0.220–1.843]	.405	0.661 [0.224–1.952][b]	.453[b]
Secondary outcome						
Obliteration, n (%)	34/40 (85.0)	43/44 (97.7)	7.588 [0.871–66.080]	.066	7.591 [0.849–67.884][b]	.070[b]
New deficit, n (%)	2/40 (5.0)	11/44 (25.0)	6.333 [1.308–30.661]	**.022**	6.175 [1.256–30.349][b]	**.025**[b]
Hemorrhage, n (%)	4/40 (10.0)	0/44 (0)	NA[e]	**.047**[f]	NA[e]	NA[e]
Unruptured AVMs						
Primary outcome						
Obliteration without new deficit, n (%)	8/19 (42.1)	8/15 (53.3)	1.571 [0.402–6.142]	.516	1.655 [0.309–8.859][c]	.556[c]
Secondary outcome						
Obliteration, n (%)	9/19 (47.4)	15/15 (100.0)	NA[d]	**.001**[f]	NA[d]	NA[d]
New deficit, n (%)	4/19 (21.1)	7/15 (46.7)	3.281 [0.733–14.683]	.120	4.351 [0.707–26.776][c]	.113[c]
Hemorrhage, n (%)	2/19 (10.5)	0/15 (0)	NA[e]	.492[f]	NA[e]	NA[e]

OR = odds ratio; CI = confidence interval; AVM = arteriovenous malformation; NA = not applicable; n = number. Bold values indicates statistical significance at a *P*-value of <0.05.
[a] Adjusted for age, and prior AVM embolization.
[b] Adjusted for age.
[c] Adjusted for prior AVM embolization, and deep venous drainage.
[d] All nonruptured AVMs in the microsurgery cohort achieved obliteration.
[e] No posttreatment hemorrhage occurred in the microsurgery cohort.
[f] Fisher's exact test.

in 18 patients (31%), symptomatic in 6 (10%), and permanent in 2 (3.4%) patients. Post-SRS cyst development occurred in 1 (1.7%) patient. Ventriculo-peritoneal shunt placement, surgical treatment for wound infection, and surgical intervention for cerebrospinal fluid leak were necessary in 2 (3.4%), 2 (3.4%), and 1 (1.7%) patients of the MS cohort.

Table 5 compares the primary and secondary outcomes between the MS vs SRS cohorts, stratified by SM and supplemented SM grades. There were no significant differences between MS and SRS cohorts in the rate of primary outcome achieved for each SM grade or for a supplemented SM grade cutoff of 6. The obliteration rate was significantly higher in the MS cohort for SM grade II (100% vs 77%, $P = .011$) and III (100% vs 58%, $P = .037$) AVMs. Patients with a supplemented SM grade ≤ 6 had a higher obliteration rate after MS (100% vs 76%, $P < .001$), but also had a higher rate of new neurological deficit (28% vs 7%, $P = .005$).

Outcomes of MS vs SRS for Ruptured AVMs

In the subgroup analysis of ruptured AVMs, the primary outcome was achieved in 83% of the SRS and 75% of the MS cohorts (Table 4). This difference remained nonsignificant after adjusting for age. The AVM obliteration rates were not significantly different for ruptured AVMs between the SRS (85%) and MS (98%) cohorts. This difference remained nonsignificant after adjusting for age. The rate of new neurological deficit was significantly higher for ruptured AVMs in the MS cohort (25% vs 5%;

TABLE 5. Comparison of the Primary and Secondary Outcomes Between the Matched Microsurgery and Stereotactic Radiosurgery Cohorts, Stratified by Spetzler–Martin and Supplemented Spetzler–Martin Grades

	Microsurgery	Stereotactic radiosurgery	*P*-value
Overall			
SM I			
Obliteration without new deficit, n (%)	7/10 (70.0)	9/10 (90.0)	.582
Obliteration, n (%)	10/10 (100.0)	9/10 (90.0)	1.000
New deficit, n (%)	3/10 (30.0)	0/10 (0)	.211
Hemorrhage, n (%)	0/10 (0)	1/10 (10.0)	1.000
SM II			
Obliteration without new deficit, n (%)	24/31 (77.4)	22/31 (71.0)	.562
Obliteration, n (%)	31/31 (100.0)	24/31 (77.4)	**.011**
New deficit, n (%)	7/31 (22.6)	3/31 (9.7)	.301
Hemorrhage, n (%)	0/31 (0)	4/31 (12.9)	.113
SM III			
Obliteration without new deficit, n (%)	7/12 (58.3)	7/12 (58.3)	1.000
Obliteration, n (%)	12/12 (100.0)	7/12 (58.3)	**.037**
New deficit, n (%)	5/12 (41.7)	2/12 (16.7)	.371
Hemorrhage, n (%)	0/12 (0)	0/12 (0)	1.000
SM IV			
Obliteration without new deficit, n (%)	3/6 (50.0)	3/6 (50.0)	1.000
Obliteration, n (%)	5/6 (83.3)	3/6 (50.0)	.545
New deficit, n (%)	3/6 (50.0)	1/6 (16.7)	.545
Hemorrhage, n (%)	0/6 (0)	1/6 (16.7)	1.000
Total supplemented SM $\leq$ 6			
Obliteration without new deficit, n (%)	38/53 (71.7)	39/54 (72.2)	.952
Obliteration, n (%)	53/53 (100.0)	41/54 (75.9)	**< .001**
New deficit, n (%)	15/53 (28.3)	4/54 (7.4)	**.005**
Hemorrhage, n (%)	0/53 (0)	5/54 (9.3)	.057
Total supplemented SM > 6			
Obliteration without new deficit, n (%)	3/6 (50.0)	2/5 (40.0)	1.000
Obliteration, n (%)	5/6 (83.3)	2/5 (40.0)	.242
New deficit, n (%)	3/6 (50.0)	2/5 (40.0)	1.000
Hemorrhage, n (%)	0/6 (0)	1/5 (20.0)	.455
Ruptured AVMs			
SM I			
Obliteration without new deficit, n (%)	5/8 (62.5)	7/8 (87.5)	.569
Obliteration, n (%)	8/8 (100.0)	7/8 (87.5)	1.000
New deficit, n (%)	3/8 (37.5)	0/8 (0)	.200
Hemorrhage, n (%)	0/8 (0)	1/8 (12.5)	1.000
SM II			
Obliteration without new deficit, n (%)	21/23 (91.3)	17/20 (85.0)	.650
Obliteration, n (%)	23/23 (100.0)	18/20 (90.0)	.210
New deficit, n (%)	2/23 (8.7)	2/20 (10.0)	1.000
Hemorrhage, n (%)	0/23 (0)	2/20 (10.0)	.210
SM III			
Obliteration without new deficit, n (%)	5/9 (55.6)	6/8 (75.0)	.620
Obliteration, n (%)	9/9 (100.0)	6/8 (75.0)	.206
New deficit, n (%)	4/9 (44.4)	0/8 (0)	.082
Hemorrhage, n (%)	0/9 (0)	0/8 (0)	1.000
SM IV			
Obliteration without new deficit, n (%)	2/4 (50.0)	3/4 (75.0)	1.000
Obliteration, n (%)	3/4 (75.0)	3/4 (75.0)	1.000
New deficit, n (%)	2/4 (50.0)	0/4 (0)	.429
Hemorrhage, n (%)	0/4 (0)	1/4 (25.0)	1.000
Total supplemented SM $\leq$ 6			
Obliteration without new deficit, n (%)	32/41 (78.1)	32/39 (82.1)	.655
Obliteration, n (%)	41/41 (100.0)	33/39 (84.6)	**.011**
New deficit, n (%)	9/41 (22.0)	2/39 (5.1)	**.029**

TABLE 5 *—continued*

	Microsurgery	Stereotactic radiosurgery	*P*-value
Hemorrhage, n (%)	0/41 (0)	3/39 (7.7)	.111
Total supplemented SM > 6			
Obliteration without new deficit, n (%)	1/3 (33.3)	1/1 (100.0)	1.000
Obliteration, n (%)	2/3 (66.7)	1/1 (100.0)	1.000
New deficit, n (%)	2/3 (66.7)	0/1 (0)	1.000
Hemorrhage, n (%)	0/3 (0)	1/1 (100.0)	.250
Unruptured AVMs			
SM I			
Obliteration without new deficit, n (%)	2/2 (100.0)	2/2 (100.0)	1.000
Obliteration, n (%)	2/2 (100.0)	2/2 (100.0)	1.000
New deficit, n (%)	0/2 (0)	0/2 (0)	1.000
Hemorrhage, n (%)	0/2 (0)	0/2 (0)	1.000
SM II			
Obliteration without new deficit, n (%)	3/8 (37.5)	5/11 (45.5)	1.000
Obliteration, n (%)	8/8 (100.0)	6/11 (54.6)	**.045**
New deficit, n (%)	5/8 (62.5)	1/11 (9.1)	**.041**
Hemorrhage, n (%)	0/8 (0)	2/11 (18.2)	.485
SM III			
Obliteration without new deficit, n (%)	2/3 (66.7)	1/4 (25.0)	.486
Obliteration, n (%)	3/3 (100.0)	1/4 (25.0)	.143
New deficit, n (%)	1/3 (33.3)	2/4 (50.0)	1.000
Hemorrhage, n (%)	0/3 (0)	0/4 (0)	1.000
SM IV			
Obliteration without new deficit, n (%)	1/2 (50.0)	0/2 (0)	1.000
Obliteration, n (%)	2/2 (100.0)	0/2 (0)	.333
New deficit, n (%)	1/2 (50.0)	1/2 (50.0)	1.000
Hemorrhage, n (%)	0/2 (0)	0/2 (0)	1.000
Total supplemented SM ≤ 6			
Obliteration without new deficit, n (%)	6/12 (50.0)	7/15 (46.7)	.863
Obliteration, n (%)	12/12 (100.0)	8/15 (53.3)	**.008**
New deficit, n (%)	6/12 (50.0)	2/15 (13.3)	.087
Hemorrhage, n (%)	0/12 (0)	2/15 (13.3)	.487
Total supplemented SM > 6			
Obliteration without new deficit, n (%)	2/3 (66.7)	1/4 (25.0)	.486
Obliteration, n (%)	3/3 (100.0)	1/4 (25.0)	.143
New deficit, n (%)	1/3 (33.3)	2/4 (50.0)	1.000
Hemorrhage, n (%)	0/3 (0)	0/4 (0)	1.000

SM = Spetzler–Martin; AVM = arteriovenous malformation; n = number. Bold values indicates statistical significance at a *P*-value of <0.05.

$P = .022$). This difference remained significant, in favor of MS, after adjusting for the covariates (OR = 6.175; $P = .025$). The posttreatment hemorrhage rates for ruptured AVMs were significantly higher for the SRS cohort compared to the MS cohort (10% vs 0%; $P = .047$).

Subgroup analyses by SM and supplemented SM grades for ruptured AVMs showed no significant differences between the MS and SRS cohorts in the rate of primary outcome achieved for each SM grade or for a supplemented SM grade cutoff of 6 (Table 5). Ruptured AVMs with a supplemented SM grade ≤ 6 had a higher obliteration rate after MS (100% vs 85%, $P = .011$), but also had a higher rate of new neurological deficit (22% vs 5%, $P = .029$).

Outcomes for MS vs SRS for Unruptured AVMs

In the subgroup analysis of unruptured AVMs, the primary outcome was achieved in 42% of the SRS and 53% of the MS cohorts (Table 4). This difference remained nonsignificant after adjusting for prior AVM embolization and deep venous drainage. The obliteration rate was significantly higher for unruptured AVMs in the MS cohort (100% vs 47%; $P = .001$). The rates of new neurological deficit for unruptured AVMs were not significantly different between SRS (21%) and MS (47%) cohorts. This difference remained nonsignificant after adjusting for the covariates. The posttreatment hemorrhage rates were 10.5% for the SRS (2/19 patients) and 0% for the MS (0/15 patients) cohorts ($P = .492$).

Subgroup analysis by SM and supplemented SM grades for unruptured AVMs showed no significant differences in primary outcome between the MS and SRS cohorts in the rate of primary outcome achieved for each SM grade or for a supplemented SM grade cutoff of 6 (Table 5). For unruptured SM grade II AVMs, the rates of obliteration (100% vs 55%, $P = .045$) and new neurological deficit (63% vs 9%, $P = .041$) were both significantly higher in the MS cohort. Unruptured AVMs with a supplemented SM grade ≤ 6 had a higher obliteration rate after MS (100% vs 53%, $P = .008$), but also had a higher rate of new neurological deficit, which trended toward significance (50% vs 13%, $P = .087$).

DISCUSSION

The primary goal of brain AVM treatment is the prevention of hemorrhagic stroke, which is achieved by complete nidal occlusion and elimination of arteriovenous shunting.[36] Currently, MS remains the gold standard of treatment, since it confers immediate and durable protection from AVM hemorrhage if angiographic cure is achieved. MS outcomes have been well documented in the literature, largely by single-center, retrospective cohort studies.[34,37-41] The SM grading scale is the most commonly used classification for estimating the operative risk of MS, based on AVM features alone.[33] More recently, a supplementary grading system, factoring in patient age, prior AVM hemorrhage, and nidal morphology, has been devised to improve the predictive accuracy of the SM grade for neurological outcomes after MS.[8,34] A review of 7 MS series comprising 1476 AVM patients reported high obliteration rates of 90% to 100% across all SM grades.[19] However, the rates of poor outcome, increased substantially with SM grade; 4% for grade I, 10% for grade II, 18% for grade III, 31% for grade IV, and 37% for grade V. Due to the elevated risk of operative morbidity and mortality associated with resection of SM grade IV and V AVMs, MS is not routinely employed for these lesions. Kim et al[8] analyzed a multicenter cohort of 1009 AVM patients who underwent MS and recommended a combined SM and supplementary grade of 6 be used as a cutoff for AVM operability. Patients with a supplemented SM grade ≤ 6 had a 0% to 24% risk of functional decline after MS, whereas those with a supplemented SM grade > 6 had a 39% to 63% risk of worsening.

Single-session SRS is a minimally invasive therapeutic alternative to MS that is ideally suited for small- to medium-sized AVMs that carry an unacceptably high surgical morbidity, or for patients who are unwilling or unable to undergo a craniotomy.[36] The VRAS and RBAS are the most notable grading scales used to predict SRS outcomes for AVMs.[32,35] Obliteration rates after SRS are related to AVM volume and margin dose, but they generally range from 60% to 80% within 3 to 5 yr of treatment.[42,43] In a recent multicenter study of 2236 SRS-treated AVMs, Starke et al[12] reported an obliteration rate of 65% and a favorable outcome (defined as obliteration without post-SRS hemorrhage or permanent RIC) in 60% after a mean follow-up of 7 yr. The disadvantage of SRS compared to MS for AVMs is the latency between treatment and obliteration, which typically spans 0.5 to 3 yr, and the delayed presentation of procedural complications. Until complete endoluminal closure of the AVM is achieved by SRS, patients remain at risk for hemorrhage during the latency period.[44] Post-SRS RIC also tends to manifest before obliteration and causes neurological symptoms in approximately 10% of cases. Even after obliteration is achieved, delayed complications, such as cyst formation, can occur in approximately 1% to 3% of SRS-treated AVM patients after a mean latency period of 6.5 yr.[45]

Although the individual merits and risks of MS and SRS have been extensively characterized in the literature, the comparative effectiveness of these 2 modalities has been poorly studied, due to an absence of rigorous analyses. This may be attributed to the multidisciplinary approach used at most cerebrovascular centers for determining the management of AVM patients, which results in substantially different demographic and nidal characteristics between those treated with MS versus SRS. In contrast, many patients who underwent SRS at our institution were derived from an international referral base, while those who underwent MS tended to be regional referrals. As a result, we are uniquely positioned to perform the first ever matched cohort study comparing the outcomes of MS versus SRS for AVMs. That is, AVM patients who might otherwise be treated with MS at a different center were, instead, referred to our institution for SRS, and therefore treated with the latter modality. The primary outcome (ie, AVM obliteration without a new permanent neurological deficit) was achieved in the same proportion of patients in each cohort (69%). As one would expect, treatment with MS was significantly more likely to achieve obliteration ($P = .001$). However, this came at the cost of a significantly greater risk of new deficit in the MS cohort ($P = .011$). That is, the most common reason the primary outcome was not achieved in the MS cohort was a new neurological deficit, whereas the most common reason the primary outcome was not achieved in the SRS cohort was a lack of obliteration. Thus, in unruptured AVMs, SRS may be more appealing to patients given the lower risk of new neurological deficits. In addition, subgroup analyses by SM and supplementary SM grades demonstrated no difference in primary outcome between the 2 cohorts. The risk of posttreatment hemorrhage was significantly higher for the SRS cohort compared to the MS cohort ($P = .027$). A total of 6 hemorrhages over 404 patient-years in the SRS cohort translate into an annual hemorrhagic risk of 1.5%, consistent with prior studies.[30] However, patients with post-MS deficits can recover neurological function over time. Therefore, given the significantly longer follow-up duration ($P < .001$) of the SRS cohort, it is possible that the discrepancy in posttreatment neurological deficit rates between the 2 treatment modalities may decrease over time.

Limitations

We acknowledge that our study has several limitations that should be considered when interpreting its findings. The retrospective, single-center design subjects this study to the selection,

treatment, and referral biases of our institution and its treating physicians. Despite matching baseline patient and AVM characteristics, there may have been other covariates that were not accounted for by the matching process. It should be also recognized that this study was not designed to compare the outcomes of MS or SRS to those of curative embolization or conservative management. Additionally, MS was only compared to single-session SRS. Therefore, comparisons cannot be drawn between MS and either staged SRS (ie, dose- or volume-staged) for large AVMs or repeat SRS for residual AVMs.[45-52]

In our subgroup analyses of ruptured and unruptured AVMs, no differences were found in the primary outcome between treatment with MS or SRS. MS-treated patients with ruptured AVMs had higher rates of new deficit ($P = .025$) with similar obliteration rates compared to those treated with SRS. However, ruptured AVM patients who presented with large-volume, cortically based or cerebellar hemorrhages underwent urgent surgical intervention. Although the matching process included a history of prior AVM hemorrhage, we were unable to account for the size or severity of the hemorrhage at the ictus of AVM rupture. Therefore, it is possible that AVM hemorrhages in the SRS cohort were less debilitating than in the MS cohort, which may confound our results.[36,53]

For patients with unruptured AVMs, MS achieved a significantly higher rate of obliteration ($P = .001$), while the rates of new deficit were not significantly different between the 2 cohorts. However, due to the small number of unruptured AVMs in each treatment cohort, the subgroup analysis may have been underpowered to detect a significant difference in neurological outcomes. Therefore, one cannot extrapolate a definitive benefit of MS over SRS for unruptured AVMs based on our results. We emphasize this limitation, given the substantial and ongoing controversy regarding the merits of intervention versus conservative management for unruptured AVMs. Despite the findings of worse outcomes from intervention than conservative management from A Randomized Trial of Unruptured Brain AVMs (ARUBA) and the Scottish Audit of Intracranial Vascular Malformations prospective AVM cohort study, multiple retrospective, single-arm interventional studies have been published, each reporting reasonable outcomes for the treatment of appropriately selected patients with unruptured AVMs.[54-66]

The findings of this study may not be generalizable to all AVMs, since pediatric patients were excluded and there were no SM V AVMs.[67-70] We did not design the study to evaluate the effect of partial AVM embolization on MS and SRS outcomes, and we were also unable to account for the potentially disparate objectives of upfront nidal embolization prior to MS versus SRS.[15,71-73] In addition, embolization may have divergent effects on SRS versus MS, as obliteration rates of SRS may be dampened by preprocedural embolization.[15] Due to the nature of being a tertiary referral center for AVM treatment, detailed clinical follow-up regarding functional status, Engel classification of seizure outcomes, and quality of life could not be obtained for some patients.[29,74-80] As with any retrospective study, the current one even though matched is subject to the inherent biases of a retrospective design including selection and referral biases. Although the mean radiological follow-up period for the SRS cohort was 7 yr, we acknowledge that the employment of a 2-yr minimum follow-up is somewhat arbitrary, and may not reflect the maximum potential of SRS. That is, a minimum follow-up duration of 2 yr in the SRS cohort may bias our results toward less favorable outcomes, due to an insufficiently long latency period after SRS to allow for AVM obliteration. However, a longer minimum follow-up (eg, 3 yr) could, conversely, bias our results toward more favorable outcomes by underrepresenting the proportion of AVMs that failed to achieved obliteration after SRS.

Finally, obliteration was determined by MRI alone in 3% and 19% of the MS and SRS cohorts, respectively, although previous studies have shown MRI to be an acceptably accurate substitute to angiography for evaluating nidal patency after SRS.[81-83] O'Connor et al[82] reported a significant correlation between MRI accuracy in evaluating AVM obliteration after SRS and nidus volume; for a nidal volume > 2.8 mL, MRI had an accuracy of 90%, whereas for a nidal volume < 2.8 mL, MRI had an accuracy of 70%. In a more recent study by Lee et al[81] evaluating the predictive value of MRI in assessing AVM obliteration after SRS between 2 blinded observers, the investigators found sensitivities of 85% and 77%, and specificities of 89% and 95%. Despite the utility of MRI for determining post-SRS obliteration, angiography remains the gold standard in confirming obliteration.

CONCLUSION

MS and SRS afford equivalent rates of deficit-free AVM obliteration for patients with angioarchitecturally comparable nidi. MS-treated AVM patients were more likely to achieve nidal obliteration, but they also incurred a greater risk of new permanent neurological deficit. Higher quality evidence is needed to better define the optimal treatment approach for AVMs in which patients are both eligible and willing to undergo SRS and MS.

Disclosure

The authors have no personal, financial, or institutional interest in any of the drugs, materials, or devices described in this article.

REFERENCES

1. van Beijnum J, van der Worp HB, Buis DR, et al. Treatment of brain arteriovenous malformations. *JAMA*. 2011;306(18):2011-2019.
2. Conger JR, Ding D, Raper DM, et al. Preoperative embolization of cerebral arteriovenous malformations with silk suture and particles: technical considerations and outcomes. *J Cerebrovasc Endovasc Neurosurg*. 2016;18(2):90-99.
3. Cohen-Inbar O, Ding D, Sheehan JP. Stereotactic radiosurgery for deep intracranial arteriovenous malformations, part 2: Basal ganglia and thalamus arteriovenous malformations. *J Clin Neurosci*. 2016;24:37-42.
4. Ding D, Liu KC. Predictive capability of the Spetzler-Martin versus supplementary grading scale for microsurgical outcomes of cerebellar arteriovenous malformations. *J Cerebrovasc Endovasc Neurosurg*. 2013;15(4):307-310.

5. Ding D, Yen CP, Starke RM, Xu Z, Sheehan JP. Effect of prior hemorrhage on intracranial arteriovenous malformation radiosurgery outcomes. *Cerebrovasc Dis*. 2015;39(1):53-62.
6. Oermann EK, Rubinsteyn A, Ding D, et al. Using a machine learning approach to predict outcomes after radiosurgery for cerebral arteriovenous malformations. *Sci Rep*. 2016;6 (1):21161.
7. Starke RM, Ding D, Kano H, et al. International multicenter cohort study of pediatric brain arteriovenous malformations. Part 2: outcomes after stereotactic radiosurgery. *J Neurosurg Pediatr* 2017;19(2):136-148.
8. Kim H, Abla AA, Nelson J, et al. Validation of the supplemented Spetzler-Martin grading system for brain arteriovenous malformations in a multicenter cohort of 1009 surgical patients. *Neurosurgery*. 2015;76(1):25-33; discussion 31-22; quiz 32-23.
9. Saatci I, Geyik S, Yavuz K, Cekirge HS. 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(1):78-88.
10. Ding D, Starke RM, Sheehan JP. Radiosurgery for the management of cerebral arteriovenous malformations. *Handb Clin Neurol*. 2017;143:69-83.
11. Ding D, Yen CP, Xu Z, Starke RM, Sheehan JP. Radiosurgery for patients with unruptured intracranial arteriovenous malformations. *J Neurosurg*. 2013;118(5):958-966.
12. Starke RM, Kano H, Ding D, et al. Stereotactic radiosurgery for cerebral arteriovenous malformations: evaluation of long-term outcomes in a multicenter cohort. *J Neurosurg*. 2017;126(1):36-44.
13. Ding D, Sheehan JP, Starke RM, et al. Embolization of cerebral arteriovenous malformations with silk suture particles prior to stereotactic radiosurgery. *J Clin Neurosci*. 2015;22(10):1643-1649.
14. Oermann EK, Ding D, Yen CP, et al. Effect of prior embolization on cerebral arteriovenous malformation radiosurgery outcomes. *Neurosurgery*. 2015;77(3):406-417; discussion 417.
15. Russell D, Peck T, Ding D, et al. Stereotactic radiosurgery alone or combined with embolization for brain arteriovenous malformations: a systematic review and meta-analysis. *J Neurosurg*. 2017;1-11. doi: 10.3171/2016.11.JNS162382.
16. Crowley RW, Ducruet AF, Kalani MY, Kim LJ, Albuquerque FC, McDougall CG. Neurological morbidity and mortality associated with the endovascular treatment of cerebral arteriovenous malformations before and during the Onyx era. *J Neurosurg*. 2015;122(6):1492-1497.
17. Ding D, Xu Z, Starke RM, et al. Radiosurgery for cerebral arteriovenous malformations with associated arterial aneurysms. *World Neurosurg*. 2016;87:77-90.
18. Ding D, Xu Z, Shih HH, Starke RM, Yen CP, Sheehan JP. Stereotactic radiosurgery for partially resected cerebral arteriovenous malformations. *World Neurosurg*. 2016;85:263-272.
19. Spetzler RF, Ponce FA. A 3-tier classification of cerebral arteriovenous malformations. *J Neurosurg*. 2011;114(3):842-849.
20. Potts MB, Lau D, Abla AA, Kim H, Young WL, Lawton MT. Current surgical results with low-grade brain arteriovenous malformations. *J Neurosurg*. 2015;122(4):912-920.
21. Potts MB, Young WL, Lawton MT. Deep arteriovenous malformations in the basal ganglia, thalamus, and insula. *Neurosurgery*. 2013;73(3):417-429.
22. 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(1):11-20.
23. Ding D, Starke RM, Kano H, et al. Stereotactic radiosurgery for Spetzler-Martin grade III arteriovenous malformations: an international multicenter study. *J Neurosurg*. 2017;126(3):859-871.
24. Ding D, Yen CP, Starke RM, Xu Z, Sun X, Sheehan JP. Radiosurgery for Spetzler-Martin grade III arteriovenous malformations. *J Neurosurg*. 2014;120(4):959-969.
25. Ding D, Yen CP, Starke RM, Xu Z, Sun X, Sheehan JP. Outcomes following single-session radiosurgery for high-grade intracranial arteriovenous malformations. *Br J Neurosurg*. 2014;28(5):666-674.
26. Ding D, Yen CP, Xu Z, Starke RM, Sheehan JP. Radiosurgery for low-grade intracranial arteriovenous malformations. *J Neurosurg*. 2014;121(2):457-467.
27. Ding D, Yen CP, Xu Z, Starke RM, Sheehan JP. Radiosurgery for primary motor and sensory cortex arteriovenous malformations. *Neurosurgery*. 2013;73(5):816-824; discussion 824.
28. Pikus HJ, Beach ML, Harbaugh RE. Microsurgical treatment of arteriovenous malformations: analysis and comparison with stereotactic radiosurgery. *J Neurosurg*. 1998;88(4):641-646.
29. Wang JY, Yang W, Ye X, et al. Impact on seizure control of surgical resection or radiosurgery for cerebral arteriovenous malformations. *Neurosurgery*. 2013;73(4):648-656; discussion 655-646.
30. Yang W, Hung AL, Caplan JM, et al. Delayed hemorrhage after treatment of brain arteriovenous malformations (AVMs). *World Neurosurg*. 2016;87:98-109.
31. Yang W, Wang JY, Caplan JM, et al. Predictors of functional outcome following treatment of posterior fossa arteriovenous malformations. *J Clin Neurosci*. 2015;22(2):357-362.
32. Starke RM, Yen CP, Ding D, Sheehan JP. A practical grading scale for predicting outcome after radiosurgery for arteriovenous malformations: analysis of 1012 treated patients. *J Neurosurg*. 2013;119(4):981-987.
33. Spetzler RF, Martin NA. A proposed grading system for arteriovenous malformations. *J Neurosurg*. 1986;65(4):476-483.
34. 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.
35. Pollock BE, Flickinger JC. Modification of the radiosurgery-based arteriovenous malformation grading system. *Neurosurgery*. 2008;63(2):239-243; discussion 243.
36. Derdeyn CP, Zipfel GJ, Albuquerque FC, et al. Management of brain arteriovenous malformations: a scientific statement for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. 2017;48(8):e200-e224.
37. Hartmann A, Stapf C, Hofmeister C, et al. Determinants of neurological outcome after surgery for brain arteriovenous malformation. *Stroke*. 2000;31(10):2361-2364.
38. Heros RC, Korosue K, Diebold PM. Surgical excision of cerebral arteriovenous malformations: late results. *Neurosurgery*. 1990;26(4):570-578; discussion 577-578.
39. Hamilton MG, Spetzler RF. The prospective application of a grading system for arteriovenous malformations. *Neurosurgery*. 1994;34(1):2-6; discussion 6-7.
40. 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(4):547-554.
41. 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(3):498-505; discussion 504-495.
42. Flickinger JC, Pollock BE, Kondziolka D, Lunsford LD. A dose-response analysis of arteriovenous malformation obliteration after radiosurgery. *Int J Radiat Oncol Biol Phys*. 1996;36(4):873-879.
43. Pollock BE, Flickinger JC, Lunsford LD, Maitz A, Kondziolka D. Factors associated with successful arteriovenous malformation radiosurgery. *Neurosurgery*. 1998;42(6):1239-1244; discussion 1244-1237.
44. Maruyama K, Kawahara N, Shin M, et al. The risk of hemorrhage after radiosurgery for cerebral arteriovenous malformations. *N Engl J Med*. 2005;352(2):146-153.
45. Ilyas A, Chen CJ, Ding D, et al. Cyst formation after stereotactic radiosurgery for brain arteriovenous malformations: a systematic review. *J. Neurosurg*. 2017;1-10. doi: 10.3171/2016.12.JNS162478.
46. Ilyas A, Ding D, Robert Hixson H, Xu Z, Starke RM, Sheehan JP. Volume-staged stereotactic radiosurgery for large intracranial arteriovenous malformations. *J Clin Neurosci*. 2017;43:202-207.
47. Moosa S, Chen CJ, Ding D, et al. Volume-staged versus dose-staged radiosurgery outcomes for large intracranial arteriovenous malformations. *Neurosurg Focus*. 2014;37(3):E18.
48. Ding D, Xu Z, Shih HH, et al. Worse outcomes after repeat vs initial stereotactic radiosurgery for cerebral arteriovenous malformations. *Neurosurgery*. 2016;79(5):690-700.
49. Awad AJ, Walcott BP, Stapleton CJ, Ding D, Leed CC, Loeffler JS. Repeat radiosurgery for cerebral arteriovenous malformations. *J Clin Neurosci*. 2015;22(6):945-950.
50. Seymour ZA, Sneed PK, Gupta N, et al. Volume-staged radiosurgery for large arteriovenous malformations: an evolving paradigm. *J. Neurosurg*. 2016;124(1):163-174.
51. Kano H, Kondziolka D, Flickinger JC, et al. Stereotactic radiosurgery for arteriovenous malformations, Part 3: outcome predictors and risks after repeat radiosurgery. *J Neurosurg*. 2012;116(1):21-32.
52. Kano H, Kondziolka D, Flickinger JC, et al. Stereotactic radiosurgery for arteriovenous malformations, Part 6: multistaged volumetric management of large arteriovenous malformations. *J Neurosurg*. 2012;116(1):54-65.

53. Ding D, Yen CP, Starke RM, Xu Z, Sheehan JP. Radiosurgery for ruptured intracranial arteriovenous malformations. *J Neurosurg*. 2014;121(2):470-481.
54. Ding D, Starke RM, Kano H, et al. Radiosurgery for unruptured brain arteriovenous malformations: an international multicenter retrospective cohort study. *Neurosurgery*. 2017;80(6):888-898.
55. Ding D, Starke RM, Kano H, et al. Radiosurgery for cerebral arteriovenous malformations in a randomized trial of unruptured brain arteriovenous malformations (ARUBA)-eligible patients. *Stroke*. 2016;47(2):342-349.
56. Ding D, Starke RM, Kano H, et al. Stereotactic radiosurgery for ARUBA (a randomized trial of unruptured brain arteriovenous malformations)–eligible Spetzler-Martin grade I and II arteriovenous malformations: a multicenter study. *World Neurosurg*. 2017;102:507-517.
57. Wong J, Slomovic A, Ibrahim G, Radovanovic I, Tymianski M. Microsurgery for ARUBA trial (a randomized trial of unruptured brain arteriovenous malformation)–eligible unruptured brain arteriovenous malformations. *Stroke*. 2017;48(1):136-144.
58. Pollock BE, Link MJ, Brown RD. The risk of stroke or clinical impairment after stereotactic radiosurgery for ARUBA-eligible patients. *Stroke*. 2013;44(2):437-441.
59. Tonetti DA, Gross BA, Atcheson KM, et al. The benefit of radiosurgery for ARUBA-eligible arteriovenous malformations: a practical analysis over an appropriate follow-up period. *J Neurosurg*. 2017;1-5. doi: 10.3171/2017.1.JNS162962.
60. Hong CS, Peterson EC, Ding D, et al. Intervention for a randomized trial of unruptured brain arteriovenous malformations (ARUBA)— eligible patients: an evidence-based review. *Clin Neurol Neurosurg*. 2016;150:133-138.
61. Starke RM, Sheehan JP, Ding D, et al. Conservative management or intervention for unruptured brain arteriovenous malformations. *World Neurosurg*. 2014;82(5):e668-e669.
62. Yen CP, Ding D, Cheng CH, Starke RM, Shaffrey M, Sheehan J. Gamma knife surgery for incidental cerebral arteriovenous malformations. *J Neurosurg*. 2014;121(5):1015-1021.
63. Nerva JD, Mantovani A, Barber J, et al. Treatment outcomes of unruptured arteriovenous malformations with a subgroup analysis of ARUBA (a randomized trial of unruptured brain arteriovenous malformations)-eligible patients. *Neurosurgery*. 2015;76(5):563-570; discussion570; quiz 570.
64. Moon K, Levitt MR, Almefty RO, et al. Safety and efficacy of surgical resection of unruptured low-grade arteriovenous malformations from the modern decade. *Neurosurgery*. 2015;77(6):948-953; discussion 952-943.
65. Al-Shahi Salman R, White PM, Counsell CE, et al. Outcome after conservative management or intervention for unruptured brain arteriovenous malformations. *JAMA*. 2014;311(16):1661-1669.
66. 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(9917):614-621.
67. Ding D, Xu Z, Yen CP, Starke RM, Sheehan JP. Radiosurgery for unruptured cerebral arteriovenous malformations in pediatric patients. *Acta Neurochir (Wien)*. 2015;157(2):281-291.
68. Patibandla MR, Ding D, Xu Z, Sheehan JP. Stereotactic radiosurgery for pediatric high-grade brain arteriovenous malformations: our experience and review of literature. *World Neurosurg*. 2017;102:613-622.
69. Blauwblomme T, Bourgeois M, Meyer P, et al. Long-term outcome of 106 consecutive pediatric ruptured brain arteriovenous malformations after combined treatment. *Stroke*. 2014;45(6):1664-1671.
70. Kano H, Kondziolka D, Flickinger JC, et al. Stereotactic radiosurgery for arteriovenous malformations, part 2: management of pediatric patients. *J Neurosurg Pediatr* 2012;9(1):1-10.
71. Buell TJ, Ding D, Starke RM, Webster Crowley R, Liu KC. Embolization-induced angiogenesis in cerebral arteriovenous malformations. *J Clin Neurosci*. 2014;21(11):1866-1871.
72. Andrade-Souza YM, Ramani M, Scora D, Tsao MN, terBrugge K, Schwartz ML. Embolization before radiosurgery reduces the obliteration rate of arteriovenous malformations. *Neurosurgery*. 2007;60(3):443-452; discussion 451-442.
73. Morgan MK, Davidson AS, Koustais S, Simons M, Ritson EA. The failure of preoperative ethylene-vinyl alcohol copolymer embolization to improve outcomes in arteriovenous malformation management: case series. *J Neurosurg*. 2013;118(5):969-977.
74. Chen CJ, Chivukula S, Ding D, et al. Seizure outcomes following radiosurgery for cerebral arteriovenous malformations. *Neurosurg Focus*. 2014;37(3):E17. doi: 10.3171/2014.6.FOCUS1454.
75. Ding D, Quigg M, Starke RM, et al. Radiosurgery for temporal lobe arteriovenous malformations: effect of temporal location on seizure outcomes. *J Neurosurg*. 2015;123(4):924-934.
76. Ding D, Quigg M, Starke RM, et al. Cerebral arteriovenous malformations and epilepsy, Part 2: predictors of seizure outcomes following radiosurgery. *World Neurosurg*. 2015;84(3):653-662.
77. Przybylowski CJ, Ding D, Starke RM, et al. Seizure and anticonvulsant outcomes following stereotactic radiosurgery for intracranial arteriovenous malformations. *J Neurosurg*. 2015;122(6):1299-1305.
78. Yang SY, Kim DG, Chung HT, Paek SH. Radiosurgery for unruptured cerebral arteriovenous malformations. *Neurology*. 2012;78(17):1292-1298.
79. Josephson CB, Bhattacharya JJ, Counsell CE, et al. Seizure risk with AVM treatment or conservative management: prospective, population-based study. *Neurology*. 2012;79(6):500-507.
80. Baranoski JF, Grant RA, Hirsch LJ, et al. Seizure control for intracranial arteriovenous malformations is directly related to treatment modality: a meta-analysis. *J NeuroIntervent Surg*. 2014;6(9):684-690.
81. Lee CC, Reardon MA, Ball BZ, et al. The predictive value of magnetic resonance imaging in evaluating intracranial arteriovenous malformation obliteration after stereotactic radiosurgery. *J Neurosurg*. 2015;123(1):136-144.
82. O'Connor TE, Friedman WA. Magnetic resonance imaging assessment of cerebral arteriovenous malformation obliteration after stereotactic radiosurgery. *Neurosurgery*. 2013;73(5):761-766.
83. Pollock BE, Kondziolka D, Flickinger JC, Patel AK, Bissonette DJ, Lunsford LD. Magnetic resonance imaging: an accurate method to evaluate arteriovenous malformations after stereotactic radiosurgery. *J Neurosurg*. 1996;85(6):1044-1049.

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COMMENTS

In this excellent study, the authors found that the primary outcome of AVM obliteration without a new permanent neurological deficit, in patients who underwent either microsurgical resection (MS) or stereotactic radiosurgery (SRS), was identical at 69%. This was derived using a matched cohort design of 59 patients in each group who underwent MS or SRS from an institutional database spanning 13 years, comprising 68 and 1400 patients treated with microsurgery or radiosurgery, respectively. The authors' ability to match microsurgical cases with comparable radiosurgical ones, of which the majority were Spetzler-Martin grades I-II, and previously ruptured, stems from the substantial institutional referrals specifically for radiosurgery. Not surprisingly, the rates of obliteration as well as new neurological deficit were significantly higher in the microsurgical cohort. This is contrasted to the 72% obliteration and 10% post-treatment hemorrhage rates in the SRS cohort. Therefore, the primary outcome was not achieved in the MS cohort most commonly due to a new neurological deficit, whereas the reason for not achieving the primary outcome in the SRS cohort was most often due to lack of obliteration. Although the cohorts are small and thus limit subgroup comparisons, the findings further elucidate the outcomes that can be achieved for carefully selected patients. However, concluding that long-term outcomes with MS or SRS are equivalent, because the primary outcome as variably defined for each group is comparable, would be an extreme oversimplification.

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The management of brain arteriovenous malformations (AVMs) is controversial and dependent on a center's experience and expertise. In general, microsurgery (MS) and stereotactic radiosurgery (SRS) are considered primary curative modalities, and endovascular embolization is reserved for adjunct therapy. Despite its flaws, ARUBA appropriately advanced the discussion regarding the treatment of unruptured AVMs and subsequently numerous clinical outcome studies have been published.

This manuscript describes the first matched cohort study comparing MS and SRS for the treatment of AVMs MS had higher rates of radiographic obliteration but higher rates of new neurological deficit compared to SRS leading to similar rates of deficit-free obliteration overall and regardless of grade or rupture status in subgroup analysis. The authors acknowledge that follow-up was significantly longer in the SRS cohort. In addition, the modified Rankin scale or similar disability index was not employed for the outcome analysis, so it is unknown to what extent the new deficits affected overall outcome.

The overwhelming majority (95.4%) of AVMs at this center were treated with SRS over a 13-year period (1400 and 68 patients, respectively). While not a criticism of this center's expertise or referral patterns, this finding demonstrates an obvious bias toward the use of SRS in AVM management. The patients were appropriately matched; however, this imbalance favors SRS outcomes. In keeping with this, the rates of new deficit are higher than those published in recent surgical series especially for low grade and unruptured AVMs It is well-established that MS has higher upfront neurological risks and higher rates of obliteration than SRS, but the equivalency of the 2 modalities for deficit-free obliteration is likely not as clear-cut as presented in this manuscript.

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