Predictors of Total Obliteration in Endovascular Treatment of Cerebral Arteriovenous Malformations

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SUMMARY – *Endovascular therapy is a therapeutic option that can achieve total obliteration of cerebral arteriovenous malformations (AVMs). The objective of this study was to determine the predictive factors of total obliteration in the endovascular treatment of AVMs. A prospective study was carried out in 71 patients with cerebral AVMs having undergone 147 embolization sessions with n-BCA, performed between 2006 and 2011. A univariate analysis was carried out, followed by a logistic regression analysis to determine the predictive factors of total obliteration. Total obliteration was achieved in 18.3% of the patients and angiographic control after 12 months showed the permanency of total occlusion in 100% of the AVMs with initial total obliteration. Angiographic characteristics found favorable for total eradication were: AVM size under 3 cm and the presence of a single arterial pedicle. Predictive factors of total obliteration were an AVM diameter smaller than 3 cm (OR: 50.9; IC: 7.41 - 349, 0; $P = 0.000$), and opposing factors, a 3-6 cm diameter (OR: 11.7; IC: 2.49 - 55, 4; $P = 0.002$) and afferences of more than two vessels of the Willis polygon (OR: 7.0; IC: 1.12-43.9; $P = 0.038$). An AVM diameter smaller than 3 cm is a predictive factor of total obliteration. Total postembolization obliteration persisted in 100% of the cases after 12 months.*

Introduction

Current therapeutic options for the treatment of arteriovenous malformations (AVMs) include vascular microsurgery, radiosurgery and endovascular embolization. Embolization is a well-established treatment option that is usually combined with vascular microsurgery or radiosurgery. The final objective of embolization comprises total obliteration curing the AVM, reduction of its size before microsurgery or radiosurgery, and palliative embolization.

In some case series¹⁻⁵, complete resolution is reported in 5-40% of AVMs treated by the endovascular technique. In micro-AVMs total obliteration rates of 84.6% are reported⁶. In groups with favorable angiographic characteristics rates of complete resolution up to 74% have been reported, as opposed to 40% resolution in the whole series³.

Literature reports evaluating the predictive factors of total obliteration of AVMs by the endovascular method are scarce. Most reports deal with the characteristics considered favorable for total obliteration and the rates of permanent cure^{1,3,6-10} and many articles have evaluated the predictive factors of total obliteration through radiosurgery¹¹⁻¹⁸. Our objective in this study was to determine the predictive factors of total obliteration in the endovascular treatment of cerebral AVMs in our series.

Materials and Methods

A prospective study was carried out in 71 patients with cerebral AVMs having undergone 147 embolization sessions with n-butyl cyanoacrylate (n-BCA) between April 2006 and April 2011, in the endovascular therapy unit

of our Medical Surgical Research Center. With the objective of determining the predictive factors of total occlusion in the endovascular treatment of AVMs, demographic, morphological, clinical and treatment data of the postembolization results were collected. Percentage occlusion figures, per session and total, were documented, as well as the stability of total devascularization, evaluated by means of control angiographies after three months and one year.

Endovascular Techniques

Cerebral panangiography was carried out using transfemoral access in angiographs featuring digital subtraction and roadmapping (Philips Integris and Siemens Artis). A flow-guided Magic 1.2 or 1.5 microcatheter and Balt Sorcerer 0.009 microguide were inserted, placing the microcatheter as close as possible to the nidus or intranidal, and superselective angiography was carried out, followed by a superselective test with Propofol; then, embolization with n-BCA was performed.

AVM sizes (mm) were measured in three dimensions, and the product of these halved, considering the ellipsoidal shape of the AVMs, to calculate their volume^{7,19,20}, using the formula: $V = d1 \times d2 \times d3 \times \frac{1}{2}$ where d1, d2 and d3 are the three dimensions of the malformation in cm, and V is the volume in mm^{3,7,21}.

Statistical Analysis

A univariate analysis was carried out to determine the validity as predictive factors of total obliteration of morphological characteristics such as location, number of afferences, Spetzler and Martin's components and grades, deep afferences and associated aneurysms.

The predictors and all the variables exhibiting a significant relationship in the univariate analysis ($P < 0.05$), or according to expert criteria were included in the multiple logistic regression model to evaluate their independent relationship with total obliteration.

The analyses were carried out using Stata 9.2 software (StatCorp 2007, release 10, College Station, TX, USA).

Results

During the follow-up period, 31.1 ± 17.5 months (mean $\pm$ SD), 71 patients having undergone $147 (2.07 \pm 1.09 (1-6))$ embolization

sessions, with a total of $174 (2.28 \pm 1.17) (1-6)$ arterial pedicles were subjected to embolization. The clinical, demographic, morphological and general treatment characteristics of AVMs in the series are shown in Table 1.

Eleven total devascularizations were performed in a single session, corresponding to grade 2 AVMs (four monopedicular and two bipedicular), grade 3 AVMs (one monopedicular, one bipedicular and one with three arterial pedicles) and grade 1 AVMs (two monopedicular).

A complete and stable cure of the AVMs with n-BCA was achieved in 13 patients (18.3%) with total devascularization, confirmed after three months and one year by means of control angiography.

The rate of total occlusion of AVMs according to morphological parameters decreases with increased AVM size, gradation in the Spetzler and Martin's scale, number of pedicles and the presence of afferences of two or more vessels of the Willis polygon (Table 2).

Favorable angiographic characteristics for total occlusion were sizes under 3 cm and the presence of a single arterial pedicle.

Keeping in mind the diameter and maximum volume of the AVMs, it is worth noting how total devascularization was achieved in AVMs with appreciably smaller mean diameters and volumes. This is clearly assessed if we compare the mean $\pm$ SD values (range) of the group in which total occlusion was achieved with that in which it was not: $21 \pm 12 (7-35)$ mm, and $6 \pm 7 (0.5-21)$ ml for the former and $46 \pm 19 (13-90)$ mm and $26 \pm 41 (1.5-180)$ ml for the latter (Table 3).

In a univariate analysis (Table 4) to evaluate the factors that negatively influence total devascularization of AVMs, significance was found for the presence of afferences of two or more vessels of the Willis polygon, with OR = 5.89 (IC: 1.2-28, 9; $P = 0.029$), and a 3-6 cm size, with OR = 8.5 (IC: 2.24-32, 2; $P = 0.002$). A favoring factor was size under 3 cm, with OR = 0.08 (IC: 0.04-0.13; $P = 0.000$). This coincides with the results of the univariate analysis performed to evaluate factors favoring total devascularization, where only size under 3 cm was statistically significant; with OR = 41.3 (IC: 7.89-215.8; $P = 0.000$).

On the other hand, in the multiple logistic regression analysis to evaluate the factors that negatively influence total devascularization of AVMs (Table 5), a diameter of 3-6 cm and afferences of more than two vessels of the Willis polygon showed the highest ORs: 11.7 (IC:

Table 1 Clinical-demographic, morphologic and treatment characteristics of patients under endovascular treatment.

Mean age $\pm$ SD (range)		30.4 $\pm$ 12.0 (11 - 68)
Age groups (years) n (%)	10 - 20	18 (25.4)
	21 - 30	18 (25.4)
	31 - 40	20 (28.2)
	41 - 50	13 (18.2)
	51 - 70	2 (2.8)
Sex, n (%)	Male	41 (57.7)
	Female	30 (42.3)
Racial morphotype, n (%)	White	45 (63.4)
	Black	8 (11.3)
	Mixed race	18 (25.4)
Initial presentation, n (%)	Intracranial hemorrhage	52 (73.2)
	Epileptic seizures	8 (11.3)
	Headache	51 (71.8)
	Convulsions	13 (18.3)
	Focal neurologic deficit	20 (28.2)
	Other / Asymptomatic	4 (5.6)
Associated pathologies	Epilepsy	13 (18.3)
	HBP	15 (21.1)
	Bronchial asthma	2 (2.8)
Maximum diameter of AVM (mean $\pm$ SD (range)), mm		41 $\pm$ 18 (7 - 90)
Maximum volume of AVM (mean $\pm$ SD (range)), ml		22 $\pm$ 38 (0.5 - 180)
Deep arterial afferences, n (%)		8 (11.3)
Choroidal afferences, n (%)		1 (1.4)
Afferences of more than two vessels of the Willis polygon, n (%)		32 (45.1)
Associated aneurysms, n (%)		9 (12.7)
Spetzler & Martin's components, n (%)	Small AVM (< 3 cm)	12 (16.9)
	Average AVM (3 - 6 cm)	50 (70.4)
	Large AVM (> 6 cm)	9 (12.7)
	Deep venous drainage	25 (35.2)
	Location in eloquent area	48 (67.6)
Spetzler & Martin's grades, n (%)	Grade 1	2 (2.8)
	Grade 2	13 (18.3)
	Grade 3	42 (59.2)
	Grade 4	12 (16.9)
	Grade 5	2 (2.8)
Embolization sessions, n (mean $\pm$ SD (range))		147: 2.07 $\pm$ 1.09(1 - 6)
Final devascularization percentage, mean $\pm$ SD (range)		69.2 $\pm$ 26.7(10-100)
Embolized pedicles, n: mean $\pm$ SD (range)		174: 2.28 $\pm$ 1.17 (1 - 6)
Follow-up time, months, mean $\pm$ SD),		31.1 $\pm$ 17.5
Vascular microsurgery after embolization, n (%)		12 (16.9)
Radiosurgery after embolization, n (%)		11 (15.5)

Table 2 Total AVM obliteration rate with respect to morphologic parameters.

<i>Parameters</i>	<i>Total number (%)</i>	<i>Number occluded</i>	<i>Percentage occluded</i>
Limit size in mm			
< 3 cm	12 (16.9)	9	75
3 - 6 cm	50 (69.0)	4	8.2
> 6 cm	10 (14.1)	—	—
Deep venous drainage			
Yes	25 (35.2)	3	12
No	46 (64.8)	10	21.7
Eloquent area			
Yes	48 (67.6)	10	20.8
No	23 (32.4)	3	13.04
Spetzler & Martin's Classification			
Grade 1	2 (2.8)	2	100
Grade 2	13 (18.3)	6	46.2
Grade 3	42 (59.2)	5	11.9
Afferences of more than two vessels of the Willis Polygon			
Yes	32 (45.1)	2	6.3
No	39 (54.9)	11	28.2
AVM Location			
Supratentorial	63 (88.7)	11	17.5
Infratentorial	8 (11.3)	2	25
Number of afferences			
1 pedicle	7 (9.)	7	100
2 pedicles	12 (16.9)	4	33.3
3 pedicles	22 (30.9)	2	9.1

Table 3 Relationship between AVM diameter / volume and percentage devascularization.

<i>Parameters</i>	<i>Total of AVMs</i>	<i>Devascularization < 100 %</i>	<i>100 % Devascularization</i>
<i>Number</i>	71	58	13
<i>Diameter</i> mean $\pm$ SD (range) mm	41 $\pm$ 18 (7 - 90)	46 $\pm$ 19(13 - 90)	21 $\pm$ 12 (7 - 35)
<i>Volume</i> mean $\pm$ SD (range)ml	22 $\pm$ 38 (0.5 - 180)	26 $\pm$ 41(1.5 - 180)	6 $\pm$ 7 (0.5 - 21)

2.49-55.4; $P = 0.002$) and 7.0 (IC: 1.12-43.9; $P = 0.038$) respectively. In contrast, in the multiple logistic regression analysis to determine factors that positively influence devascularization, a diameter smaller than 3 cm showed an OR = 50.9 (IC: 7.41-349.0; $P = 0.000$). This means that a diameter under than 3 cm causes a 50-fold increase in the possibility of total occlusion of an AVM.

Discussion

Approximately five to ten per cent of all AVMs embolized can be cured by embolization alone. These are typically small AVMs, with relatively few arterial pedicles and drainage veins²²⁻²⁷. The rate of total occlusion in our series is in the reported range. According to the literature, the endovascular treatment

Table 4 Factors with a negative influence on total AVM devascularization. Univariate analysis.

Characteristics	No (%)	OR	IC: 95 %	P
Supratentorial location (n = 71)	63 (88.7)	1.58	0.28 - 8.87	0.606
Deep afferences (n = 71)	8 (11.3)	1.65	0.86 - 14.68	0.655
Afferences of more than two vessels of Willis polygon (n = 71)	32 (45.1)	5.89	1.2 - 28.9	0.029
Associated aneurisms (n = 71)	9 (12.7)	1.92	0.22 - 16.9	0.556
<i>Spetzler & Martin's components, n (%)</i>				
Small AVM (< 3 cm)	12 (16.9)	0.08	0.04 - 0.13	0.000
Average sized AVM (3 - 6 cm)	50 (70.4)	8.5	2.24 - 32.2	0.002
Large AVM (> 6 cm)	9 (12.7)	—	—	—
Deep venous drainage	25 (35.2)	0.49	0.12 - 1.98	0.317
Location in eloquent area	48 (67.6)	1.75	0.43 - 7.1	0.431
<i>Spetzler & Martin's grades, n (%)</i>				
Grade 1	2 (2.8)	—	—	—
Grade 2	13 (18.3)	0.14	0.04 - 0.48	0.002
Grade 3	42 (59.2)	2.08	0.68 - 6.33	0.199
Grade 4	12 (16.9)	—	—	—
Grade 5	2 (2.8)	—	—	—

Note: In univariate analysis to determine factors with a positive influence on total AVM devascularization, diameter < 3 cm showed OR = 41.3 (IC: 7.89 – 215.8; P = 0.000).

Table 5 Factors with a negative influence on total AVM devascularization. Multiple logistic regression.

Parameters	OR	IC: 95 %	P
3 - 6 cm diameter	11.7	2.49 - 55.4	0.002
Deep venous drainage	2.4	0.43 - 13.0	0.320
Supratentorial location	1.4	0.16 - 12.01	0.76
Afferences of more than 2 vessels of the Willis polygon	7.0	1.12 - 43.9	0.038
Associated aneurysms	2.58	0.22 - 30.5	0.45

Note: In the multiple logistic regression analysis to determine factors with a positive influence on total AVM devascularization, diameter < 3 cm showed OR 50.9 (IC: 7.41 – 349.0; P = 0.000).

of AVMs as sole treatment (without surgery) achieves complete occlusion in five to 40% of cases¹⁻⁵. An extensive retrospective review of embolization results in 32 series covering a 35-year period⁵ divides the data in two series, before and after 1990, indicating that total cure by embolization was 4% before 1990 and 5% afterwards.

Recent advances in embolizing substances (Onyx is one example) and improvements in other aspects of the endovascular treatment will contribute to achieve better results from embolization. Maimon et al. (2010) reported a total occlusion rate of 55% using Onyx and a Sonic Microcatheter²⁸.

Healing rates by means of embolization reported in the literature vary considerably due

to the selection criteria and also differ in therapeutic and technical objectives. Small AVMs with few afferences have the highest probability of being cured by the endovascular technique. Valavanis and Yasargil reported a total healing rate by embolization of 74% in subgroups of patients with favorable angiographic characteristics, characterized by the presence of one or few afferent pedicles, absence of perinidal angiogenesis and fistulous nidus, in contrast with 40% healing by embolization for the whole series of 387 patients³.

In recent reviews, the primary curing rate by embolization only varied in the 9-84.6% range, especially in AVMs under 1 cm⁸. Gobin et al.² reported the results of treatment of 125 patients via embolization and radiosurgery,

showing curing rates of 76-78% for AVMs smaller than 4 cm, 59% for those measuring 4-6 cm, and 7% for those larger than 6 cm. Wikholm et al.⁷ reported an 11.2% total occlusion in their series. The totally occluded AVMs differed in size and volume from the whole group: they were smaller, which is comparable with our findings. On the other hand, in AVMs up to 3 cm in diameter 42.3% total occlusion was achieved, and in those larger than 3 cm occlusion was only 3.7%. This observation coincides with our results, in which an increased size decreases the possibility of total occlusion. Viñuela et al.⁹, in their series of 405 patients,

reported a total occlusion rate of 9.9% in small and average sized AVMs with fewer than four arterial pedicles.

Conclusions

Favorable angiographic characteristics for total occlusion in our series were size under 3 cm and the presence of only one dominant arterial pedicle, or a maximum of three. Diameter under 3 cm is a predictor factor of total obliteration. Total postembolization obliteration persisted in 100% of the cases for 12 months.

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