

EVALUATION OF CEREBRAL ARTERIOVENOUS MALFORMATIONS (AVMS): POSTOPERATIVE ENDOVASCULAR INTERVENTION CLINICAL AND RADIOLOGICAL OUTCOME IN AL-AZHAR HOSPITALS

By

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ABSTRACT

Background: Arteriovenous malformation (AVMs) is a collection of dysplastic plexiform vessels that is supplied by one or more arterial feeders and drained by one or more venous channels. AVMs may have a pure plexiform nidus or contain a mixed plexiform fistulous nidus.

Objective: To evaluate cerebral AVMs postoperative endovascular embolization by intervention, clinical and radiological outcome in a sample of Egyptian patients.

Patients and Methods: This was a retrospective study of all consecutive patients who had underwent endovascular embolization for cerebral AVMs between December 2006 up to April 2021. One hundred sixty-nine (169) patients (91 female and 78 males) with cerebral arteriovenous malformations were treated by embolization at the Neurointervention Unit at Al-Hussein Hospital University

Results: The mean age in our study was 32.85 years with a range of 6-80 years, and the standard deviation was 14.875 years. The sex distribution showed slight higher incidence in females (53.8%) than in males (46.2%), and twenty eight patients (16.6%) were with family history of cerebral AVMs. The most common presentation was intracranial hemorrhage (presented as weakness), seizure came second, and headache came third other neurological deficits (focal deficits, learning disability and cognitive impairment) were due to AVM itself were significant difference in nidus diameter, and the Spetzler and Martin grading of the cerebral AVMs after embolization in comparison to before embolization.

Conclusion: The endovascular treatment of the cerebral AVMs was safe, efficient and achieved high rates of total and near total occlusion.

Keywords: Cerebral Arteriovenous Malformations (AVM), and Postoperative Endovascular Intervention Clinical, Radiological Outcome.

INTRODUCTION

Arteriovenous malformation (AVMs) is a collection of dysplastic plexiform vessels that is supplied by one or more arterial feeders and drained by one or

more venous channels. AVMs may have a pure plexiform nidus or contain a mixed plexiform fistulous nidus (*Gross and Sacho, 2021*).

The AVMs detection rate is 1.1-1.2/100,000 people/year and the incidence of AVM hemorrhage is 0.42/100,000 persons/year (*Nitzan-Hirsh and Golan, 2020*).

The vast majority of all AVMs are located in the cerebral hemispheres (85% supratentorial) large majority located superficially, whereas only 10% are located deep in the cerebral hemisphere, including the basal ganglia, ventricles and corpus callosum. Only 15% occur in the posterior fossa, cerebellar hemisphere is a more common site than brainstem (*Ganaw et al., 2019*).

Patients with AVMs present with hemorrhage in 50% of the cases which is considered the most common presentation; seizures in 30%; headaches in 10% and neurological deficit in 10%, any one of these symptoms may occur alone. The pathophysiological mechanisms may lead to more than one mode of presentation (*Williams et al., 2019*).

Until recently, the gold standard for diagnosing AVMs is conventional angiography (*Pezeshkpour et al., 2020*).

Modern treatment of cerebral AVMs comprises the following interventions alone or in combination: microsurgical excision, stereotactic radiosurgery, and endovascular embolization (*Zuurbier and Salman, 2019*).

Endovascular embolization can be used for a curative embolization, nidus reduction before surgery or radiosurgery and palliative embolization. The goal of curative embolization is the complete and permanent obliteration of the AVMs nidus with the restoration of the normal arterial

blood flow and the preservation of venous drainage (*Al-Mufti et al., 2021*).

The most commonly used embolic agent is the rapidly polymerizing liquid embolic agent n-Butyl Cyano-Acrylate (nBCA). The use of nBCA for brain AVMs requires experience and skill, because of the intra-nidal flow and polymerization of nBCA are both quick and largely unpredictable (*Hill et al., 2018*).

After the introduction of the Onyx liquid embolic system (EV3, Irvine, CA) which is less adhesive, more slowly polymerizing and accordingly much more advantageous than nBCA, nBCA was largely replaced as an agent for AVMs embolization (*Al-Mufti et al., 2021*).

The present work aimed to evaluate cerebral AVMs postoperative endovascular embolization by intervention, clinical and radiological outcome in a sample of Egyptian patients.

PATIENTS AND METHODS

This was a retrospective review of all consecutive patients who had undergone endovascular embolization for cerebral AVMs between December 2006 and April 2021. One hundred sixty-nine (169) patients (91 females and 78 males) with cerebral arteriovenous malformations were treated by embolization at the Neurointervention Unit in Al-Hussein Hospitals Al-Azhar University.:

Inclusion criteria: All patients presented by cerebral AVMs and subjected to Al-Azhar Neurointervention Units, ie. since December 2006 up to April 2021 (ruptured or unruptured AVM) either symptomatic or discovered accidentally,

with high bleeding risk due to small size (< 3 cm), deep venous drainage, and/or associated aneurysm. Patients with recent intracranial hemorrhage were post-poned for at least 2 weeks (hematomas may interfere with good angiographic assessment).

Preprocedural assessment:

- Complete medical history.
- Complete general and neurological examinations.
- Laboratory investigations with stressing on:
 - Complete blood picture.
 - Coagulation profile.
 - Hepatitis markers.
 - Liver function tests.
 - Renal function tests.
- Radiological investigations:
 - CT (without contrast) was done for all patients for diagnosis after the presentation as an investigative study, for localization of the site of the AVMS, associated infarction or hydrocephalus.
 - CT (with contrast) was done for some patients for diagnosis after the presentation as an investigative study, for localization of the site of the AVMS, associated infarction or hydrocephalus
 - MRI was done for all patients and used as a good diagnostic tool in revealing pathological anatomy, edema, gliosis and associated venous varix and nidal aneurysm.
 - MRA and CTA were done in some patients, and used as good

diagnostic tools in revealing arterial feeders, venous drainage and associated venous varix and nidal aneurysm

- Intra-Arterial Digital Subtraction Angiography (IA-DSA) was done for all patients.

Follow up by IA-DSA and repeated scoring on Spetzler-Martin AVMS grading system were done within 6 months after embolization.

Modified Rankin scale was applied for patients presented with weakness before embolization and follow up after 6 months. Less than 3 indicated improvement and 3 or more indicated disability.

0= No symptoms at all.

1= No significant disability despite symptoms, able to carry out all usual duties and activities.

2= Slight disability, unable to carry out all previous activities, but able to look after own affairs without assistance.

3= Moderate disability, requiring some help, but able to walk without assistance.

4= Moderate to severe disability, unable to walk without assistance, and unable to attend to on bodily needs without assistance.

5= Severe disability, bedridden, incontinent, requiring constant nursing care and attention.

Statistical analysis:

Qualitative data were presented as numbers and percentages and tested with Monte-Carlo method were performed. Quantitative data were presented as

mean± standard deviation and the differences in quantitative data between groups were tested with t-test or Wilcoxon Signed Ranks Test.

P value <0.05 was considered significant.

Statistical Package for the Social Sciences (SPSS) v 26 was used

RESULTS

One hundred sixty-nine patients with cerebral arteriovenous malformations fulfilled the criteria of inclusion in this study were embolized. The mean age in our study was 32.85 years with range of 6-

80 years and the standard deviation was 14.875 years. The sex distribution showed slight higher incidence in females (53.8%) than in males (46) (**Table 1**).

Table (1): Age and sex distribution

Factors	Frequency (n =169)	Percentage
Gender		
Males	78	46.2
Females	91	53.8
Age		
Mean ± SD	32.85 ± 14.875	Mean ± SD
Max. – Min.	6 – 80	Max. – Min.

There was twenty-eight patients (16.6%) with family history of cerebral AVMs, there was forty-eight patients (28.4%) with hypertension of cerebral

AVMs, there was forty-one (24.3%) with diabetes mellitus of cerebral AVMs, there was fifty-seven patient (33.7%) with smoking of cerebral AVMs (**Table 2**).

Table (2): Risk factors among the study

Risk factors	Frequency (n =169)	Percentage
HTN		
No	121	71.6
Yes	48	28.4
DM		
No	128	75.7
Yes	41	24.3
Smoking		
No	112	66.3
Smoker	57	33.7
Family history		
No	141	83.4
Yes	28	16.6

In our study, 75 patients (44.38%) were presented with focal neurological deficit due to Hemorrhage, 42 patients (24.85%) with fits, 36 patients (21.30%) with headache and 16 patients with other

neurological deficit (focal deficits, learning disability and cognitive impairment) due to AVM itself (9.47%) (Table 3).

Table (3): Clinical presentation of cerebral AVMs in the study

Factor	Patients (n =169)	Percentage
Presentation		
Neurological deficit due to Hemorrhage	75	44.38
Fits	42	24.85
Headache	36	21.30
Others neurological deficit due to AVMs itself	16	9.47

There was a significant difference in nidus diameter in all patients after

embolization in comparison to before embolization (p = 0.000) (Table 4).

Table (4): Nidus diameter before and after embolization in our study by cm

Nidus diameter	Before embolization	After embolization	p value
Mean ± SD	3.96 ± 0.81	1.39 ± 0.7	0.01

SD: standard deviation. Paired p-test was used to compare between the repeated continuous data.

Nidus diameter and number of nidus less than 3 cm significantly reduced after

the intervention compared to baseline values (P < 0.0001).

Table (5): Number of patient with AVMs nidus more than 8cm less than 3cm before and after embolization

Groups Nidus diameter	Before		After		P value
	Number	Percentage	Number	Percentage	
≤ 3 cm	20	11.8	158	93.5	0.00
> 3 cm	149	88.2	11	6.5	

McNemar Test was used to compare between the repeated qualitative data.

There was significant difference in Spetzler and Martin grading system before and after embolization ($p = 0.001$). Spetzler and Martin score of the cerebral

AVMs was significantly improved after 6 months of the intervention compared to the initial grading score ($P < 0.0001$). (Table 6).

Table (6): Spetzler and Martin grading of the cerebral AVMs before and 6-month follow up after embolization

Spetzler And Martin grading	Groups		Before embolization		After embolization		P
	No	%	No	%			
Grade I	0	0	0	0	<0.01		
Grade II	24	14.2	149	88.2			
Grade III	93	55	0	0			
Grade IV	35	20.7	0	0			
Grade V	17	10	0	0			
Complete occlusion	0	0	20	11.8			
Total	169	100	169	100			

Wilcoxon Signed Ranks Test was used to compare between the repeated qualitative ordinal data.

Modified Rankin scale score for patients presented with side weakness was significantly improved after 6 months of

the intervention compared to the initial grading score (Table 7).

Table (7): Modified Rankin scale before and 6-month follow up after embolization

Modified Rankin scale	Groups		Before embolization		After embolization		P value
	No	%	No	%			
Grade I	0	0	15	50	<0.01		
Grade II	0	0	8	25			
Grade III	16	50	12	25			
Grade IV	22	50	3	0			
Grade V	0	0	0	0			
Total	38	100	38	100			

Wilcoxon Signed Ranks Test was used to compare between the repeated qualitative ordinal data.

As regards the final outcome, 20 patients (11.83%) showed complete occlusion of the nidus and 149 patients

(88.17%) had Suitable for radiosurgery (Table 8).

Table(8): Final outcome in our study

Outcome	No	%
Complete occlusion	20	11.83
Suitable for radiosurgery	149	88.17
Total	169	100

DISCUSSION

The mean age of the patients in our study was 32.85 years with range of 6-80 years and the standard deviation was 14.875 years. The age distribution recorded incidence peaks in the 3rd and 4th decade as the mean age of the patients was 32.85 years which was supported by *Krithika and Sumi (2020)* who reported that the mean age at diagnosis is 31.2 years.

The sex distribution showed slight higher incidence in females (53.8%) than in males (46.2%) which agreed with the study done by *Ganaw (2019)* who reported that higher incidence in females (57.8%) than in males (42.2%).

This did not go with the results which reported that 60.67% were males and 39.32% were females *Cai et al. (2020)*, also with *He et al. (2018)*.

Hypertension, diabetes mellitus, smoking, and family history were risk factors. Smoking was most significantly associated risk factor, present in 33.7 % of patients, followed by hypertension in 28.4 %.that was controversy to *Bokhari and Bokhari (2020)* who presented smoking as the most significant association followed by hypertension, due to which could be low incidence of smoking in Egyptian females which constituted 53.8% of our patients.

This was in agreement with the studies conducted by *Deng et al (2020)* where they found smoking as number one risk factor in 58.8% of cases, followed by hypercholesterolemia 21%, then hypertension comes in 19.8% of cases, diabetes with 6.2%, and family history is

the last factor which was present in only 1.1%.

Regarding the presentation of the cerebral AVMs in our study, presented with neurological deficit due to hemorrhage, 24.85% with fits, 21.30% with headache and other neurological deficit (focal deficits, learning disability and cognitive impairment) due to AVM itself 9.47% which was going strongly with *Wang et al. (2020)* who showed that 48% presented with hemorrhage, 21% with seizure, 16% with headache and 10% with no symptoms.

A systematic literature review by *Abecassis and colleagues (2014)* found that between 36% to 38% of new cases presented as a first-time hemorrhag which runs in the same line with our results. Also, *Bokhari and Bokhari (2020)* reported that seizure is second presenting disorder in 15 to 40% of patients. Also these has controversy to the study done by *De Sousa et al. (2020)* that showed the commonest clinical presentation was unspecific headache in 46% of cases, followed by epilepsy in 23% of cases, while only 20% came with intracerebral hemorrhage as first presentation and 11% accidentally discovered.

Chen et al. (2019) proved that headache was the second common presentation following the intracranial hemorrhage, and seizure was the third common presentation accounting for about 17.3% which did not go with our study.

Regarding AVMs characteristics as side, site, size, venous drainage and dural supply, our study showed that the AVMs were located in the right hemisphere in 55.62% and in the left hemisphere in

44.38%. The location of the AVMs in order of decreasing frequency was parieto-occipital 29.6%, parietal 26.6%, temporo-parietal 14.8%, temporal 14.8%, frontal 8.3% and cerebellar hemisphere 5.9%. These results are in agreement with AA, *et al.* (2014).

Our study showed that Nidus diameter before embolization of the AVMs was < 3 cm in 11.83%, 3 – 6 cm in 79.88% and > 6 cm in 8.28%. The venous drainage of the AVMs was multiple in 30.76%, single in 69.23%. The number of feeders in our study was multiple in 41.42%, single in 58.57%. The dural supply of the AVMs was positive in 20.1% and negative in 79.9%. These results agreed to some extent and differed in some characteristics, with the study done by *Dagli et al.* (2021).

Commonly used grading scale for brain AVMs was Spetzler-Martin Grade (SMG) scale, which was a composite score of nidus size (3 cm, 3-6 cm, 6 cm; 1-3 points), eloquence of adjacent brain (one point if located; brainstem, thalamus, hypothalamus, cerebellar peduncles or sensorimotor, language or primary visual cortex), and presence of deep venous drainage (one point if any or all drainage was through deep veins, such as internal cerebral veins, basal veins or precentral cerebellar veins *Bokhari and Bokhari* (2020).

The Spetzler and Martin grading of the cerebral AVMs before embolization was grade I in 0 patient (0%), grade II in 14.2%, grade III in 55%, grade IV in 20.7% and grade V in 10%.

This was in agreement with AA, *et al.* (2014). Who found that 0 patients were grade I (0%), 15 patients were grade III

(60%) and 5 patients were grade IV (20%). This disagreed to some extent with *Narsinh et al.* (2021) who found in their series that 25 patients were grade I or II, 10 patients were grade III and 12 patients were grade IV or V.

In this work, 360 sessions of injection were done to all patients. The majority of patients received 1-4 sessions. The nidus diameter reduction after embolization was complete reduction (total occlusion) in 11.8% and partial reduction 88.2%.

There was a marked reduction in nidus diameter after embolization which 6.5% had nidus diameter > 3 cm, while 81.6% had nidus diameter ≤ 3 cm. There was a significant difference in nidus diameter in all patients after embolization in comparison to before embolization.

Total occlusion occurred in 11.8%, while the remaining 88.2% had cerebral AVMs with grade II according to the Spetzler and Martin classification of the cerebral AVMs. There was a significant difference in Spetzler and Martin grading system before and after embolization.

Regarding the modified Rankin scale before embolization and 6-months follow up after embolization for patients presented with weakness (less than 3 indicates improvement and 3 or more indicates disabled). All patients were disabled before embolization with grade III weakness or more on the MRS and only 25% were disabled after embolization with grade III weakness on the MRS. Modified Rankin scale score for patients presented with side weakness was significantly improved after 6 months of the intervention compared to the initial grading score.

Our results were near to that of *Ly et al. (2011)* found in their series that clinically significant deficit was detected in 5% of the patients and 4.1% were disabled, and *De Sousa et al. (2020)* who observed that 10% of patients had modified Rankin scale 3 to 5 after AVMs embolization. In contrast these results were inconsistent with *Wang et al. (2020)* who found 2% had persistent neurological deficit (modified Rankin scale 3 to 5, and *Narsinh et al. (2021)* who found that 14% of patients were disabled after AVMs embolization.

Regarding the outcome of epilepsy after 6 months, we found that 76.2% had epilepsy and controlled, while in the 23.8%, the fits became infrequent. This could be explained by presence of edema and inflammation surrounding the nidus.

Well controlled seizure, if the patient had no seizures was in the last 3 months and infrequent seizure if the patient had one to six seizures per year. Regarding the outcome of headache after 6 months, we found that 89% improved and 11% did not improve. These results were in agreement with *AA, S, et al. (2014)* showed that 83.3% improved and 16.7% was not improved.

As regards the final outcome, 11.83% showed complete occlusion of the nidus and 88.17% had partial reduction of the nidus and were candidate for radiosurgery.

There results were in agreement with *AA, S, et al. (2014)*. Who showed that 20% with complete occlusion of the nidus and 80% had partial reduction of the nidus, and were candidate for radiosurgery.

CONCLUSION

The endovascular treatment of the cerebral AVMs was safe, efficient and can achieve high rates of total and near total occlusion. Indicated that curative embolization of AVMs can achieve high rates of total and near total occlusion with acceptable complications.

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التقييم الاكلينيكي و الاشعاعي من خلال الأشعة لعلاج حالات انصمام التشوهات الشريانية الوريدية المخية ما بعد التدخل بالقساطر متناهية الصغر وحقن المواد المجلطة في مستشفيات جامعة الأزهر

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خلفية البحث: دراسه حشديه تراجعيه لجميع المرضى الذين خضعوا للعلاج بالقسطره التداخليه والذين يعانون من تشوه الشرياني الوريدي الدماغى فى الفترة من ديسمبر 2006 حتى أبريل 2021 حيث تم علاج مائة تسعة وستين (169) مريضاً (91 إنثاء و 78 ذكورا) كانوا يعانون من التشوهات الشريانية الوريدية الدماغية و تم علاجهم عن طريق القسطره التداخليه فى وحدة القسطره المخيه بمستشفى الحسين الجامعي.

الهدف من البحث: تقييم وعلاج التشوه الشرياني الوريدي الدماغى بعد العلاج التداخلي بالقسطره المخيه فى عينة من المرضى المصريين.

المرضى وطرق العلاج: علاج جميع المرضى الذين يعانون من التشوه الشرياني الوريدي الدماغى فى وحدة القسطره المخيه منذ ديسمبر 2006 حتى أبريل 2021 سواء حدث انفجار للتشوه او لم يحدث (سواء كان عرضياً أو تم اكتشافه بالصدفة) مع وجود مخاطر نزيف عالية بسبب الحجم الصغير (أقل من 3 سم)، والتصريف الوريدي العميق، و/ أو تمدد الأوعية الدموية المصاحب فى مستشفيات جامعه.

نتائج البحث: وجدنا أن غالبية حالات التشوه الشرياني الوريدي الدماغى تظهر متوسط الاعمار الذين يعانون من التشوه (32) عاماً ووجدنا أيضاً ثمانية وعشرين مريضاً (16.6%) لديهم تاريخ مرضى فى العائله للتشوه الشرياني الوريدي الدماغى. و كان العرض الأكثر شيوعاً هو النزيف داخل الجمجمة، وجاء الصرع فى المرتبة الثانية، وجاء الصداع فى المرتبة الثالثة واعراض عصبية آخرا بسبب

التشوه الشرياني الوريدي نفسه. و كشفت دراستنا أن موقع التشوه الشرياني الوريدي الدماغى فى نصف الكرة الأيمن أكثر من نصف الكرة الأيسر. وكانت أهم الملاحظات فى دراستنا هى الاختلاف المهم الواضح فى قطر بؤره التشوه الشرياني الوريدي، وتصنيف اسبيتزلىر و مارتن للتشوه الشرياني الوريدي الدماغى بعد العلاج بالقسطره المخيه مقارنةً بما قبل العلاج بالقسطره المخيه. كما كشفت دراستنا أن إمداد الجافية كان سالبًا فى غالبية المرضى. وكانت نتيجة دراستنا بعد 320 جلسة فى 169 مريضًا هى الانسداد الوعائى الكامل ل20 مريضًا، والانخفاض الجزئى فى قطر النيدوس فى 129 مريضًا وتحويل 20 مريضًا للجراحة الاشعاعيه.

الاستنتاج: إلى أن العلاج القسطره المخيه التداخليه للتشوه الشرياني الوريدي الدماغى آمن وفعال ويمكن أن يحقق معدلات عالية الغلق الكامل والشبه الكامل.

الكلمات الدالة: التشوهات الشريانية الوريدية المخية، بعد التدخل بالقسطره المخية، التقييم الأكلينيكي و الأشعاعى.

قبول للنشر 14 / 9 / 2021