Available online at www.sciencedirect.com

ScienceDirect

journal homepage: http://www.elsevier.com/locate/pjnns

Original research article

Early outcomes and periprocedural complications of transarterial embolization of brain arteriovenous malformations with Onyx®

Wojciech Poncyljusz [a], Marcin Sawicki [b,*], Katarzyna Lubkowska [c], Monika Rać [d]

[a] Department of Interventional Radiology, Pomeranian Medical University, Neurointerventional Cath Lab MSW Hospital, Rybacka 1, 70204 Szczecin, Poland
[b] Department of Diagnostic Imaging and Interventional Radiology, Pomeranian Medical University, Rybacka 1, 70204 Szczecin, Poland
[c] Euromedic Lowersilesian Medical Center, Interventional Neuroradiology CathLab, Traugutta 116, 50420 Wrocław, Poland
[d] Department of Biochemistry and Medical Chemistry, Pomeranian Medical University, Rybacka 1, 70204 Szczecin, Poland

ARTICLE INFO

Article history:
Received 5 July 2016
Accepted 23 March 2017
Available online 5 April 2017

Keywords:
Brain arteriovenous malformation
Embolization
Onyx

ABSTRACT

Background: Brain arteriovenous malformation (BAVM) is a rare pathology diagnosed mostly in young adults. However, due to its hemorrhagic complications, it constitutes an important clinical problem. Treatment modalities available include endovascular, surgery and radiosurgery.

The aim of the study was to assess the efficacy and safety of endovascular treatment of BAVM with Onyx® by reporting one-center experience.

Material and methods: Between 2006 and 2013, 54 patients with BAVM were embolized with Onyx. The group consisted of 24 males and 30 females, aged 10 to 65 years (mean 42.6 ± 15.4). Clinical manifestations of BAVMs were: hemorrhage in 27 (50.0%), headaches in 12 (22.2%), seizures in 7 (13.0%) and focal neurologic deficits in 2 (3.7%) patients. Six (11.1%) patients were asymptomatic. A majority of BAVMs were of II and III grade in Spetzler-Martin scale (19 and 22 cases respectively).

Results: A total number of 108 endovascular procedures were performed (mean 2.00 ± 0.98 sessions/patient). Complete obliteration of malformation was achieved in 25 (46.3%) patients, mostly with grade II and III BAVMs. In 29 (53.7%) patients, embolization led to a decrease in size of BAVM that made it feasible for other treatment modality. Morbidity and mortality rates were 5.6% and 1.8% respectively. The rate of hemorrhagic complications was 9.3%.

Conclusion: Embolization of BAVM with Onyx® is an effective and safe method of treatment. However, regarding type and consequences of complications, the technique needs further improvement.

* *Corresponding author.*
E-mail addresses: wponcyl@poczta.onet.pl (W. Poncyljusz), msaw@pum.edu.pl (M. Sawicki), k.lubkowska@interia.pl (K. Lubkowska), carmon12@gmail.com (M. Rać).

http://dx.doi.org/10.1016/j.pjnns.2017.03.006
0028-3843/

1. Introduction

Endovascular treatment is one of the modalities, alongside neurosurgical excision and radiosurgery, which is nowadays available for the management of brain arteriovenous malformations (BAVM). The first liquid embolic agent introduced to the treatment of BAVM was *n*-butyl cyanoacrylate (n-BCA). However, due to its fast polymerization after contact with ionic substances in blood and poor intraoperative control, n-BCA enables complete occlusion of BAVM in very limited number of patients, even if used by an experienced neurointerventionist [1,2]. Onyx (Covidien ev3, Irvine, CA, USA) is polymer of ethyl vinyl alcohol dissolved in dimethyl sulfoxide (DMSO), which precipitates and thus allows slower injection with better control and penetration to the nidus of BAVM. It seems to be more promising and safer for both patients and neurointerventionist [3,4]. Onyx was approved in Europe in 1999 and became a commonly used embolic agent in everyday endovascular practice around 2004/2005 [5]. Since then, the indications for use of n-BCA were reduced and accessibility of endovascular treatment of BAVM was facilitated. This method of treatment became available beyond selected experienced centers. Although, a complexity of the pathology and its low incidence still requires the highest level of expertise from a medical team dealing with this problem.

The aim of the report was to define the efficacy of endovascular treatment of BAVM with Onyx with particular emphasis on its safety and complete cure rate by reporting single-center experience with this method.

2. Material and methods

2.1. Patient's selection

The Onyx liquid embolic agent has European Conformity Marking (CE Mark) and is routinely utilized in our institution. Application of Onyx did not require ethical committee approval for this observational study. The study was performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. Informed consent was obtained from all patients.

The studied population included patients with the diagnosis of BAVM confirmed by preoperative digital subtraction angiography (DSA) who underwent endovascular treatment using Onyx in one interventional neuroradiological center from 2006 to 2013. All patients were qualified for endovascular therapy by a multidisciplinary team of physicians experienced in BAVM treatment, representing at least three medical specialties: neurosurgery, interventional neuroradiology and anesthesiology. In the center included in this report, embolization was established as the first line treatment of malformations with an intention to cure. All of the patients with a non-hemorrhagic manifestation of BAVM have been treated before publication of ARUBA trial (A Randomized Trial of Unruptured Brain Arteriovenous Malformations) partial results in November 2013 [6].

2.2. Endovascular procedure

Endovascular treatment in all patients was performed with intention to cure that is to completely occlude BAVM. Neuroradiologist with over 10-years experience in endovascular neurointerventions performed all embolizations. Onyx was used as a sole embolic agent in all cases and its injection was determined by the possibility of distal access to the nidus and anatomy of BAVM.

Each procedure was performed under general anesthesia, through femoral access using Avanti 6F sheath introducer (Cordis, Bridgewater, NJ, USA) and was preceded by intravenous bolus of 2000 IU of heparin in a case of unruptured BAVM. Guiding catheter Envoy 6F (Cordis, Bridgewater, NJ, USA) or Guider Soft (Boston Scientific, Fremont, CA, USA) was then placed under fluoroscopy in either internal carotid or vertebral artery being main supply to the malformation. Subsequently, DMSO compatible microcatheter Sonic (Balt Extrusion, Montmorency, France) with detachable tip, or undetachable microcatheter Marathon (Covidien ev3, Irvine, CA, USA) was introduced into the feeding artery over guidewire SilverSpeed (Covidien ev3, Irvine, CA, USA), Traxcess (Microvention Terumo, Tustin, CA, USA) or Hybrid (Balt Extrusion, Montmorency, France). A proper working position of microcatheter was confirmed by monoplane microangiography. Microcatheter was then flushed with recommended volume of DMSO and its dead space filled with Onyx, which was injected slowly under continuous control of monoplane subtraction fluoroscopy with 30–120 s breaks for building reflux over the tip of microcatheter in the feeding pedicle. The injection was stopped and microcatheter removed when control angiography showed a total occlusion of the whole nidus or its intended part or the length of reflux was considered critical (15 mm). Control 3-vessel DSA completed each procedure. If no complications occurred, a patient was woken up from general anesthesia and observed first in ICU, then in neurosurgery ward for at least 24 h with continuous monitoring of BP.

2.3. Data collection

For all patients, age and gender were noted. The following data describing the clinical presentation were recorded: intracranial hemorrhage, headaches, seizures and neurological deficits. The following data regarding BAVM were analyzed: localization categorized as the cerebral hemisphere, cerebellum, basal ganglia incl. thalamus and corpus callosum; nidus size divided into categories: <3 cm, 3–6 cm and >6 cm; outflow type categorized as superficial or deep; number of outflows and feeding arteries as single or multiple; additional anatomical risk factors, such as aneurysm of the feeding artery, ectasia, stenosis of the draining vein and fistula. All lesions were categorized according to the Spetzler-Martin grading scale. A number of embolization sessions was noted.

The angiographic result was categorized as complete (100%) or incomplete ($<100\%$) obliteration of BAVM, based on post-procedural DSA. Initial and final DSA was assessed by the neuroradiologist performing embolization. Procedural complications of embolization were noted during one-month

follow-up period after the last session. In cases with incomplete obliteration, information about complementary surgery and/or radiosurgery was collected. As the aim of the study was to assess the efficacy and safety of Onyx embolization, the techniques and results of complementary treatment were not analyzed.

2.4. Statistical analysis

Age, Spetzler-Martin grading, and number of embolization sessions were considered continuous variables, with gender, initial signs and symptoms, localization of BAVM, nidus size, outflow type, number of outflows, number of feeding arteries and additional anatomical risk factors as categorical variables. The Mann–Whitney U test was used to compare continuous variables because the distributions of most of them were significantly different from the normal distribution ($p < 0.05$, Shapiro–Wilk test). The chi-squared test (χ^2) was used for categorical variables. A multivariate logistic regression model was used to find independent demographic and clinical predictors of negative treatment outcome. $p < 0.05$ was considered statistically significant. Statistica 12 software (StatSoft Inc., Tulsa, OK, USA) was used for the statistical analysis. A medical statistician evaluated the tests.

3. Results

3.1. Patient's and BAVM's population

The studied population consisted of 54 patients (30 females) at a mean age of 42.6 ± 15.4 years (range 10–65 years). Characteristics of the patients and BAVMs features are presented in Table 1.

Table 1 – Characteristics of the patients and BAVMs.

Characteristics	No. (n = 54) and percentage
Symptoms	
Hemorrhage	27 (50.0)
Neurological deficits	2 (3.7)
Seizures	7 (13.0)
Headaches	12 (22.2)
Incidental	6 (11.1)
Location	
Hemisphere	27 (50.0)
Basal ganglia incl. thalamus	12 (22.2)
Corpus callosum	3 (5.6)
Cerebellum	12 (22.2)
Size	
<3 cm	28 (51.9)
3–6 cm	25 (46.3)
>6 cm	1 (1.8)
Outflow type	
Deep	40 (74.1)
Superficial	14 (25.9)
Number of outflows	
Single	22 (40.7)
Multiple	32 (50.3)
Number of feeding arteries	
Single	28 (51.9)
Multiple	26 (48.1)
Additional features	
No additional features	24 (44.4)
Associated aneurysm	7 (13.0)
Fistula	11 (20.4)
Ectasia of the draining vein	8 (14.8)
Stenosis of the draining vein	4 (7.4)
Spetzler-Martin grade	
I	5 (9.3)
II	19 (35.2)
III	22 (40.7)
IV	7 (13.0)
V	1 (1.8)

3.2. Results of endovascular treatment

The aim of embolization that is complete obliteration of the lesion was achieved in 25 (46.3%) patients. Among 29 patients with incomplete occlusion, over 75% of BAVM was obliterated in 13 (44.8%) patients. Detailed results of embolization are presented in Table 2. Up to 4 sessions were performed in a single patient with a total number of 108 sessions (mean 2.00 ± 0.98 sessions/patient) (Fig. 1).

Undetachable catheters were used in 62 (57.4%) sessions, catheters with detachable tip in 46 (42.6%) sessions.

Two causes of a failure to achieve complete occlusion were identified. In some cases, it was impossible to place the catheter in a proper working position close enough to nidus. The other cause was an unacceptably long reflux, which occurred before the lesion was completely occluded.

Univariate statistical analysis showed, that risk factors for failure of complete occlusion were presence of multiple feeding arteries, nidus size ≥ 3 cm and Spetzler-Martin grade III–V – see Table 2.

Analysis of multivariate logistic regression revealed, that the only independent predictor of the failure to achieve complete occlusion was the presence of multiple feeding arteries (OR 4.00; 95%CI 1.04–16.64; $p = 0.04$).

3.3. Procedural complications

Complications occurred in 6 out of 108 procedures (5.6% per procedure). One of them was ischemic and 5 hemorrhagic, including 4 intracerebral hematomas and 1 subarachnoid hemorrhage. A detailed description of complications is presented in Table 3.

Among these 6, we noted one ischemic and one hemorrhagic complication related to catheters. In both cases undetachable microcatheters were used. The difference in complication rate between undetachable and detachable catheter group was statistically insignificant ($p > 0.5$; chi-squared test). However this result could be biased by small number of complications.

In the first case ischemic stroke occurred in Spetzler-Martin II plexiform BAVM with stenotic draining veins. In this case undetachable microcatheter was trapped in the single feeder (PCA) and ruptured during forceful retrieval. Motor and neuropsychological rehabilitation resulted in partial regression of symptoms.

The second case was a fatal complication. In this patient, SAH resulted from tearing of feeding pedicle during retrieval of trapped undetachable microcatheter. In the following days,

Table 2 – Results of BAVM embolization.

Characteristics	Total	Complete occlusion	Incomplete occlusion	*p* value
Presentation				
Hemorrhagic	27	12 (44%)	15 (56%)	0.57
Non-hemorrhagic	27	13 (48%)	14 (52%)	
Location				
Hemisphere	27	13 (48%)	14 (52%)	0.21
Basal ganglia incl. thalamus	12	4 (33%)	8 (67%)	
Corpus callosum	3	1 (33%)	2 (67%)	
Cerebellum	12	7 (58%)	5 (42%)	
Nidus size				
<3 cm	28	21 (75%)	7 (25%)	<0.001
≥3 cm	26	4 (15%)	22 (85%)	
Outflow type				
Deep	40	17 (43%)	23 (57%)	0.39
Superficial	14	8 (57%)	6 (43%)	
Number of outflows				
Single	22	10 (45%)	12 (55%)	0.12
Multiple	32	15 (47%)	17 (53%)	
Number of feeding arteries				
Single	28	21 (75%)	7 (25%)	<0.001
Multiple	26	4 (15%)	22 (85%)	
Additional features of BAVM				
No additional features	24	12 (50%)	12 (50%)	0.19
Associated aneurysm	7	3 (43%)	4 (57%)	
Fistula	11	4 (36%)	7 (64%)	
Ectasia of the draining vein	8	4 (50%)	4 (50%)	
Stenosis of the draining vein	4	2 (50%)	2 (50%)	
Spetzler-Martin grade				
I–II	24	19 (79%)	5 (21%)	0.004
III–V	30	6 (20%)	24 (80%)	

SAH induced cerebral edema resistant to treatment and the patient died.

In the remaining 4 cases with intracerebral bleedings venous congestion was observed before the nidus was completely occluded. The complications resulted in permanent deficits in two patients while on the other two the symptoms resolved completely.

This gave procedure-related hemorrhagic complications rate of 9.3%, morbidity of 5.6% and mortality of 1.8%.

3.4. *Complementary treatment*

Complementary treatment was performed in 8 patients with incomplete occlusion of BAVM: 7 of them received radiosurgery and one patient underwent surgery. Additionally, 4 patients refused complementary treatment. As the aim of the study was to assess the efficacy and safety of Onyx embolization, the technique and results of complementary treatment were not analyzed.

4. Discussion

BAVMs constitute a group of complex and rare pathological vascular shunts. Their incidence is estimated at approximately 1 per 100,000 per year and they are usually diagnosed in patients between 30 and 40 years affecting both genders at the same percentage [7–11]. The cumulative risk of BAVM bleeding is 2–4%, increasing to 6% in the first year after the first hemorrhagic episode. A major risk and clinical consequence of BAVM is the possibility of its rupture resulting in intracranial bleeding. Less severe symptoms include headaches, seizures, vertigo, tinnitus and, occasionally, focal neurological deficits (not caused by bleeding but by the malformation itself) [7,12,13]. BAVM may also remain silent for long periods or may never manifest any clinical symptoms [9,14]. It is well known and accepted, that patients presenting with hemorrhage have to be treated. The biggest clinical and decision—making dilemma remains, whether to treat or not to treat the patients with unruptured BAVMs as soon as we are not able to predict the clinical course of malformations and distinguish between patients more susceptible for hemorrhage and those with minor risk of complications. The bleeding risk of untreated BAVM is estimated as 2–3% per year [15–18] with mortality of 10–30% and approximately 20% of permanent significant morbidity [19–22]. The decision making process has become even more difficult after recently published ARUBA trial partial results, which showed that the risk of death or stroke was significantly lower in the medical management group than in the interventional therapy group (hazard ratio 0.27, 95% CI 0.14–0.54) [6]. Considering a short observation time in the study (mean follow-up 33.3 months) and controversies in designing it, there are still neither algorithms nor guidelines for BAVM treatment.

The primary goal of the treatment of brain AVMs is to prevent bleeding and for this purpose, complete occlusion of the AVM has to be obtained. Various techniques are available to treat brain AVMs (surgery, radiosurgery and embolization) and a combination of techniques is often necessary to obtain a complete cure of the AVM. Embolization is often the first step

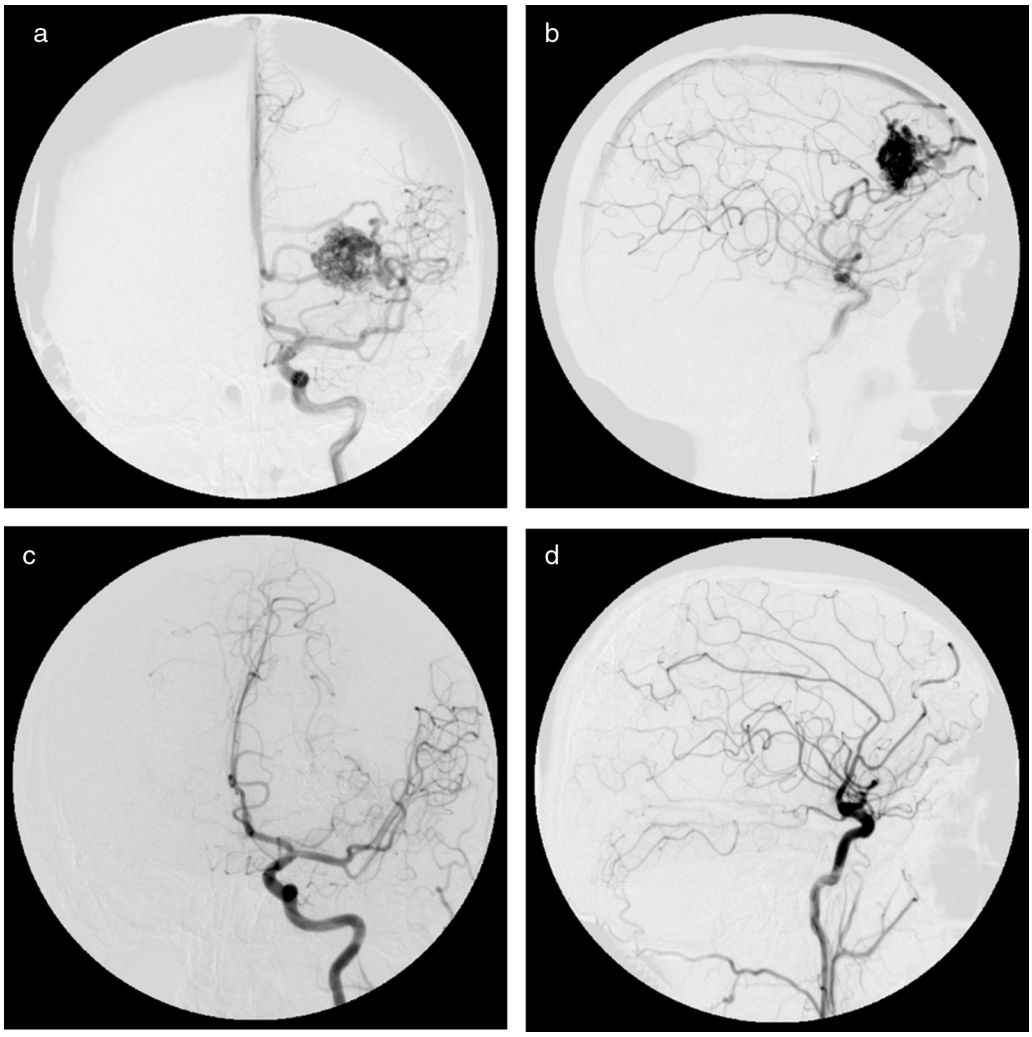

Fig. 1 – The case of 37 y/o woman with unruptured BAVM in the left frontal lobe presenting partial seizures, numbness and altered personality manifesting as severe anger toward her family. Left internal carotid artery injection: a and b – anteroposterior and lateral view of grade II BAVM; c and d – anteroposterior and lateral view after Onyx embolization.

employed to obtain a complete occlusion of the nidus or to reduce the size of the nidus for subsequent treatment (surgery or radiosurgery). For embolization n-BCA or Onyx are used. Using n-BCA, prolonged injections are not possible, and only a limited volume of the nidus can usually be occluded by in a single injection [4]. In contrast to *n*-BCA, Onyx is a nonadhesive liquid. This basic characteristic eliminates the risk of gluing the catheter to the vessel wall and therefore allows a longer injection time and a wider range of different injection rates. Both facilitate occluding larger nidus portions per injection [23].

The purpose of this retrospective study was to describe experience our group has made in using Onyx and to compare our results and complications with those in the literature. Our results show that this treatment is associated with acceptable mortality (1.8%), morbidity (5.6%) and hemorrhagic complications rate (9.3%) with a complete occlusion rate in 46.3% of patients. These results are quite similar to those reported in the previous series of patients with brain AVMs treated with Onyx (Table 4).

Particularly, the mortality rate is similar to that reported in the previous series (0.0–4.3%) [1,5,24–32]. Morbidity is more heterogeneous from one series to another and ranged from 3.5 to 15.5% [1,5,24–32]. However in more recent series, morbidity was between 3.5 and 5.1% [30–32]. Finally, our cohort confirms the results of previous single- and multicentre studies that show a hemorrhagic complications rate between 4.0 and 12.2% [29–32].

There were no deaths among non-bleeding patients and one patient died of procedure—related complications in the bleeding group. Most of the complications were hemorrhagic (83%), which corresponds to the results of other authors [1,24,26–32]. The causes of hemorrhagic complications in our series included rupture of feeding pedicle during retrieval of trapped microcatheter (in 1 patient) or hemodynamic changes in the nidus caused by passage of embolic agent to the venous side of malformation (in 4 patients). Mounayer et al. and Maimon et al. [1,33] reported the same complications in their series. We noted two catheter related complications; associated with retrieval of trapped undetachable catheter in both

Table 3 – Complications of endovascular treatment.

S-M grade	AVM location	AVM characteristics	Catheter used	Complication	Clinical presentation	Treatment	Outcome
II	Cerebellar	Nidus 2.5 cm, plexiform, 1 feeder (right PCA), multiple draining veins superficial and deep with stenosis	Undetachable	Ischemic stroke due to rupture of trapped microcatheter during retrieval	Ataxia, vertigo, partially resolved after rehabilitation	Conservative	Permanent moderate disability
II	Cerebellar	Nidus 2 cm, plexiform, 2 feeders, 1 deep draining vein with stenosis	Detachable	Small ICH in 2nd session probably due to venous stagnation; AVM completely occluded in 3 sessions	Transient diplopia, unilateral deafness	Conservative	Permanent unilateral deafness probably not related to embolization
V	Left fronto-parietal	Nidus 6.5 cm, fistulous, 3 feeders, 7 draining veins (3 deep, 4 superficial)	Undetachable	ICH in 4th session due to venous stagnation; 60% occlusion was achieved	Disturbance of consciousness, psychomotor hyperactivity, right sided hemiparesis	Conservative	Permanent disability (GOS 4)
IV	Left temporo-parietal	Nidus 4 cm, fistulous, 3 feeders, 5 deep draining veins	Undetachable	ICH in 2nd session due to venous stagnation; 70% occlusion was achieved	Right sided hemiparesis	Craniectomy and hematoma evacuation	Transitory disability (GOS 3)
III	Left temporo-parietal	Nidus 2 cm, plexiform, 1 feeder (left MCA), 3 draining veins (1 deep, 2 superficial)	Detachable	ICH with intraventricular bleeding after complete occlusion in 1 session, probably due to venous stagnation	Right sided hemiparesis	EVD	Transitory disability (GOS 3)
III	Cerebellar	Nidus 3 cm, plexiform, 1 feeder (right PICA), 1 deep draining vein	Undetachable	SAH due to tearing of feeding pedicle during retrieval of trapped microcatheter	Refractory cerebral edema	Decompressive craniectomy	Death

Table 4 – Clinical and anatomical results of the endovascular treatment of BAVMs using Onyx.

Study author and year	No.	Hemorrhagic complications	Morbidity	Mortality	Complete occlusion
Perez-Higueras, 2005 [24]	45	8.9%	15.5%	2.0%	22.2%
Song, 2005 [25]	50	6.0%	10.0%	0.0%	20.0%
Van Rooij, 2007 [26]	44	6.8%	4.6%	2.3%	16.0%
Weber, 2007 [5]	93	–	12.0%	0.0%	20.0%
Mounayer, 2007 [1]	94	8.5%	8.5%	3.2%	49.0%
Katsaridis, 2008 [27]	101	5.9%	8.0%	3.0%	53.9%
Pierot, 2009 [28]	50	8.0%	8.0%	2.0%	8.3%
Panagiotopoulos, 2009 [29]	82	12.2%	3.8%	2.4%	24.4%
Xu, 2011 [30]	86	7.0%	3.5%	1.2%	18.6%
Saatci, 2011 [31]	350	4.0%	4.3%	1.1%	50.9%
Pierot (BRAVO study), 2013 [32]	127	8.5%	5.1%	4.3%	23.5%
Present series	54	9.3%	5.6%	1.8%	46.3%

cases. This favors the usage of devices with detachable tip, although these available on the market are little less navigable in comparison to undetachable ones. A major consideration during endovascular treatment remains still a control of hemodynamic changes within the nidus and the venous side of malformation, that was the cause of bleeding in 4 cases in this study.

It is difficult to compare the rate of complete occlusion from one series to another because two different strategies in embolization are used. For some groups, embolization is used and optimized in order to provide the higher possible rate of complete occlusion with embolization alone and to appropriately prepare the incompletely embolized AVMs for further treatment (surgery or radiosurgery). For other groups, embolization is used as a first step treatment to prepare for a second step (surgery or radiosurgery). Results are heterogeneous from one series to another (8.3–53.9%) [1,5,24–32]. In the present study, complete occlusion of BAVM by embolization alone was achieved in 46.3% of cases, which is similar to the results reported in the literature from the centers where endovascular treatment has the intention to cure.

We identified two causes of a failure to achieve complete occlusion. The first one was an inability to catheterize some small and tortuous feeders close enough to the nidus. One of the possible solutions in endovascular treatment of BAVMs with difficult arterial access could be a transvenous approach described by Pereira et al. in 2013 [34]. However, the application of this new technique is limited to small lesions (<3 cm) with a single, not greatly dilated draining vein. Besides, improvements in designing more maneuverable microcatheters are needed as well.

The second cause of the failure in the present cohort was unacceptably long reflux which occurred before the sufficient tidal penetration of Onyx was achieved. This could be avoided by the usage of pressure cooker technique introduced by Chapot et al. in 2014 [35]. This technique creates an anti-reflux plug by trapping the detachable part of an Onyx-compatible microcatheter with coils and glue in order to obtain wedge-flow conditions and controlled Onyx embolization. The other possible solution is double—catheterization technique described by Abud et al. in 2011 [36] which in selected cases of small BAVMs, provides better control on the inflow to the malformation and, thus, on the efferents, making embolization more predictable.

An important role of these two factors is supported by the results of statistical analysis of predictors for the complete occlusion failure. In the present study, the factors predicting the failure included nidus size above 3 cm, S-M grade III-V and multiple feeders. However, the only independent predictor of incomplete occlusion was the presence of multiple feeding arteries. This could be explained by the fact that multiple feeders are usually found in large BAVMs with high S-M grade. The difficulty of the treatment of large, high grade BAVMs with multiple feeders was reported in previous studies [1,33]. In such BAVMs it is more difficult to achieve complete occlusion due to competitive flow from the remaining feeding arteries. Despite developing new techniques, endovascular treatment of BAVMs grade III-V still remains challenging.

5. Conclusions

Endovascular embolization of BAVM using Onyx is an effective method of treatment. The risk of complications is acceptable in cases of ruptured BAVMs, but the technique has to be developed to achieve lower complication rate and decrease morbidity among patients, who are asymptomatic or present symptoms other than hemorrhage.

Conflict of interest

None declared.

Acknowledgement and financial support

None declared.

Ethics

The work described in this article has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans; Uniform Requirements for manuscripts submitted to Biomedical journals.

REFERENCES

[1] Mounayer C, Hammami N, Piotin M, Spelle L, Benndorf G, Kessler I, et al. Nidal embolization of brain arteriovenous malformations using Onyx in 94 patients. AJNR Am J Neuroradiol 2007;28:518–23.

[2] Yamashita K, Taki W, Iwata H, Nakahara I, Nishi S, Sadato A, et al. Characteristics of ethylene vinyl alcohol copolymer (EVAL) mixtures. AJNR Am J Neuroradiol 1994;15:1103–5.

[3] Jalaly J, Dalfino J, Mousa SA. Onyx® in the management of cranial arteriovenous malformations. Expert Rev Med Dev 2013;10:453–9.

[4] Murayama Y, Vinuela F, Ulhoa A, Akiba Y, Duckwiler GR, Gobin YP, et al. Nonadhesive liquid embolic agent for cerebral arteriovenous malformations: preliminary histopathological studies in swine rete mirabile. Neurosurgery 1998;43:1164–75.

[5] Weber W, Kis B, Siekmann R, Jans P, Laumer R, Kuhne D. Preoperative embolization of intracranial arteriovenous malformations with Onyx. Neurosurgery 2007;61:244–52. discussion 52-4.

[6] Starke RM, Komotar RJ, Connolly ES. A randomized trial of unruptured brain arteriovenous malformations. Neurosurgery 2013;73:N13–5.

[7] Al-Shahi R, Warlow C. A systematic review of the frequency and prognosis of arteriovenous malformations of the brain in adults. Brain 2001;124:1900–26.

[8] Jessurun GA, Kamphuis DJ, van der Zande FH, Nossent JC. Cerebral arteriovenous malformations in The Netherlands Antilles. High prevalence of hereditary hemorrhagic telangiectasia-related single and multiple cerebral arteriovenous malformations. Clin Neurol Neurosurg 1993;95:193–8.

[9] Arteriovenous malformations of the brain in adults. N Engl J Med 1999;340:1812–8.

[10] Hofmeister C, Stapf C, Hartmann A, Sciacca RR, Mansmann U, terBrugge K, et al. Demographic, morphological, and clinical characteristics of 1289 patients with brain arteriovenous malformation. Stroke 2000;31:1307–10.

[11] Ogilvy CS, Stieg PE, Awad I, Brown Jr RD, Kondziolka D, Rosenwasser R, et al. AHA Scientific Statement: 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: 1458–71.

[12] Kader A, Goodrich JT, Sonstein WJ, Stein BM, Carmel PW, Michelsen WJ. Recurrent cerebral arteriovenous malformations after negative postoperative angiograms. J Neurosurg 1996;85:14–8.

[13] Mast H, Mohr JP, Osipov A, Pile-Spellman J, Marshall RS, Lazar RM, et al. 'Steal' is an unestablished mechanism for the clinical presentation of cerebral arteriovenous malformations. Stroke 1995;26:1215–20.

[14] Olivecrona H, Riives J. Arteriovenous aneurysms of the brain, their diagnosis and treatment. Arch Neurol Psychiatry 1948;59:567–602.

[15] Brown Jr RD, Wiebers DO, Forbes G, O'Fallon WM, Piepgras DG, Marsh WR, et al. The natural history of unruptured intracranial arteriovenous malformations. J Neurosurg 1988;68:352–7.

[16] Fults D, Kelly Jr DL. Natural history of arteriovenous malformations of the brain: a clinical study. Neurosurgery 1984;15:658–62.

[17] Graf CJ, Perret GE, Torner JC. Bleeding from cerebral arteriovenous malformations as part of their natural history. J Neurosurg 1983;58:331–7.

[18] Wilkins RH. Natural history of intracranial vascular malformations: a review. Neurosurgery 1985;16:421–30.

[19] Forster DM, Steiner L, Hakanson S. Arteriovenous malformations of the brain. A long-term clinical study. J Neurosurg 1972;37:562–70.

[20] Hartmann A, Mast H, Mohr JP, Koennecke HC, Osipov A, Pile-Spellman J, et al. Morbidity of intracranial hemorrhage in patients with cerebral arteriovenous malformation. Stroke 1998;29:931–4.

[21] Mast H, Young WL, Koennecke HC, Sciacca RR, Osipov A, Pile-Spellman J, et al. Risk of spontaneous haemorrhage after diagnosis of cerebral arteriovenous malformation. Lancet 1997;350:1065–8.

[22] Ondra SL, Troupp H, George ED, Schwab K. The natural history of symptomatic arteriovenous malformations of the brain: a 24-year follow-up assessment. J Neurosurg 1990;73:387–91.

[23] Jahan R, Murayama Y, Gobin YP, Duckwiler GR, Vinters HV, Vinuela F. Embolization of arteriovenous malformations with Onyx: clinicopathological experience in 23 patients. Neurosurgery 2001;48:984–95. discussion 95-7.

[24] Perez-Higueras A, Lopez RR, Tapia DQ. Endovascular treatment of cerebral AVM: our experience with Onyx. Interv Neuroradiol 2005;11:141–57.

[25] Song D, Leng B, Gu Y, Zhu W, Xu B, Chen X, et al. Clinical analysis of 50 cases of BAVM embolization with Onyx, a novel liquid embolic agent. Interv Neuroradiol 2005;11: 179–84.

[26] van Rooij WJ, Sluzewski M, Beute GN. Brain AVM embolization with Onyx. AJNR Am J Neuroradiol 2007;28:172–7. discussion 8.

[27] Katsaridis V, Papagiannaki C, Aimar E. Curative embolization of cerebral arteriovenous malformations (AVMs) with Onyx in 101 patients. Neuroradiology 2008;50:589–97.

[28] Pierot L, Januel AC, Herbreteau D, Barreau X, Drouineau J, Berge J, et al. Endovascular treatment of brain arteriovenous malformations using Onyx: results of a prospective, multicenter study. J Neuroradiol 2009;36: 147–52.

[29] Panagiotopoulos V, Gizewski E, Asgari S, Regel J, Forsting M, Wanke I. Embolization of intracranial arteriovenous malformations with ethylene-vinyl alcohol copolymer (Onyx). AJNR Am J Neuroradiol 2009;30:99–106.

[30] Xu F, Ni W, Liao Y, Gu Y, Xu B, Leng B, et al. Onyx embolization for the treatment of brain arteriovenous malformations. Acta Neurochir 2011;153:869–78.

[31] Saatci I, Geyik S, Yavuz K, Cekirge HS. Endovascular treatment of brain arteriovenous malformations with prolonged intranidal Onyx injection technique: long-term results in 350 consecutive patients with completed endovascular treatment course. J Neurosurg 2011;115:78–88.

[32] Pierot L, Cognard C, Herbreteau D, Fransen H, van 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;23:2838–45.

[33] Maimon S, Strauss I, Frolov V, Margalit N, Ram Z. Brain arteriovenous malformation treatment using a combination of Onyx and a new detachable tip microcatheter, SONIC: short-term results. AJNR Am J Neuroradiol 2010;31:947–54.

[34] Pereira VM, Marcos-Gonzalez A, Radovanovic I, Bijlenga P, Narata AP, Moret J, et al. Transvenous embolization of a

ruptured deep cerebral arteriovenous malformation. A technical note. Interv Neuroradiol 2013;19:27–34.
[35] Chapot R, Stracke P, Velasco A, Nordmeyer H, Heddier M, Stauder M, et al. The pressure cooker technique for the treatment of brain AVMs. J Neuroradiol 2014;41:87–91.
[36] Abud DG, Riva R, Nakiri GS, Padovani F, Khawaldeh M, Mounayer C. Treatment of brain arteriovenous malformations by double arterial catheterization with simultaneous injection of Onyx: retrospective series of 17 patients. AJNR Am J Neuroradiol 2011;32:152–8.