Original Article

Onyx in Brain Arteriovenous Malformation Embolisation

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Abstract

Introduction: **Embolisation has long been used as an adjunct to surgical resection in the treatment of brain arteriovenous malformation (bAVM). The most commonly used embolic material, n-butylcyanoacrylate glue, requires experience and skill to handle its quick and unpredictable flow and polymerisation. A new liquid embolic agent, ethylene vinyl alcohol copolymer (Onyx), is less adhesive and polymerises slowly, which provides better control for radiologists performing embolisation.**

Objective: **To report our experience in embolisation using Onyx alone or in combination with histoacryl for bAVM embolisation in our tertiary referral centre.**

Methods: We retrospectively reviewed the anatomy, technical conditions, complications and clinical outcome of all bAVM patients embolised at our centre using Onyx alone or in combination with n-butylcyanoacrylate glue.

Results: **Between 2010 and 2013, 13 patients [6 (46.2%) male; 7 (53.8%) female; aged, 14–57 years] were included, and a total of 31 embolisations were performed. Clinical presentation included hemorrhage [9 (69.2%)], seizures [2 (15.4%)], and headache [2 (15.4%)]. Most AVMs were located in the brain hemispheres [12 (92.3%)] and measured <3 cm [7 (53.8%]. Complete occlusion of the AVM was obtained in 2 (15.4%) patients; 11 (84.6%) patients had partial occlusion [6 (54.5%) had <50% nidus occlusion]. Complications occurred in four procedures involving 3 patients (morbidity, 23.1%). This resulted in the death of 1 patient (mortality, 7.7%) and complete recovery with no disability in 2 patients.**

Conclusion: **The total nidal occlusion achieved herein is comparable to other similar studies. Our morbidity and mortality were higher compared to other studies which may be attributed to the small number of patients. More data is being collected which may better reflect on our experience.**

Keywords: *therapeutic embolisation; arteriovenous malformations; angiography; butylcyanoacrylate; Onyx copolymer*

Introduction

An arteriovenous malformation (AVM) is a tangled cluster of vessels (known as nidus) in which feeder arteries connect directly to draining veins without any intervening capillary bed. The most common presenting symptom is hemorrhage (71%), followed by seizures [24%] (1). The goal of treatment is to prevent hemorrhage; seizure control and stabilisation of neurological deficits are also occasionally a goal of treatment (2).

Embolisation has been used as an adjunct to surgical resection. The goal of embolisation is to reduce the size of the nidus by occluding the arterial feeders and the nidus itself. Several different embolic materials have been used in endovascular embolisation, such as balloons, polyvinyl alcohol particles, and most commonly, n-butylcyanoacrylate (n-BCA) glue. The intranidal flow and polymerisation of n-BCA glue are quick and unpredictable, requiring experience and skills to handle it (3). A new liquid embolic agent, ethylene vinyl alcohol copolymer (Onyx; Covidien/ev3, Irvine, CA, USA) is less adhesive and polymerises slowly, which provides better control for the radiologist performing the embolisation. Herein, we describe our experience using Onyx alone or in combination with n-BCA glue for embolisation of brain AVM (bAVM).

Research Methodology

The current study was a retrospective review of medical records and previous imaging of all patients with bAVM that underwent embolisation between January 2010 and January 2013 at our tertiary referral centre. A total of 115 embolisations were performed at our centre during this period for a variety of indications, including treatment of cerebral and spinal vascular disorders and pre-operative embolisation of tumors. Thirty-eight embolisations were done for bAVM. Patients with incomplete pre-embolisation images archived in our hospital's picture archiving and communication system (PACS) were excluded. These were patients who had imaging done at another hospital and were referred to our centr efor embolisation. The pre-embolisation images may have been kept by the patient and not archived into the PACS.

Patient demographics and number of embolisations were recorded. Other variables reviewed included image evaluation completed by a neuroradiologist and an interventional neuroradiologist and AVM anatomy, which was evaluated by cross-sectional imaging and digital subtraction angiogram. The outcome of embolisation was assessed by evaluating the percentage of nidal occlusion post-embolisation based on digital subtraction angiogram images. Any recorded complications that occurred and steps taken to remedy them were also reviewed. Each patient's clinical status post-embolisation recorded in their medical record was also reviewed using the Modified Rankin Scale.

Results

The current results are presented based on the BRAVO study (4). Our review included 13 patients [6 (46.2%) male; 7 (53.8%) female] aged 14 to 57-years-old treated for bAVM by embolisation at our hospital between January 2010 and January 2013. The majority of patients presented with intracranial hemorrhage [9 (69.2%)], while the rest presented with seizure [2 (15.4%)], and headache [2 (15.4%)]. No patient presented with neurological deficit or was an incidental finding. Table 1 summarises the anatomy of AVM among our patients.

A total of 31 embolisations were done on these 13 patients (median, 2 embolisations per patient) and a range of one to five procedures per patient (Table 2).

In reviewing the number of embolizations performed, we included those which were attempted but abandoned for various reasons, but mainly due to spontaneous nidal occlusion or failure to cannulate feeder arteries. In six procedures (19.4%), no embolic agents were used (Table 2). We included these procedures because in our opinion, these embolisations were indicated in order to achieve as much nidal occlusion as possible and are reflected in the number of embolisations needed per patient. Embolisation outcomes are described in Table 3. Complications occurred in four procedures involving 3 patients (morbidity, 23.1%). This resulted in the death of 1 patient (mortality, 7.7%) and complete recovery with no disability in 2 patients (Table 4).

Table 1: Anatomy of AVM

Total no. of patients: 13									
Location	**n (%)**	**Size**	**n (%)**	**Venous drainage**	**n (%)**	**Associated aneurysm n (%)**	**Direct Fistula n (%)**	**Spetzler – Martin Grade n (%)**	
Right	7(53.8)	3cm	7(53.8)	Deep	3(23.1)	2 (15.4)	0 (0)	1	1(7.7)
Left	6(46.2)	3–6cm	6(46.2)	Superficial	6(46.2)			2	7(53.8)
Hemisphere	12(92.3)	>6cm	0(0)	Deep & Superficial	4(30.8)			3	2(15.4)
Basal Ganglia	1 (7.7)			Unique	5(38.5)			4	3(23.1)
Cerebellum	0 (0)			Multiple	8(61.5)				
Corpus Callosum	0 (0)								
Eloquent	7 (53.8)								
Non eloquent	6 (46.2)								

Table 2: Technical Results

Total embolisations performed	**31**
No. of embolisations/patient	Median = 2 (Range: 1–5)
Embolic materials used:	**n (%)**
Onyx	17 (54.8)
Glue	6 (19.4)
Onyx & Glue	2 (6.5)
None (embolisation attempted but abandoned)	6 (19.4)

Table 3: Outcome of AVM treatment

No. of patients embolised = 13			
Nidal occlusion	**Size <3cm**	**Size 3-6cm**	**Total n(%)**
100%	1	1	2 (15.4)
75 – 99%	1	0	1 (7.7.)
50 – 74%	1	3	4 (30.8)
<50%	4	2	6 (46.2)
Complementary treatment for partially embolised AVM = 11			
Patients		**n(%)**	
Awaiting radiosurgery		4 (36.4)	
Refused further intervention		1 (9.1)	
Lost to follow up		6 (54.5)	

Table 4: Complications from embolisations

Patient	Procedure	Type of complication	Treatment for complication	MRS post treatment	Outcome post treatment
A	1	Intra-op perforation of feeder artery	Embolisation of perforated artery	0	Achieved <50% nidal occlusion
	2	Post op Intracranial haemorrhage – treatment related	Decompression surgery	5	Death
B	3	Post op Intracranial haemorrhage – disease related	Conservative	0	Regression of AVM without further intervention, refused further treatment
C	4	Cortical venous thrombosis with no venous infarct	Conservative	0	Total nidal occlusion without further intervention

Discussion

An AVM is a tangled cluster of vessels known as nidus in which feeder arteries connect directly to draining veins usually via arteriovenous shunting without any intervening capillary bed. Due to its rarity and presence of asymptomatic patients, establishing a true prevalence rate is difficult. The prevalence of detected AVM inferred from incidence data is <10.3 per 100,000 people (5). The mean age of presentation is 33.7 years (1), and it affects men and women equally. The most common presenting symptom is hemorrhage (71%), followed by seizures [24%] (1). This is similar to our current data, where 69.2% presented with hemorrhage. The annual risk of hemorrhage is 1.3%–4.0% per year and 1.0% results in mortality per year (1, 6); mortality after initial rupture is 10%–17.6% (6).

A multidisciplinary approach consisting of surgery, endovascular embolisation, and stereotactic radiosurgery is used to treat bAVM. Surgical resection is the definitive treatment for eradication of lesions (7). However, stereotactic radiosurgery and embolisation have been increasingly used for inoperable lesions. Embolisation has also been used as an adjunct to surgical resection. The goal of embolisation is to reduce the size of the nidus by occluding the arterial feeders and the nidus itself. This facilitates surgical resection, prevents further hemorrhage, and/or reduces signs and symptoms associated with steal phenomenon, venous hypertension, and seizures (7). Typically, embolisation is done in stages. At our centre, the number of embolisations per patient ranges from one to five (median, 2). Unfortunately, complete obliteration of AVM by embolisation alone is low [13%] (8). Thus, it is usually used in a multidisciplinary treatment program.

Several different embolic materials have been used in endovascular embolisation, such as balloons, polyvinyl alcohol particles, and n-BCA glue. The intranidal flow and polymerisation of n-BCA glue are quick and unpredictable, requiring extensive experience and skill when handling it (3). The embolic agent Onyx is less adhesive and polymerises slowly, which provides better control during the embolisation procedure.

Our data shows 2/13 patients (15.4%) achieved total occlusion, which is similar to other studies. van Rooij et al. reported total occlusion in 16% of their 44 patients (3), while Pierot et al. reportedly achieved total occlusion in 23.5% of their 117 patients, and Katsaridis et al. attained total occlusion in 53.9% of their 52 patients (4, 9). In our opinion, the number of total occlusions achieved herein was not directly due to the embolic material used or the technical aspects of embolisation. As seen in Table 3, 54.5% of our patients were lost to follow-up. We might have achieved a higher number of total occlusions if we were able to continue embolisation in these patients.

The safety and efficacy of Onyx has been reported in several studies. In a study of 44 patients with a total of 52 embolisations, van Rooij et al. reported a morbidity and mortality of 4.6% and 2.3%, respectively (3). In the BRAVO study on 117 patients by Pierot et al., 5.1% morbidity and 4.3% mortality were reported (4). Katsaridis et al. also reported similar results in 52 patients where the morbidity and mortality were 8% and 3%, respectively (9).

In the present study, morbidity (23.1%) and mortality (7.7%) were higher than what has been reported previously. This is likely due to the small number of patients included in our study. We have one death which resulted from the treatment. Herein, a 51-year-old man underwent his fourth embolisation. The AVM nidus measured 3–6 cm and had been partially embolised previously, achieving <50% occlusion. The latest embolisation was uneventful, and three vials of Onyx were used to achieve 50%–75% occlusion. He was extubated with full GCS recovery, and no neurological deficit was noted while in the angio suite. However, his GCS dropped 6 h later. A computed tomography scan showed a left temporoparietal intra parenchymal bleed with mass effect and midline shift, likely due to a venous infarct. Onyx cast was seen within the draining vein (Figure 1).

There were also smaller Onyx casts seen in the internal cerebral and cortical veins, and he underwent decompression surgery to treat the intracranial bleed. However, the patient eventually lost his brainstem function and passed away. We postulate that the presence of Onyx in the draining vein contributed towards the venous thrombosis, which subsequently resulted in venous infarct and intra parenchymal hemorrhage. Due to the inhomogeneity of the radio-opacity of Onyx, it is difficult to visualise, particularly when it is not in the targeted site.

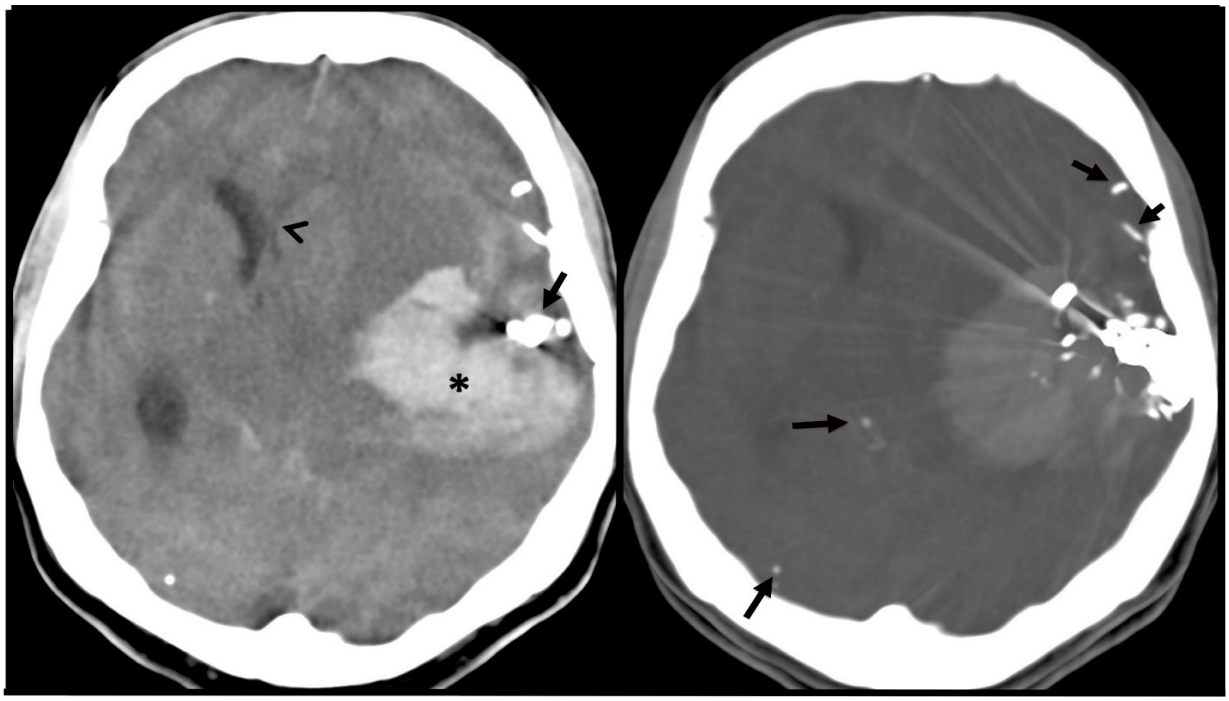

Figure 1: Non- contrasted CT Brain showed a left temporo-parietal bleed (*) causing midline shift to the left and compression of left lateral ventricle (arrowhead). Onyx casts were seen in the draining vein and cortical veins (black arrow).

Conclusion

The total nidal occlusions achieved in our centre is comparable to other similar studies. However, this number can certainly be improved, not only with respect to technical aspects, but also by improving our patients' commitment to their treatment and preventing their loss to medical follow-up. We also hope to improve our morbidity and mortality. More data is being collected which may better reflect on our experience with this procedure and new embolic agent.

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Conflict of Interest

None

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Authors Contributions

Conception and design, Analysis and interpretation of the data, Drafting of the article, Statistical expertise, Collection and assembly of data: HH
Conception and design, Analysis and interpretation of the data, Critical revision of the article for important intellectual content, Final approval of the article, Provision of study materials or patients: ASM
Provision of study materials or patients, Collection and assembly of data, Final approval of the article, Administrative, technical, or logistic support: AAA & ZAH

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References

1. Ondra SL, Troupp H, George ED, Schwab K. The natural history of symptomatic arteriovenous malformations of the brain: A 24-year follow-up assessment. Journal of *Neurosurgery*. 1990;**73(3):**387–391. http://dx.doi.org/10.3171/jns.1990.73.3.0387

2. Ogilvy CS, Stieg PE, Awad I, Brown RD, Kondziolka D, Rosenwasser R, et al. Recommendations for the management of intracranial arteriovenous malformations: a statement for healthcare professionals from a special writing group of the stroke council, American Stroke Association. *Stroke*. 2001;**32(6):**1458–1471. http://dx.doi.org/10.1161/01.STR.32.6.1458

3. van Rooij WJ, Sluzewski M, Beute GN. Brain AVM Embolization with Onyx. *American Journal of Neuroradiology*. 2007;**28(1):**172–177.

4. Pierot L, Cognard C, Herbreteau D, Fransen H, Rooij WJ, Boccardi E, et al. Endovascular treatment of brain arteriovenous malformations using a liquid embolic agent: results of a prospective, multicentre study (BRAVO). *Eur Radiol*. 2013;**23(10)**:2838–2845. http://dx.doi.org/10.1007/s00330-013-2870-6

5. Berman MF, Sciacca RR, Pile-Spellman J, Stapf C, Connolly ES, Jr., Mohr JP, et al. The epidemiology of brain arteriovenous malformations. *Neurosurgery*. 2000;**47(2):** 389–396; discussion 97. http://dx.doi.org/10.1097/00006123-20000 8000-00023

6. Fleetwood IG, Steinberg GK. Arteriovenous malformations. *Lancet*. 2002;**359(9309):**863–873. http://dx.doi.org/10.1016/S0140-6736(02)07946-1

7. Plasencia AR, Santillan A. Embolization and radiosurgery for arteriovenous malformations. *Surgi Neurol Int*. 2012;**3(Suppl 2):**S90. http://dx.doi.org/10.4103/2152-7806.95420

8. van Beijnum J, van der Worp HB, Buis DR, Al-Shahi Salman R, Kappelle LJ, Rinkel GJ, et al. Treatment of brain arteriovenous malformations: a systematic review and meta-analysis. *JAMA*. 2011;**306(18):**2011–2019. doi: 10.1001/jama.2011.1632. http://dx.doi.org/10.1001/jama.2011.1632

9. Katsaridis V, Papagiannaki C, Aimar E. Curative embolization of cerebral arteriovenous malformations (AVMs) with Onyx in 101 patients. *Neuroradiology*. 2008;**50(7):**589–597. http://dx.doi.org/10.1007/s00234-008-0382-x