Surgical outcome of brain arteriovenous malformation according to the location, A retrospective study

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Date of submission: 25th January 2023 Date of acceptance: 29th May 2023 Date of Publication 24th June 2023

Abstract

Background and Objective: The goal of this study was to analyze the association of brain arteriovenous malformations (AVMs) location and its outcome after microsurgical excision. The relation of outcome using modified Ranklin Scale (mRS) at time of discharge, early and last follow ups with respect to location of AVM.

Methods: Demographic data, AVM characteristics, and treatment outcomes were evaluated in 47 bAVMs treated with microsurgery between November 2009 and April 2021. For this series, 47 patients were retrospectively reviewed. The mRS was used to assess functional outcome post-surgery with respect to its location

Outcomes: Forty-seven patients (32% female) and 68% male; average age 33.4 years) with brain AVMs were included in this review. Among the AVMs, the mean size was 5.5cm, 83% with hemorrhage, 63% with deep drainage, mean SM grade is 2.74. The non-eloquent AVM comprised of 25.5%. The most common eloquent location was language (36.2%), followed by sensorimotor (23.4%), visual 8.5% and coordination 6.4%. Motor mapping was done in all cases of brain AVM with sensorimotor eloquence. There was no statically significant difference in the baseline patient and AVM characteristics among different subtypes of eloquence. Favorable outcome (mRS 0-2) was seen on both eloquent (100% in visual) and non-eloquent AVMs. Age and AVM size were significant predictor for good overall outcome in last follow-up.

Conclusion: Although the sample size of this study is a limitation, the result of our case series demonstrated excellent surgical outcome for visual eloquence, good outcome in sensorimotor and language eloquence. Coordination eloquence had worse overall outcome.

Key words: AVMs, brain arteriovenous malformation, eloquence location, microsurgery, Spetzler-Martin grades, functional outcome

Access this article online
Website: https://www.nepjol.info/index.php/NJN
DOI: https://doi.org/10.3126/njn.v20i2.51780
HOW TO CITE
Karki P, Sharma GR, Joshi S, Paudel P, Shah DB, Sharma A. Surgical outcome of brain arteriovenous malformation according to the location- A retrospective study. NJNS. 2023;20(2):17-27.

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ISSN: 1813-1948 (Print), 1813-1956 (Online)

Introduction

The location of brain AVM plays key role in the neurological outcome of the patient after surgical resection. Grading schemes are used to predict the associated risk, when surgery is planned. Among the factors used in grading system, location is one of the major components. The most frequently used prediction model is Spetzler-Martin (S-M) grading system which grades AVMs on a scale from 1 to 5 based on size, venous drainage, and eloquence. [1]

The grading system does not differentiate the location type, therefore patient with language eloquence will receive same grading as with motor strip eloquence which gives variable impact on overall neurological outcome after surgical resection. In fact, the Spetzler-Martin grading system gives eloquent location a negative prognostic value in the overall predictive score. This underscores the challenges of achieving a favorable outcome with resection for an AVM located in eloquent regions of the brain. As reported earlier, the results of microsurgical resection of AVMs located in eloquent locations of the brain are associated with morbidity and significant functional disability. [2, 3] There are some reports in the lesion-to-eloquence distance (LED) [4, 5] but a study assessing the risk of resection in specific eloquence types is lacking.

The purpose of our study was to describe the effect of microsurgical resection on the clinical outcomes of a cohort of patients with AVMs. We also evaluated the effect of eloquent cortex on the outcome of surgically treated AVMs compared with those in noneloquent cortex locations.

Materials and Methods

This was a retrospective study conducted in our institutes (Bir, Dhirgayu, Mediciti Hospitals) in Kathmandu, Nepal from 2009 -2021 April including 47 patients who underwent microsurgical resection of brain AVM. This study was approved by Nepal Health Research Council (NHRC) following an authorization from the Institutional review committee (IRC); IRC-RP-2077/78-0029 and was conducted in accordance with the institutional ethics guidelines. The Nepal Mediciti Hospital brain AVM study group database is a prospectively collected database containing demographics, clinical and radiological information. We also had hard copies of patient profiles and follow-ups in brain AVM Performa collection. To identifiy patients with brain AVMs treated by microsurgical resection at our institute between 2009 and 2021 April, the profoma was used. All patients with intracerebral AVM and treated with microsurgery were included in the study. Brain AVM was categorized by Spetzler Martin Grading system (SMG) and Supplemented SMG. Diagnosis and surgical planning in all patients were based on brain MRI, CT angiography and for large and complex AVM, Digital Subtraction Angiogram (DSA). Intraoperative ICG, Doppler and Neurophysiological monitoring were routinely used in all cases.

Clinical follow-up was performed at 1 week, 1, 3 to 6 months post hospital discharge and at annual intervals thereafter. Post-operative cerebral angiogram after 1 week prior to discharge was routinely performed and follow-up CT angiogram whenever required or necessary. Exclusion criteria included evidence of operated for other vascular malformations like cavernoma, venous angioma, body AVM or any treatment without microsurgical resection of AVM. All AVM cases were diagnosed based on magnetic resonance imaging, computed tomography angiogram and DSA in complex large cases. The AVM location was categorized into eloquent and non-eloquent location where eloquence was further divided intThe relation of different variables were analyzed with location of the AVM (Eloquent and non-eloquent). The association of the location of AVM was studies and was analyzed with dichotomized modified Ranklino sensorimotor, visual, language and coordination. Scale (mRS) favorable mRS (0-2) and non-favorable mRS (>2) to find out the outcome at time of discharge and at last follow-up (minimum being 3 months).

Statistical analysis

IBM SPSS Statistics 20 was used for statistical analysis. Independent- samples t test was used to test significance of association. A subtype analysis was performed by comparison of different variables with non-eloquent and eloquent (sensorimotor, visual, language and coordination). Statistical significance was defined as a value of $P<05$. Univariate analysis was performed to assess the associations of AVM location with postoperative mRS score as good and poor outcomes. We used chi-square to assess differences between groups for categorical characteristics in univariate analyses of factors affecting postoperative mRS.

Results

From 2009 to 2021 April, 47 bAVMs patients were treated with microsurgical resection.

One of the example cases is illustrated in Figures 1A-E of left frontal AVM which had mRS score of 0 on 6 months follow-up and in Figure 2A-H of left occipital AVM with mRS score of 0 on 6 months follow-up. Baseline demographics, clinical presentation, and AVM characteristics are presented in Table 1. The mean age at presentation was 33.4 years, there were 15 females (32%) and 32 males (68%). The most AVM were in eloquent location i.e. 74.5% among which 23.4% in Sensori motor, 8.5% in visual, 36.2% in language and 6.4% in coordination. 25.5% AVM was in non-eloquent area. 63.8%% of AVM had deep venous drainage. Most of the AVM were 3-6cm (61.7%), 23.4% were more than 6cm and 14.9% were less than 3cm. SM grading was distributed accordingly: 1 grade 1 (2.1%), 20 grade 2 (46.8%), 13 grade 3 (29.8%), 7 grade 4 (17%) and 2 grade 5 bAVMs (4.3%). Supplemented SM grading was also distributed as: 1 grade 2 (2.1%), 5 grade 3 (10.6%), 11 grade 4 (25.5%), 14 grade 5 (31.9%), 4 grade 6 (10.6%), 6 grade 7 (14.9%) and 2 grade 8 (4.3%). The minimum follow-up period was 3months.

There was no statistically significant difference in the baseline patient and AVM characteristics among the different subtypes of eloquence (Table 2). Mean SM grade was highest in sensorimotor eloquence (p-value-0.017). Associated aneurysm was in 0% in non-eloquent, 18.2% in sensori-motor, 25% in visual eloquence, 41% in language eloquence and 33.3% in coordination eloquence. Complication was also highest in sensorimotor eloquence (81%) with borderline significance (p-value-0.076).

Non Eloquent location is not associated with aneurysm whereas eloquent location are mostly associated with aneurysms. This associated can explain the high rate of hemorrhage in eloquent location (100% in visual, 88.2% in language, 72.7% in sensorimotor and 66.7% in coordination). We found that both sensorimotor and language eloquence have associations with poor outcome in comparison to visual eloquence Figure 3A, B. 100% visual eloquent AVM had hemorrhage with surprising 100% favorable outcome (mRS 0-2), overall unfavorable outcome was seen 3 times higher in eloquent location (p-value- 0.353) when compared to non-eloquent location Figure 3B, C.

In univariant analysis (Table 3), among the patients with visual eloquence, 100% had favorable outcome after surgical excision of brain AVM in comparison to 81.8% of those with sensorimotor eloquence, 76.5% of those with language eloquence and 66.7% of those with coordination eloquence. 91.7% of non-eloquent brain AVM had favorable outcome. Therefore, favorable outcomes were seen in both eloquent and non-eloquent AVMs, where unfavorable outcome was seen almost 3 times higher in eloquent location with borderline significance (p-value- 0.353).

The Chi-square test (Table-4) identified age (p-value < 0.030) and AVM size (p value < 0.000) as a significant predictor for the good overall outcome in last follow-up.

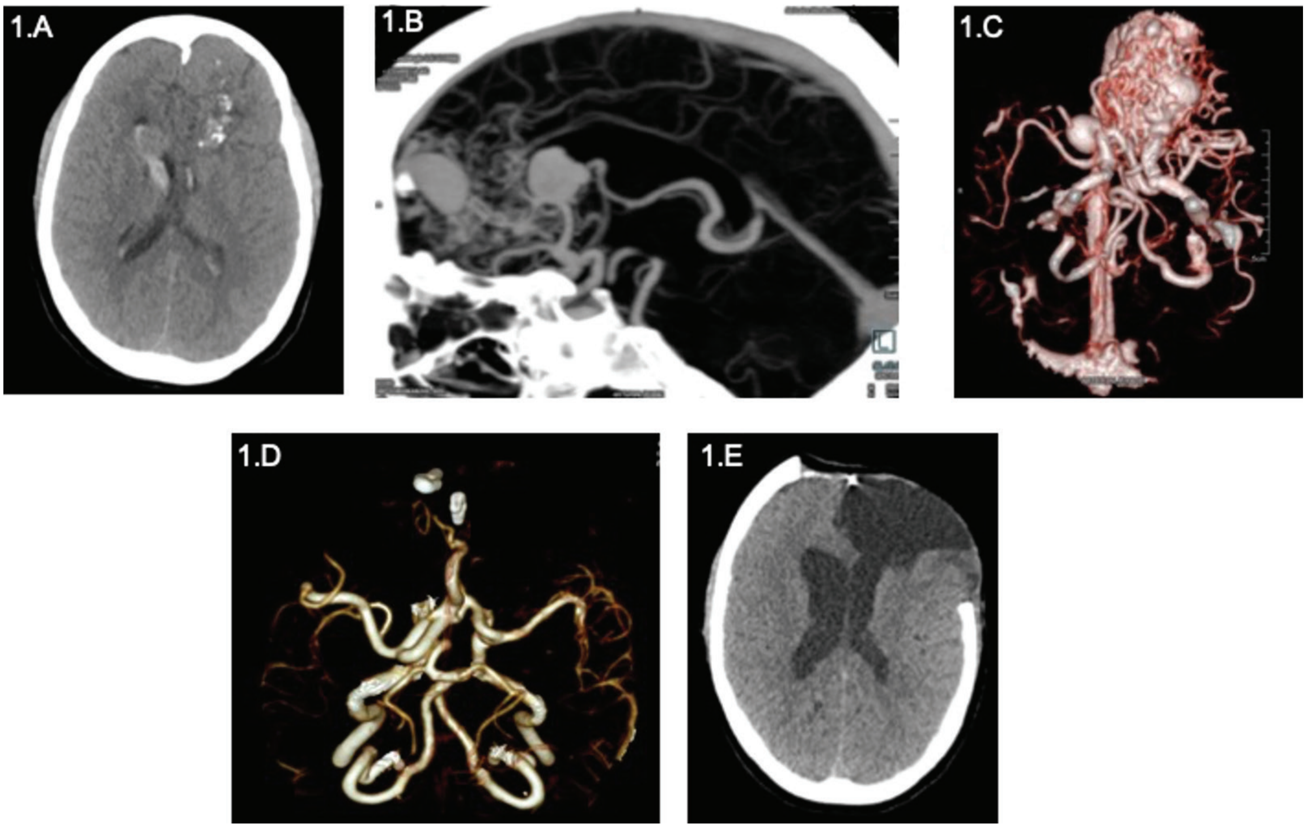

Figure 1: Left frontal AVM of SMG V and Supplemented SMG 7

A. Plain Computed Tomography scan showing evidence of calcified lesion on left frontal lobe with hyper-density in ventricle showing intraventricular hemorrhage.

B. Computed Tomography Angiogram sagittal view with intravenous contrast showing large left frontal AVM with feeders from left Middle cerebral artery, anterior cerebral artery, internal carotid artery and draining into vein of Galen to straight sinus.

C. 3D reconstruction of Computed Tomography Angiogram axial view with intravenous contrast showing larger left frontal AVM.

D. Post-operative 3D reconstruction of Computed Tomography Angiogram axial view with intravenous contrast showing complete excision of AVM with normal cerebral vessels and two aneurysm clips in anterior circulation.

E. Post-operative plain Computed Tomography scan showing complete excision of left frontal AVM with cranial defect over left fronto-temporal and part of right frontal bone.

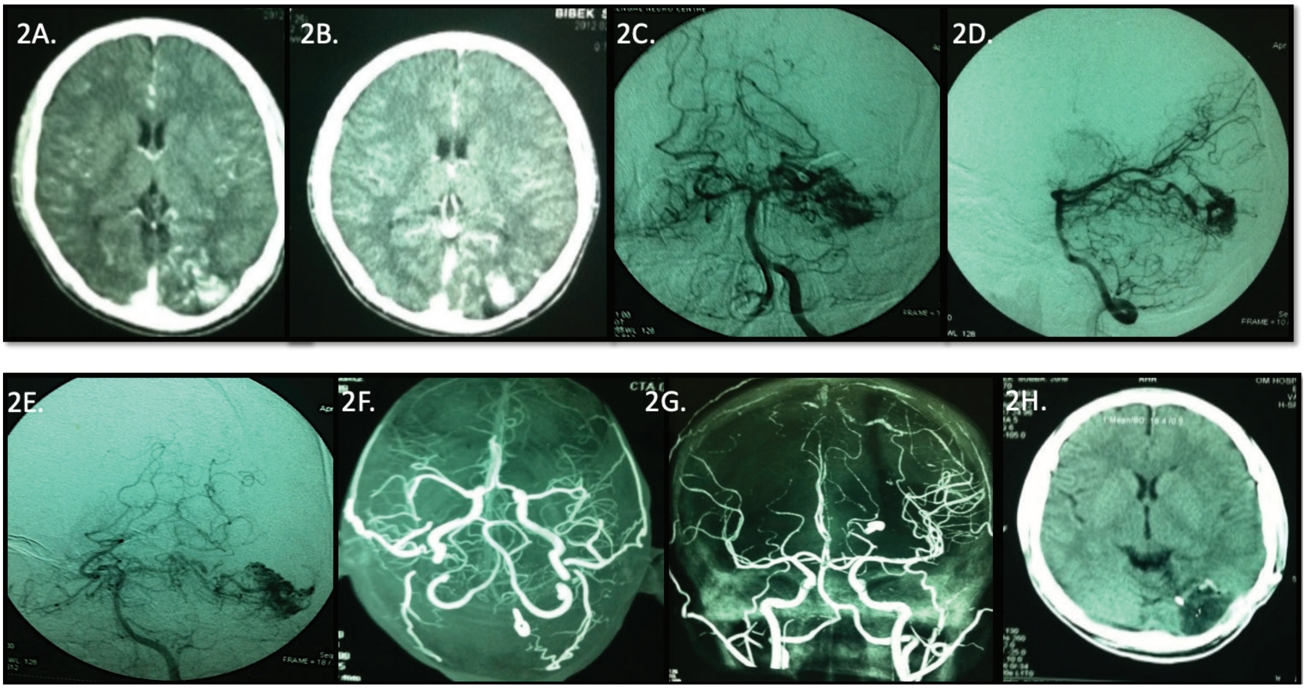

Figure 2: Left occipital AVM of SMG

A. Plain Computed Tomography scan showing evidence of calcified lesion on left occipital hemorrhage with hyperdense calcified area.

B. Plain Computed Tomography scan showing evidence of calcified lesion on left occipital hemorrhage with hyperdense calcified area and occipito-parietal edema.

C. Digital subtraction angiogram with left vertebral artery dye injection, anterior-posterior view showing AVM with occipital branche of posterior cerebral artery as a feeder and draining into left transverse sinus.

D. Digital subtraction angiogram lateral view showing AVM with feeder from posterior cerebral artery branche and draining into left transverse sinus.

E. Digital subtraction angiogram with left vertebral artery dye injection, anterior-posterior view showing AVM with occipital branch of posterior cerebral artery as a feeder and evidence of transverse sinus filling.

F. Post AVM excision 3D Computed Tomography angiogram axial view showing complete excision of AVM with evidence of one aneurysm clip at occipital region.

G. Post AVM excision 3D Computed Tomography angiogram coronal view showing complete excision of AVM.

H. Post-operative plain Computed Tomography scan showing complete excision of left occipital AVM.

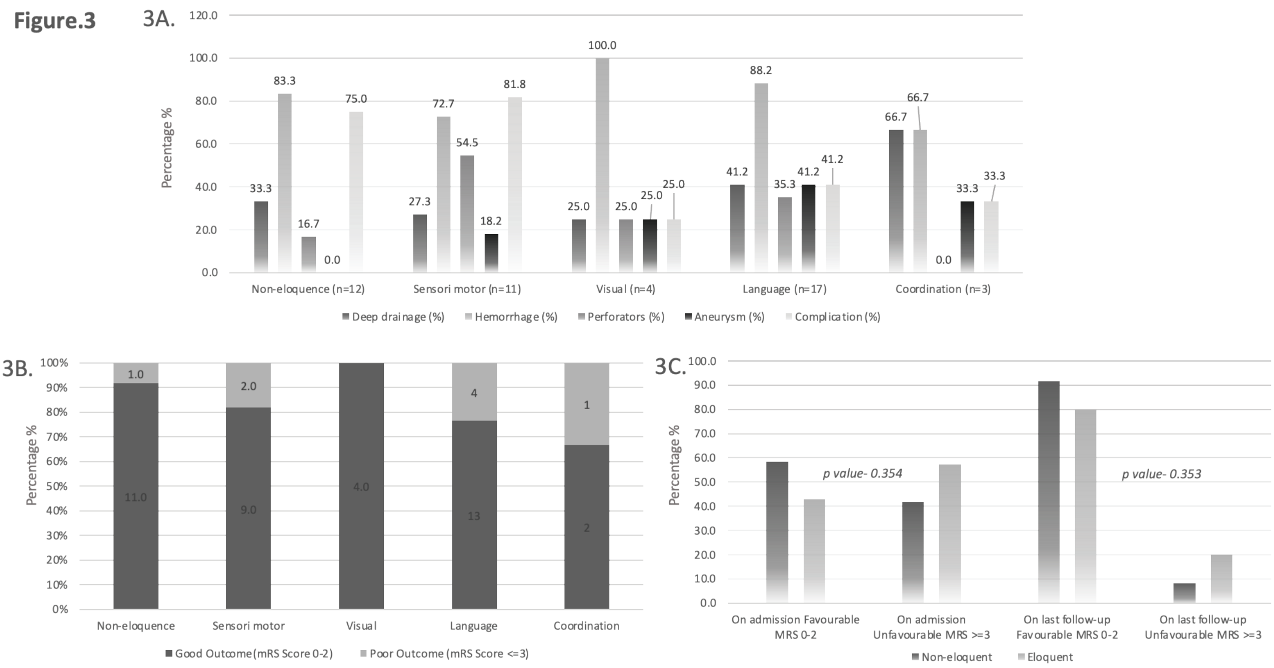

Figure 3: Bar-diagrams

A. The bar diagram showing comparision of non eloquence and eloquence subtype in relation to different variables.

B. The bar-diagram showing comparision of outcomes in non eloquence and eloquence subtype in relation to Follow-up Modified Ranklin Scale.

C. The bar diagram showing pre and post surgery outcomes in relation to location of AVM where favorable outcomes were seen on last follow-up in both eloquent and non eloquent AVMs.

Table 1: Baseline patient and AVM characteristics

Variable	No.	Standard deviation
No. of patients	47	
Mean age in yrs.	33.4	Std. Dev. 18.7
Age group		
<20	15 (32.0)	
20-40	16 (34.0)	
>40	16 (34.0)	
Sex		
F	15 (32.0)	
M	32 (68.0)	
Mean AVM Size (cm)	5.5	Std. Dev. 3.3
AVM size		
<3 cm	7 (14.9)	
3-6 cm	29 (61.7)	
>6 cm	11 (23.4)	
Hemorrhage	39 (83.0)	
Deep drainage	30 (63.8)	
Mean SM grade	2.74	Std. Dev. 0.9
SM grade		
I	1 (2.1)	
II	22 (46.8)	
III	14 (29.8)	

IV	8 (17.0)	
V	2 (4.3)	
Mean supplemented grade	5	Std. Dev. 1.4
Supplemented grade		
2	1 (2.1)	
3	5 (10.6)	
4	12 (25.5)	
5	15 (31.9)	
6	5 (10.6)	
7	7 (14.9)	
8	2 (4.3)	
AVM location/ eloquence		
Non-eloquence	12 (25.5)	
Sensori motor	11 (23.4)	
Visual	4 (8.5)	
Language	17 (36.2)	
Coordination	3 (6.4)	
Values are expressed as the mean and standard deviation or as the number of patients (%)		

Table 2: Comparison of non-eloquence and eloquence subtype with different variables

Variable	Non eloquent	Eloquent				p Value
	Non-eloquence (n=12)	Sensori motor (n=11)	Visual (n=4)	Language (n=17)	Coordination (n=3)	
Age (Mean yrs.)	40.8	27.8	20.5	34.5	35.7	0.308
Male sex (%)	75.0	63.6	25.0	70.6	100.0	0.264
Mean AVM Size (cm)	4.3	5.1	7.3	6.5	3.5	0.217
Deep drainage (%)	33.3	27.3	25.0	41.2	66.7	0.731
Hemorrhage (%)	83.3	72.7	100.0	88.2	66.7	0.638
Mean SM grade	2.3	3.5	2.3	2.8	2.7	0.017
Mean supplemental grade	4.6	5.7	3.8	5.0	5.7	0.095
Perforators (%)	16.7	54.5	25.0	35.3	0.0	0.243
Aneurysm (%)	0.0	18.2	25.0	41.2	33.3	0.136
Complication (%)	75.0	81.8	25.0	41.2	33.3	0.076

Table 3: Comparison of outcomes in location subtype in relation to Follow-up mRS

AVM Eloquence	On last follow-up Good outcome (mRS score 0-2)	Poor outcome (MRS >=3)	p-Value
Non-Eloquent	28.2	12.5	0.353
Eloquent	71.8	87.5	
	On last follow-up		
Eloquence subtype, no. (%)	**Good Outcome (mRS Score 0-2)**	**Poor Outcome (mRS Score >=3)**	**p Value**
Non-eloquent	11 (91.7)	1 (8.3)	0.636
Sensori motor	9 (81.8)	2 (18.2)	
Visual	4 (100.0)	0 (0.0)	
Language	13 (76.5)	4 (23.5)	
Coordination	2 (66.7)	1 (33.3)	

Table 4: Chi-square test of variables associated with last follow-up

Variable	Associated with last follow-up, P value [a]
Sex	0.287
5-yr age group	0.030
Caste/ethnicity	0.672
AVM size (cm)	0.000
Eloquence location	0.666
Perforators	0.477
Deep veins	0.396
Hemorrhage	0.946
Aneurysm	0.437
Spetzler-Martin grade	0.948
Supplemented SMG	0.975
[a]P values are derived from a Chi-square test.	

Discussion

Microsurgical resection of brain AVM is an established treatment in the management of arteriovenous malformation of the brain. [1-6] The goal is to completely obliterate the AVM with minimal side effects, thus, reducing the risk of temporary or permanent deficit. The ARUBA (A Randomised Trial of Unruptured Brain Arteriovenous Malformations) results indicated that medical management was superior to intervention in unruptured AVMs, with stroke and death as the primary endpoints. [5] The Spetzler-Martin surgical grading system classifies critical (or eloquent) brain location (including sensorimotor cortex) as a significant risk for poorer outcome after AVM resection. [1]

Given the natural history of the AVM rupture risk of 4%–5% for untreated lesions and the postresection risk of 0%–0.6%, microsurgical resection is arguably the most optimal treatment strategy for selected patients. [7]

Previous report suggest that preservation of a good functional status posttreatment is highest in surgically treated groups. [7, 8] Even though, microsurgery is considered optimal treatment for AVM, AVM located in eloquent location is associated with significant morbidity after surgery. [9, 10] Schaller and Schramm [11] reported a 6.1% rate of permanent, significant neurological deficits after microsurgical removal of small AVMs (Spetzler-Martin Grades I–III) in eloquent regions. Central or deep AVMs (Basal ganglia, Thalamus, Insula) account for around 3–13% of all intracranial AVMs. [12, 13] Higher risk of neurological complications (4%) is reported after microsurgery of deep seated and eloquent AVM in pediatric patients, these complications were reported as high as 28.5%. [14, 15] O' Laoire et al., [16] reported 11% severe disability and 5% mortality. Kunc [17] reported 61% reduced capacity to work and 11% disability rate. Heros et al., [18] reported 7.8% morbidity and 0.6% mortality rates. Some reports show that even in deep brain AVM microsurgery is best suited treatment, such as, Potts MB et al [12], reported 48 patients with deep AVM where AVM resection was complete in 34 patients (71%) and incomplete in 14 patients (29%). Likewise, temporal locations of an AVM were concluded to be a risk factor for bleeding by Crawford et al [19], in a large series of 216 nontreated cases. The depth of the malformation was not a significant factor in the same study, but deep-seated AVMs made up only 7% of the total group. Another study reported 100% obliteration rate of pediatric AVM located in Rolandic area after microsurgical resection with neurological deficit in 2 patients out of 23 patients. [20]

Higher rate of complication after surgical resection of eloquent AVM may be due to motor or language function shift in the presence of an AVM from its anatomic location to an adjacent gyrus or even to the contralateral hemisphere. [21, 22] This explains higher complication rate in sensorimotor eloquence (81%) compared to other eloquent areas in our study (***Borderline significance- 0.076***). Furthermore, the higher complication rate could also be due to highest mean SM grade in Sensorimotor eloquence (***p-value- 0.017***) in our studies.

In pediatric patient increased surgical tolerance and better recovery may be due to increased brain plasticity, a more aggressive microsurgical management than in adult bAVM. [14] Likewise in our study, Chi square test identified age (p value < 0.030) as a significant predictor for the good overall outcome in last follow-up. On the other hand, in older patients, surgical intervention is probably ineffective in terms of functional recovery, and because of the shorter life expectancy of this group, the cumulative risk of bleeding is considerably lower. [23]

Despite the immediate therapeutic benefits of curative resection, there are conflicting data on the role of microsurgery for AVM lesions within eloquent cortex. For such lesions, radiosurgery has been recommended as an alternative treatment approach to decrease the likelihood of postoperative complications. [24-27] Previous study compared results of radiation therapy in eloquent vs at other intracranial locations. The obliteration rate was 74%, higher incidence of symptomatic radiation changes (15% vs. 5%) and higher incidence of hemorrhage in the period of latency (9.4% vs. 3%) were noted in patients with central AVMs. [28] Flickinger et al. in their risk prediction model predicted a very high incidence of symptomatic permanent post-radiosurgery injury in patients with central AVMs ranging from 8–92% depending on the volume (2–40 cm3) of AVM compared to 0–40% in patients with AVMs at other locations. [29] Moreover, there are potential long-term radiation-related complications, including malignancy and developmental delay. [30-32] Regarding radiosurgery, an overall occlusion rate of 64% has been reported. When only large and deep-seated lesions are considered, occlusion rates can fall as low as 32%. We should also consider that the annual risk of bleeding after radiosurgery, which is reported to be 2.2%; on the other hand, the risk of death as a result of hemorrhage has been reported to be between 0.6% and 1.3%. In large clinical series study, radiosurgery did not improve patients` performance and in fact resulted in new or worsened neurological symptoms in approximately 11%. [33, 34]

Therefore, radiosurgery for AVM in eloquent areas like motor cortex, there are pitfalls of such intervention, moreover, our results along with other studies indicate that surgical resection of critical location AVM can result in complete obliteration without significant reoccurrence and complications. [23]

The hemorrhagic risk of AVM is as high as 6% to 7% in the first year after clinical presentation with hemorrhage. [35, 36] Morbidity after AVM rupture is as high as 53% to 81% [35], whereas mortality after initial rupture is 10% to 17.6%. [35, 37, 38] Regarding function, Hartmann et al [39] demonstrated that 16% of patients were moderately or severely disabled after hemorrhage, which is greater than the treatment-related morbidity in most modern series. Whereas in our series even though AVM in visual eloquence had 100% hemorrhage, the post-surgical outcome was also 100% favorable. As previous reports, the main advantage of surgical treatment over other modalities is that patient exposure to the risk of bleeding is minimized immediately after the procedure. [40]

AVM resection with preoperative adjuncts such as angiography, and neurophysiological monitoring would enable effective obliteration of the AVM lesion with limited neurological morbidity. The intraoperative electrophysiological monitoring of SEPs and MEPs represents a critical additional tool for surgeons. [23] The findings of previous reports, suggest that more extensive functional imaging and/or tractography will be necessary to refine eloquence beyond what can be done with angiography and MRI. [41]

Even though, our study did not use functional imaging or tractography due to its unavailability, our results indicate that the resection of AVMs within eloquent cortex is feasible with operative adjuncts and provides treatment benefits of immediate AVM obliteration with long-term cure rates.

We hypothesized that sensorimotor eloquence would have a greater association with poor outcome than the other eloquence subtypes. We found that both sensorimotor and language eloquence have associations with poor outcome in comparison to visual eloquence. Non Eloquent location is not associated with aneurysm whereas eloquent location are mostly associated with aneurysms. This associated can explain the high rate of hemorrhage in eloquent location (100% in visual, 88.2% in language, 72.7% in sensorimotor and 66.7% in coordination). Although, 100% visual eloquent AVM had hemorrhage with surprising 100% favorable outcome (mRS 0-2), overall unfavorable outcome was seen 3 times higher in eloquent location (p-value- 0.353) when compared to non-eloquent location. As described earlier by Hartmann et al, [39] moderate to severe disability was related to associated hemorrhage rather than morbidity related to treatment, which explains our finding on higher rate of unfavorable outcome and associated hemorrhage in eloquent location. Our results regarding coordination eloquence are likely difficult to interpret given the small number of patients and higher rate of complications in this subgroup.

Limitation of the study

Limitations of this study included that it was a retrospective design and sample size was small so results of comparative analysis of subgroups should be considered cautiously and may not be appropriate to generalize in clinical practice. Further clinical studies with large cohorts are needed to support our findings. The eloquence based on anatomical location may be flawed methodologically. For instance, it has been shown that eloquence can shift or translocate in the presence of AVMs and the distance from the AVM to eloquence may be the more important factor. [42, 43] The functional MRI or DTI, Neuronavigation, Stimulated Cortical mapping were not performed due to its unavailability.

Conclusion

Surgical resection of AVMs in eloquent areas can be considered a safe option. The result of our case series demonstrated excellent surgical outcome for visual eloquence, good outcome in sensorimotor and language eloquence. The outcome might be due to high association with AVM hemorrhage rather than treatment related morbidity. Coordination eloquence had worse overall outcome. Overall, our data suggests good outcome post-surgery but there is a need of prospective, multicentric data to better identify patients who may benefit most from microsurgical treatment alone.

Disclosure statements

There is no conflict of interest.

References

1. Spetzler RF, Martin NA. A proposed grading system for arteriovenous malformations. J Neurosurg 1986; 65(4):476-83. https://doi: 10.3171/jns.1986.65.4.0476.

2. Sasaki T, Kurita H, Saito I, Kawamoto S, Nemoto S, Terahara A, et al. Arteriovenous malformations in the basal ganglia and thalamus: Management and results in 101 cases. J Neurosur 1998; 88:285-92. https://doi: 10.3171/jns.1998.88.2.0285.
3. Lawton MT, Hamilton MG, Spetzler RF. Multimodality treatment of deep arteriovenous malformations: Thalamus, basal ganglia and brain stem. Neurosurgery 1995; 37:29-36. https://doi: 10.1227/00006123-199507000-00004.
4. Jiao Y, Lin F, Wu J, Li H, Wang L, Jin Z, et al. Lesion-to eloquent fiber distance is a crucial risk factor in presurgical evaluation of arteriovenous malformations in the temporo- occipital junction. World Neurosurgery 2016;93:355–364. https://doi: 10.1016/j.wneu.2016.06.059.
5. 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. https://doi: 10.1016/S0140-6736(13)62302-8.
6. Mohr JP, Overbey JR, von Kummer R, et al. International ARUBA Investigators. Functional impairments for outcomes in a randomized trial of unruptured brain AVMs. Neurology 2017;3;89(14):1499-1506. https://doi:10.1212/WNL.0000000000004532.
7. Yang W, Anderson-Keightly H, Westbroek EM, et al. Long- term hemorrhagic risk in pediatric patients with arteriovenous malformations. J Neurosurg Ped 2016;18(3):329–338. http://doi: 10.3171/2016.3.PEDS15715.
8. Darsaut TE, Guzman R, Marcellus ML, et al. Management of pediatric intracranial arteriovenous malformations: experience with multimodality therapy. Neurosurg 2011;69(3):540–556. http://doi: 10.1227/NEU.0b013e3182181c00.
9. Gross BA, Storey A, Orbach DB, et al. Microsurgical treatment of arteriovenous malformations in pediatric patients: the Boston Children's Hospital experience. J Neurosurg Ped 2015;15(1):71–77. http://doi: 10.3171/2014.9.PEDS146.
10. Darsaut TE, Guzman R, Marcellus ML, et al. Management of pediatric intracranial arteriovenous malformations: experience with multimodality therapy. Neurosurg 2011;69(3):540–556. http://doi: 10.1227/NEU.0b013e3182181c00.
11. Schaller C, Schramm J. Microsurgical results for small arteriovenous malformations accessible for radiosurgical or embolization treatment. Neurosurg 1997;40:664–674. http://doi: 10.1097/00006123-199704000-00003.
12. Potts MB, Jahangiri A, Jen M, et al. UCSF Brain AVM Study Project. Deep arteriovenous malformations in the basal ganglia, thalamus, and insula: multimodality management, patient selection, and results. World Neurosurgery 2014;82(3-4):386-94. http://doi: 10.1016/j.wneu.2014.03.033.
13. Malik GM, Umansky F, Patel S, Ausman JL. Microsurgical removal of arteriovenous malformations of the basal ganglia. Neurosurgery 1988;23:209–217. http://doi: 10.1227/00006123-198808000-00014.
14. Meling TR, Patet G. What is the best therapeutic approach to a pediatric patient with a deep-seated brain AVM? Neurosurg Review 2019;42(2):409-416. http://doi: 10.1007/s10143-019-01101-8.
15. Berenstein A, Ortiz R, Niimi Y, et al. Endovascular management of arteriovenous malformations and other intracranial arterio-venous shunts in neonates, infants, and children. Childs Nervous System 2010;26:1345–1358. http://doi: 10.1007/s00381-010-1206-y.
16. O'Laoire SA. Microsurgical treatment of arteriovenous malformations in critical areas of the brain. British Journal of Neurosurgery 1995;9:347-60. http://doi: 10.1080/02688699550041359.
17. Kunc Z. Surgery of arteriovenous malformation in the speech and motor-sensory regions. Journal of Neurosurgery 1974;40:293-303. http://doi: 10.3171/jns.1974.40.3.0293.
18. Heros RC, Korosue K, Diebold PM. Surgical excision of cerebral arteriovenous malformations: Late results. Neurosurgery 1990;26:570-8. http://doi: 10.1097/00006123-199004000-00003.
19. Crawford PM, West CR, Chadwick DW, Shaw MD. Arteriovenous mal- formations of the brain: natural history in unoperated patients. Journal of Neurology, Neurosurgery and Psychiatry 1986;49:1–10. http://doi: 10.1136/jnnp.49.1.1.
20. Cho N, Nga VDW, Ahmed R, Ku JC, Munarriz PM, Muthusami P, Rutka JT, Dirks P. Surgical management of pediatric rolandic arteriovenous malformations: a single-center case series. Journal of Neurosurgery Pediatrics 2020;30:1-7. http://doi: 10.3171/2020.6.PEDS18547.
21. Alkadhi H, Kollias SS, Crelier GR, Golay X, Hepp-Reymond MC, Valavanis A. Plasticity of the human motor cortex in patients with arteriovenous malformations: a functional MR imaging study. American Journal of Neuroradiology 2002;21(8):1423-1433. PMID: 11003274, PMCID: PMC7974034
22. Lazar RM, Marshall RS, Pile-Spellman J, et al. Anterior translocation of language in patients with left cerebral arteriovenous malformation.

Neurology 1997;49(3):802-808. http://doi: 10.1212/wnl.49.3.802.

23. Lepski G, Honegger J, Liebsch M, Sória MG, Narischat P, Ramina KF, Nägele T, Ernemann U, Tatagiba M. Safe resection of arteriovenous malformations in eloquent motor areas aided by functional imaging and intraoperative monitoring. Neurosurgery 2012;70(2 Suppl Operative):276-88. http://doi: 10.1227/NEU.0b013e318237aac5.
24. Gross BA, Storey A, Orbach DB, et al. Microsurgical treatment of arteriovenous malformations in pediatric patients: the Boston Children's Hospital experience. Journal of Neurosurgery Pediatrics 2015;15(1):71–77. http://doi: 10.3171/2014.9.PEDS146.
25. Starke RM, Ding D, Kano H, et al. International multicenter cohort study of pediatric brain arteriovenous malformations. Part 2: Outcomes after stereotactic radiosurgery. Journal of Neurosurgery Pediatrics 2017;19(2):136–148. http://doi: 10.3171/2016.9.PEDS16284.
26. Starke RM, Kano H, Ding D, et al. Stereotactic radiosurgery for cerebral arteriovenous malformations: evaluation of long- term outcomes in a multicenter cohort. Journal of Neurosurgery 2017;126(1):36 – 44. http://doi: 10.3171/2015.9.JNS151311.
27. Reyns N, Blond S, Gauvrit J-Y, et al. Role of radiosurgery in the management of cerebral arteriovenous malformations in the pediatric age group: data from a 100-patient series. Neurosurgery 2007;60(2):268–276. http://doi: 10.1227/01.NEU.0000249277.72063.BD.
28. Kiran NA, Kale SS, Kasliwal MK, Vaishya S, Gupta A, Singh Sharma M, Shankar Sharma B, Kumar Mahapatra A. Gamma knife radiosurgery for arteriovenous malformations of basal ganglia, thalamus and brainstem--a retrospective study comparing the results with that for AVMs at other intracranial locations. Acta Neurochirurgia (Wien) 2009;151(12):1575-82. http://doi: 10.1007/s00701-009-0335-0.
29. Karlsson B, Lax I, Soderman M, Khirlstrom L, Lindquist C. Prediction of results following gamma knife surgery for brain stem and other centrally located arteriovenpus malformations: Relation to natural course. Stereotactic and Functional Neurosurgery 1995;66(suppl 1):260–268. http://doi: 10.1159/000099817.
30. Dirks PB, Jay V, Becker LE, et al. Development of anaplastic changes in low-grade astrocytomas of childhood. Neurosurgery 1994;34(1):68–78. PMID: 8121571
31. Williams NL, Rotondo RL, Bradley JA, et al. Late effects after radiotherapy for childhood low-grade glioma. American Journal of Clinical Oncology 2018;41(3):307-312. http://doi: 10.1097/COC.0000000000000267.
32. Hanakita S, Koga T, Shin M, et al. The long-term outcomes of radiosurgery for arteriovenous malformations in pediatric and adolescent populations. Journal of Neurosurgery Pediatrics 2015;16(2):222–231. http://doi: 10.3171/2015.1.PEDS14407.
33. Sun DQ, Carson KA, Raza SM, et al. The radiosurgical treatment of arteriovenous malformations: obliteration, morbidities, and performance status. International Journal of Radiation Oncology, Biology and Physics 2011;80(2):354-361. http://doi: 10.1016/j.ijrobp.2010.01.049.
34. Wegner RE, Oysul K, Pollock BE, et al. A modified radiosurgery-based arteriovenous malformation grading scale and its correlation with outcomes. International Journal of Radiation Oncology, Biology and Physics 2011;79(4):1147-1150. http://doi: 10.1016/j.ijrobp.2009.12.056.
35. Graf CJ, Perret GE, Torner JC. Bleeding from cerebral arteriovenous malformations as part of their natural history. Journal of Neurosurgery 1983;58(3):331-337. http://doi: 10.3171/jns.1983.58.3.0331.
36. Itoyama Y, Uemura S, Ushio Y, et al. Natural course of unoperated intracranial arteriovenous malformations: study of 50 cases. Journal of Neurosurgery 1989;71(6):805-809. http://doi: 10.3171/jns.1989.71.6.0805.
37. Wilkins RH. Natural history of intracranial vascular malformations: a review. Neurosurgery 1985;16(3):421-430. http://doi: 10.1227/00006123-198503000-00026.
38. Brown RD Jr, Wiebers DO, Torner JC, O'Fallon WM. Frequency of intracranial hemorrhage as a presenting symptom and subtype analysis: a population-based study of intracranial vascular malformations in Olmsted Country, Minnesota. J Neurosurg 1996;85(1):29-32. http://doi: 10.3171/jns.1996.85.1.0029.
39. Hartmann A, Mast H, Mohr JP, et al. Morbidity of intracranial hemorrhage in patients with cerebral arteriovenous malformation. Stroke 1998;29(5):931-934. http://doi: 10.1161/01.str.29.5.931.
40. Huh SK, Lee KC, Lee KS, Kim DI, Park YG, Chung SS. Selection of treatment modalities for cerebral arteriovenous malformations: a retrospective analysis of 348 consecutive cases. Journal of Clinical Neuroscience 2000;7(5):429-433. http://doi: 10.1054/jocn.1999.0698.
41. Jiao Y, Lin F, Wu J, Li H, Wang L, Jin Z, et al. A supplementary grading scale combining lesion-to-eloquence distance for predicting surgical outcomes of patients with brain arte- riovenous malformations. Journal of Neurosurgurgery 2018;128:530–540. http://doi: 10.3171/2016.10.JNS161415.

42. Lee L, Sitoh YY, Ng I, Ng WH. Cortical reorganization of motor functional areas in cerebral arteriovenous malformations. Journal of Clinical Neurosciences 2013;20:649–653. http://doi: 10.1016/j.jocn.2012.07.007.

43. Vates GE, Lawton MT, Wilson CB, McDermott MW, Halbach VV, Roberts TP, et al. Magnetic source imaging demonstrates altered cortical distribution of function in patients with arteriovenous malformations. Neurosurgery 2002;51:614–627. PMID: 12188939