



Original Article

Outcomes of Microsurgical Resection of Low-Grade Cerebral Arteriovenous Malformations: A Descriptive Observational Multicenter Study from a Low-Middle-Income Country

Adnan Khaliq¹, Muhammad Hassan Raza², Ahtesham Khizar², Muhammad Idris Khan³, Nayab Gul⁴, Adeeb-ul-Hassan²

¹Saidu Teaching Hospital, Swat, ²Punjab Institute of Neurosciences, Lahore ³Khyber Teaching Hospital, ⁴Northwest General Hospital and Research Center, Peshawar, Pakistan

ABSTRACT

Objective: To appraise the overall outcomes of microsurgical resection of low-grade arteriovenous malformations (AVMs) in a low-middle-income country.

Materials and Methods: Data was collected from three different neurosurgical centers in Pakistan for this study and it lasted for two years. Patients who had been diagnosed with cerebral AVMs were categorized into three groups, A, B, and C, using the Spetzler-Martin (S-M) grading system. AVMs of grades 1 and 2 were included in Class A. Class B contained grade 3 AVMs, while Class C contained grade 4 and 5 AVMs. All male and female patients in Class A were eligible for this study. Patients were evaluated postoperatively for seizures, hemorrhage, focal neurological deficits, and AVM recurrence. Morbidity, mortality, and functional recovery were used to evaluate the outcome. Functional recovery and cure rate were observed after 6 months of follow-up.

Results: There were a total of 22 patients. The mean age was 36.41 ± 14.32 SD years. There were 12 (54.5%) male patients and 10 (45.5%) female patients. 13 patients (59.1%) presented with spontaneous intracerebral hemorrhage, while 9 patients (40.9%) presented with seizures. 14 patients (63.6%) had S-M grade 1 and 8 patients (36.4%) had S-M grade 2. All patients underwent microsurgical resection. We discovered 4.5% morbidity in our study. There was no postoperative mortality. According to the Glasgow outcome scale, an excellent functional outcome of 95.5% at 6 months and a 100% cure rate were noted.

Conclusion: Regarding morbidity, mortality, and cure rates for low-grade AVMs in our nation, microsurgery is a secure and efficient therapeutic option.

Keywords: AVM, Microsurgery, Neurosurgery, Multicenter study, Observational study, developing countries.

Abbreviations: AVM: Arteriovenous malformation. AVMs: Arteriovenous malformations. S-M: Spetzler-Martin. ICB: Intracerebral bleed. CT: Computed Tomography. MR: Magnetic Resonance. DTI: Diffusion tensor imaging. AEDs: Antiepileptic drugs. SRS: Stereotactic radiosurgery. SPSS: Statistical Package for Social Sciences.

Corresponding Author: Muhammad Hassan Raza Department of Neurosurgery

Punjab Institute of Neurosciences, Lahore, (PINS), Pakistan Email: mhraza512@hotmail.com

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INTRODUCTION

AVM (cerebral arteriovenous malformation) is a non-neoplastic and dysplastic vascular lesion in which venules and arterioles communicate without a capillary bed in between.^{1, 2} AVM is made up of three parts: feeding arteries, draining veins, and nidus.^{3, 4} Nidus lacks a muscle layer and dysplastic vessels. Without possesses tiny exchanging with tissue, arterial blood is shunted from arteries to veins.^{3,4} These lesions are congenital and get bigger over time. The majority of them are sporadic, and a few are connected to neurocutaneous conditions including Sturge-Osler-Weber-Rendu Weber syndrome and disease.^{5,6} Approximately 98% of cerebral AVMs are solitary, with only 2% being multiple.⁷ In most cases, AVMs present clinically as an intracerebral bleed or seizures. Smaller AVMs commonly cause intracerebral bleed (ICB), while larger ones cause seizures.⁸ An average of 2% to 4% of AVMs rupture each year.¹ AVMs affect both men and women equally. The most frequent cause of spontaneous ICB in younger individuals is an AVM rupture (age less than 35 years).⁹ AVMs in the brain cause 2% of hemorrhagic strokes.¹⁰⁻¹¹ Between 20% and 40% of AVM patients experience seizures. They respond swiftly to antiepileptic drugs and are frequently generalized.8

Cerebral AVMs are diagnosed non-invasively using computed tomography (CT) brain and CT/ Magnetic Resonance (MR) angiography. Cerebral angiography is the gold standard for diagnosis, however, due to its invasiveness, it can only be used in certain circumstances. The location, size, and aneurysms that are connected to the nidus can all be determined using radiological exams. Both intraventricular AVM and parenchymal bleeding into the ventricles can result in hemorrhage.¹² intraventricular Antiepileptic medicines (AEDs), microsurgical excision, stereotactic radiosurgery, endovascular procedures, and multimodality therapy are among the possibilities for managing 12 AVMs. The treatment goal is to eradicate AVM. Operating surgeon's skill, size and location of AVM, accessibility to the surgical or endovascular facility, venous drainage, and the presence of high-risk factors such as a feeding artery aneurysm are all aspects to be considered during an AVM management.¹³

In 1986, Spetzler and Martin created a mechanism to assign grades to cerebral AVMs. This system was based on the location of the AVM concerning the eloquent cerebral cortex, including the sensory cortex, motor cortex, Broca's/speech Wernicke's area, visual cortex, hypothalamus, brainstem, thalamus, and cerebellum, as well as the size of the nidus, the pattern of venous drainage, and the location of the AVM.¹³ AVMs are graded (1 - 5) and classified into three groups using this scale. Grades 1 and 2 are included in Class A and are treated with microsurgical resection. Grade 3 AVMs are included in Class B and are treated with a combination of angioembolization, stereotactic radiosurgery (SRS), and microsurgery. Watchful angioembolization waiting, SRS, and are recommended treatment options for AVMs in grades 4 and 5. The Spetzler-Martin grading system is employed to estimate the surgical risk of removing an AVM. High grades are linked to increased rates of surgical morbidity and mortality.^{14 b}

For low-grade AVMs, microsurgery is thought to be the gold standard treatment, but not for high-grade AVMs. The microsurgical excision of an AVM includes craniotomy, dural opening, circumferential resection of the AVM, meticulous coagulation of the feeding arteries and draining

veins, and removal of the AVM nidus. The advantage of totally obliterating the AVM nidus makes microsurgical excision superior. It is connected with various problems, such as intraoperative AVM rupture with substantial bleeding. There have also been reports of problems like seizures and hematoma formation.⁷ Adult AVMs can be completely removed through microsurgery, but child AVMs are more dynamic and may recur after removal.¹⁵ Brain AVMs are diverse, and each one's unique microanatomy and vascular architecture may lead to a different clinical outcome. In patients without risk indicators including hemorrhagic presentation, deep AVM placement, or deep venous drainage, the probability of bleeding ranges from 0.9% per year to as high as 34.4% in patients with these features.^{1,16} The use of endovascular techniques like embolization, stereotactic radiosurgery, and microsurgery have advanced significantly during the past two decades, enabling efficient multidisciplinary treatment of arteriovenous malformations, including some that were once thought to be incurable.¹⁷ In our study, we tried to evaluate the overall outcomes of microsurgical resection of low-grade AVMs operated at three different neurosurgical centers in Pakistan.

MATERIALS AND METHODS

Study Design and Setting

Data was collected from three different neurosurgical centers in Pakistan as part of a descriptive observational study. The study lasted for two years, from January 2018 to December 2020.

Inclusion Criteria

Patients with S-M Grades 1 and 2 were included in this study regardless of their age and gender differences.

Exclusion Criteria

Patients with S-M Grades 3, 4, and 5 were excluded.

Data Collection Procedure

Data was collected after the institutional ERB's ethical approval. Patients gave their informed consent for this study. All cerebral AVM patients were categorized into three classes using the Spetzler-Martin grading system: A, B, and C. Grades 1 and 2 were in Class A, grade 3 was in Class B, and grades 4 and 5 were in Class C. All male and female patients with grade 1 and grade 2 AVMs, regardless of age, were eligible. Following surgery, patients were assessed for seizures, hemorrhage, localized neurological impairments, and AVM recurrence. To assess the outcome, morbidity, mortality, and functional recovery were used. Functional recovery and cure rate were observed after 6 months of follow-up. For data collection, a proforma was created.

Data Analysis Procedure

Statistical Package for Social Sciences (SPSS) version 28.0 was used to analyze the data.

RESULTS

Age Distribution

There were a total of 22 patients. The mean age was 36.41 ± 14.32 SD years with minimum and maximum ages of 16 and 65 years, respectively (Figure 1).

Gender Distribution

There were 12 (54.5%) male patients and 10 (45.5%) female patients in this study (Table. 1).

Clinical Presentation

13 patients (59.1%) presented with spontaneous intracerebral hemorrhage, while 9 patients

(40.9%) presented with seizures (Table. 1). 8 (66.7%) male and 5 (50%) female patients presented with hemorrhage while 4 (33.3%) male and 5 (50%) female patients presented with seizures (Figure 2).

Table 1: Patients with low-grade AVMs' baselinefeatures and prognosis.				
Variables	No. of Patients			
Gender	Male	12 (54.5%)		
Gender	Female	10 (45.5%)		
Clinical	Hemorrhage	13 (59.1%)		
Presentation	Seizures	9 (40.9%)		
Location of AVM Nidus	Frontal lobe	10 (45.5%)		
	Parietal lobe	6 (27.3%)		
	Occipital lobe	3 (13.6%)		
	Temporal lobe	3 (13.6%)		
Side of AVM	Right side	13 (59.1%)		
in the Brain	Left side	9 (40.9%)		
S-M grade	Grade 1	14 (63.6%)		
S-IM grade	Grade 2	8 (36.4%)		
Outcome	Morbidity	1 (4.5%)		
	Mortality	0 (0%)		
	Functional outcome	21 (95.5%)		
	Cure rate	22 (100%)		

Location of AVM Nidus

The location of AVM nidus was the frontal lobe in 10 (45.5%), parietal lobe in 6 (27.3%), occipital lobe in 3 (13.6%), and temporal lobe in 3 (13.6%) patients (Table. 1). Location of AVM nidus among male patients was 7 (58.3%) in the frontal lobe, 3

(25%) in the parietal lobe, 1 (8.3%) in the occipital lobe and 1 (8.3%) in temporal lobe while among female patients it was 3 (30%) in the frontal lobe, 3 (30%) in the parietal lobe, 2 (20%) in the occipital lobe and 2 (20%) in the temporal lobe, respectively (Figure 3).

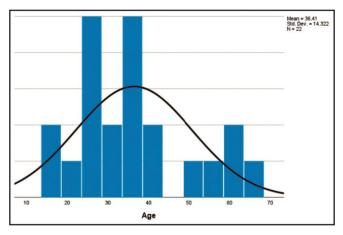


Figure 1: Age distribution among patients.

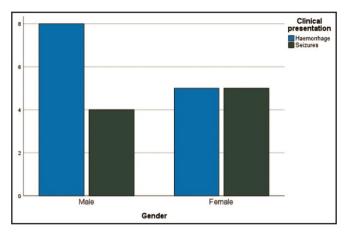


Figure 2: Clinical presentation among male and female patients.

Side of AVM in the Brain

13 (59.1%) AVMs were on the right side of the brain, while 9 (40.9%) were on the left side (Table. 1). Side of AVM in the brain was right side in 8 (66.7%) and left side in 4 (33.3%) male patients whereas it was right side in 5 (50%) and left side in other 5 (50%) female patients (Figure 4).

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S-M Grades Distribution

14 (63.6%) patients (63.6%) had S-M grade 1 and 8 patients (36.4%) had S-M grade 2 (Table. 1). 9 (75%) male patients had S-M grade 1 and 3 (25%) had S-M grade 2 while 5 (50%) female patients had S-M grade 1 and other 5 (50%) had S-M grade 2 (Figure. 5).

All patients underwent microsurgical resection. We discovered 4.5% morbidity in our patients. There was no postoperative mortality. At 6 months, an excellent functional outcome of 95.5% (according to the Glasgow outcome scale) and a 100% cure rate were observed.

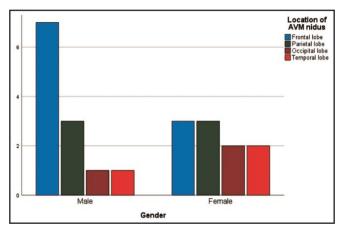


Figure 3: Location of AVM nidus among male and female patients.

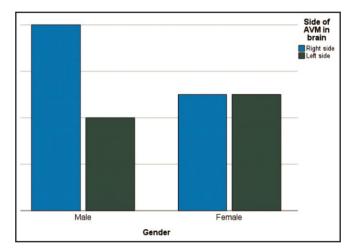


Figure 4: Side of AVM in the brain among male and female patients.

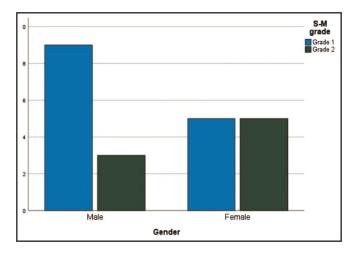


Figure 5: S-M grades distribution among male and female patients.

Table 2: Summary of surgical results of low-grade AVMs from high-income countries.					
Authors'	Year	No. of Patients	Morbidity (%)	Mortality (%)	The cure Rate (%)
Spetzler & Martin ²³	1986	44	0	NA	NA
Heros et al. ²⁴	1990	47	2.2	2.2	100
Sundt et al. ²⁵	1991	84	2.2	0	100
Sisti et al. ²⁶	1993	67	1.5	0	94
Hamilton & Spetzler ²⁷	1994	40	0	0	100
Schaller & Schramm ²⁸	1997	50	3.2	0	98

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Schaller et al. ²⁹	1998	81	0	0	NA
Pikus et al. ³⁰	1998	26	3.8	0	100
Hartmann et al. ³¹	2000	48	6.6	0	NA
Morgan et al. ³²	2004	220	0.9	0.5	100
Davidson & Morgan ³³	2010	296	0.7	0	97
Lawton ³⁴	2014	232	2.4	0.5	98
Theofanis et al. ³⁵	2014	128	1.9	2.7	100
Potts et al. ³⁶	2015	232	3	0.4	97
Moon et al. ³⁷	2015	85	3.5	3.5	NA
Ren et al. ³⁸	2017	239	NA	NA	89.3
Hung et al. ³⁹	2017	51	NA	NA	94.1
Wang et al. ¹⁸	2020	218	1.2	0.5	100
Total	-	2188	2.07	0.69	97.67

Table 3: Summary of surgical results of low-grade AVMs from low-middle-income countries.					
Authors	Year	No. of Patients	Morbidity (%)	Mortality (%)	The cure Rate (%)
Ayub et al. ⁴⁰	2011	11	9	9	100
Jean et al.41	2019	56	10	7	98
Karki et al. ⁴²	2021	21	19	0	88
Nguyen et al. ⁴³	2021	5	3.5	0	100
Total	-	93	10.4	4	96.5

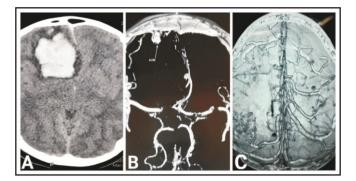


Figure 6: These Images are published after taking consent from the patient. CT; A: scan of brain plain axial view showing a right frontal lobe hemorrhage secondary to a ruptured AVM, B: Preoperative CT angiogram showing AVM nidus in right frontal lobe region, C: Postoperative CT angiogram of the same patient showing absence of AVM nidus.

DISCUSSION

With low-grade AVMs, microsurgical excision is thought to be the "gold standard" procedure (S-M grade 1 and 2). There are only two architectural options available for grades 1 and 2 in the grading system: 1) The eloquent cortex or deep venous drainage, but not both, are options if the AVM has a maximum diameter of 3 cm; 2) If neither deep venous drainage nor eloquent cortex is present, the AVM must be no more than 6 cm in diameter. Due to their straightforward architectural characteristics, low-grade AVMs are frequently determined to be safe for microsurgical resection with minimum morbidity and mortality.¹⁸

According research, hemorrhagic to appearance is a highly reliable independent predictor of further hemorrhage. Over 24 years, Ondra and colleagues studied a cohort of unoperated symptomatic brain AVM patients. They discovered a mean delay of 7.7 years between initial diagnosis and subsequent hemorrhage.¹⁹ The probability of future hemorrhage decreased among patients with hemorrhage as the initial presentation from 32.9% in the first year to 11.3% per year in the following years, according to research by Brown and colleague.²⁰ A study from Toronto discovered a 9.65% annual risk of hemorrhage during the first year and a 3.67% risk after 5 years from the initial hemorrhagic presentation. Additional possible risk factors for hemorrhage include 1) AVMs with solely deep venous drainage, 2) AVMs with associated aneurysms, 3) deep AVMs, and 4) infratentorial AVMs.⁸

In the ARUBA trial, 223 patients were enrolled for an average of 33 months across a 5-year enrollment period and any form of treatment for unruptured brain AVMs was contrasted with their natural course. The risk of death or stroke was 10.1% and 30.7% greater for the conservative and interventional care arms, respectively, according to the study. This ARUBA trial found that in all grades of unruptured brain AVMs, conservative care outperformed intervention in reducing death stroke.²¹ Due anatomical and to the characteristics of S-M grade 1 and 2 AVMs, which are better managed with microsurgery, ARUBA did not particularly evaluate the microsurgical results of patients with these AVMs.²²

According to our study, S-M grade 1 and 2 AVM patients who received microsurgical excision had outstanding results. Microsurgery is the gold standard for the vast majority of lesions, with embolization and radiosurgery reserved for risky AVMs in deep, difficult-to-reach places and eloquent regions that may be related to postoperative neurological impairments. Our findings support earlier studies on AVMs that recommended microsurgical excision as the most effective course of action for low-grade AVMs.²³⁻⁴³ AVMs that are surface-located are thought to be best for microsurgery. Seldom is corticotomy advised as a treatment for deep AVMs because it invariably leaves some sort of neurological damage. Nevertheless, not all of our centers have Diffusion Tensor Imaging (DTI) or Neuronavigation, which are imaging modalities unguestionably helpful are in such that circumstances. For better outcomes, the surgical approach to AVM is slightly different from that used to treat the other lesions that take up space in the brain.

Some of the key steps in our centers' procedures are as follows: Craniotomy of a large size, circumferential dural opening and carefully dissecting the dura from the underlying AVM nidus, dissecting the arachnoid-sulci at the AVM nidus margins, dissecting the arteries en passage, using aneurysm mini clips, coagulate as patiently and thoroughly as possible, coagulate and cut arteries first and then veins by non-stick bipolar cautery, Dissect the AVM nidus in a single piece, taking care not to tear the surrounding artery en route, Meticulous hemostasis following nidus resection, Watertight Dural closure and then closure of craniotomy defect.

The suggested technique asks for pre-and postoperative digital subtraction angiography for the accurate assessment of nidus excision, but the majority of our centers lack this capability, thus we perform cerebral CT angiography during follow-up visits in its place. Microsurgical resection, angioembolization, and radiosurgery are all forms of current AVM treatment, but in Pakistan, these options are only offered at one center in Lahore and two centers in Karachi. AVMs are ideally managed by a team of neurosurgeons, interventional neuroradiologists, and radiation therapists but such teamwork is lacking in our setups. We hope that our article will highlight the flaws in our systems and assist us in forming a better team to provide better patient care. We evaluated the outcome of microsurgical resection in terms of early morbidity, such as focal neurological deficits, seizures, and intracerebral bleeding, as well as late morbidity, such as AVM recurrence. Similarly, the mortality rate was also assessed. Figure 6 A, B & C shows one of our cases which was treated microsurgically. Our findings showed that there was 4.5% morbidity and 0% mortality. On postoperative 6-month follow-up, we had 95.5% functional outcome (according to the Glasgow outcome scale) and 100% cure rates. According to the available literature (Table. 6 & 7), a summary of surgical resection of 2188 low-grade AVMs had a morbidity rate of 2.07%, a mortality rate of 0.69%, and a cure rate of 97.67% in high-income countries but it was 10.4% morbidity, 4% mortality and 96.5% cure rate for low-middleincome countries. According to this summary, a larger sample size may result in a better assessment of morbidity and mortality. Our findings are very similar to international studies with small sample sizes. We propose further studies in the future with large sample sizes and long-term follow-up periods for better results.

CONCLUSION

For low-grade AVMs, microsurgery should be considered the first-line therapy. Microsurgery is the preferred method of treatment for low-grade AVMs due to its high surgical cure rates and excellent functional results. Radiosurgery and angioembolization are reserved for deep and inoperable AVMs. In our country, low-grade AVMs can be safely and successfully treated with microsurgery.

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Additional Information

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S. No.	Author's full name	Intellectual contribution to paper in terms of
1	Adnan Khaliq	Study Design, Methodology and Data Calculation.
2	Ahtesham Khizar	Data Analysis, Interpretation of Results and Paper Writing.
3	Muhammad Hassan Raza	Literature Review and Quality Insurer.
4	Muhammad Idris Khan	Statistical Analysis.
5	Nayab Gul & Adeeb-ul-Hassan	Literature Review.

AUTHORS' CONTRIBUTIONS