Predictors of Hemorrhagic Complications from Endovascular Treatment of Cerebral Arteriovenous Malformations

JOSÉ A JORDAN¹, JUAN CARLOS LLIBRE², FRANK VÁZQUEZ¹, RAÚL RODRÍGUEZ³, JOSÉ A. PRINCE⁴, JOSÉ CARLOS UGARTE²

¹ Department of Radiology, Centro de Investigaciones Médico Quirúrgicas (CIMEQ), Medical University of Havana; Havana, Cuba

² Department of Neurology, Stroke Unit, Instituto de Neurología y Neurocirugía (INN), Medical University of Havana; Havana, Cuba

³ Department of Anesthesia, Centro de Investigaciones Médico Quirúrgicas (CIMEQ), Medical University of Havana; Havana, Cuba

⁴ Department of Neurosurgery, Centro Internacional de Restauración Neurológica (CIREN), Medical University of Havana; Havana, Cuba

Key words: arteriovenous malformations, predictive factors, hemorrhage, embolization, n-butyl cyanoacrylate, post-embolization hypotension

Summary

Post-embolization hemorrhage is the most severe, dramatic and morbidity-mortality-related complication in the treatment of endovascular arteriovenous malformations (AVMs). The objective of this study was to determine predictive factors of post-embolization hemorrhage.

This is a retrospective study in 71 patients with cerebral AVMs having undergone 147 embolization sessions with n-butyl cyanoacrylate (n-BCA), carried out between 2006 and 2011. Clinical-demographic, morphological and treatment data as well as results were recorded. The relationship of post-procedure hemorrhage with demographic and morphological factors, percentage devascularization per session, venous drainage and whether or not post-procedure hypotension had been induced was investigated.

Six post-embolization hemorrhages occurred, all in sessions characterized by extensive devascularization without the induction of post-procedure hypotension; which disappeared after a limit to the extent of devascularization per session and post-procedure hypotension were introduced. In the multivariate analysis, hemorrhage predictors were: nidus diameter < 3 cm (OR=45.02; CI=95%:1.17-203.79; P=0.005); devascularization > 40% (OR=32.4; CI=95%: 3.142-518.6; P=0.009) per session; intranidal aneurysms

(OR=7.5; CI=95%:1.19-341.3; P=0.041) and lack of post-procedure hypotension (OR=16.51; CI=95%:1.81-324.4; P=0.049) and the association of sessions with devascularization exceeding 40% with lack of post-procedure hypotension, showed an increase in the risk of hemorrhage (OR=36.4; CI=95%:3.67-362.4; P=0.002).

Extensive devascularization and the absence of post-procedure hypotension increase the risk of hemorrhage. We suggest partial, 25-30%, devascularization per session and the induction of post-procedure hypotension, which produces a 20% decrease of the basal mean arterial pressure (MAP).

Introduction

Arteriovenous malformations (AVMs) are a very heterogeneous group of lesions, extremely variable in size, location, angio-architecture, and clinical presentation. The current therapeutic options include microvascular neurosurgery, radio neurosurgery, and endovascular embolization, the latter usually considered the first treatment option. The incidence of reported complications from endovascular treatment varies between 3% and 25%¹⁻¹². The rates of permanent morbidity and mortality vary in the 3.8-14% and 1.0-3.7% ranges, respectively¹³.

The most severe complication, causing significant morbidity-mortality and post-procedure incapacity is post-embolization hemorrhage. However, modest attention has been paid in the literature to the predictive factors of this complication, whereas many studies have addressed the predictors of neurological deficit. The rates of hemorrhagic complications associated with embolization involve 1.6-15% of patients, and 0.6-5.6% of procedures^{3,9,12,14-25}, while complications reported in large series are only 1.6-3.1% for patients^{12,21,23}. Among the mechanisms described as causing these complications are hemodynamic changes, the occlusion of drainage veins and specific morphological characteristics. However, there is little clarity on the influence of these factors on the risk of hemorrhagic complications and also the ways of counteracting their effects.

The objective of this study was to determine predictive factors of hemorrhagic complications from endovascular treatment of cerebral AVMs, after noticing that the hemorrhagic complications in our series occurred in sessions characterized by extensive devascularization without hemodynamic control, and disappeared when devascularization was reduced to 25-30% per session and post-procedure hypotension was kept 20% below the basal mean arterial pressure (MAP). The identification of predictors of hemorrhagic complications should allow the implementation of strategies to decrease its incidence and thus improve the results of endovascular treatment.

Materials and Methods

A retrospective 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 the Medical-Surgical Research Center, CIMEQ. Clinical-demographic, morphological and treatment data as well as post-embolization results were recorded. Patients with post-procedure hemorrhage and those whose interventions showed no complications were compared, keeping in mind AVM morphology and the morphological changes induced by embolization. This scrutiny was focused on the percentage devascularization per session, venous drainage, demographic factors, and post-intervention monitoring, particularly blood pressure (BP)

control, with the objective of determining predictive factors of hemorrhagic complications from endovascular treatment of arteriovenous malformations.

Endovascular Techniques

Cerebral pan-angiography was carried out by means of transfemoral access and local anesthesia, in angiographs with digital subtraction and road-mapping (Philips Integris and Siemens Artist). Systemic heparinization was established achieving an activated coagulation time (ACT) two to three times the basal value. The catheters used were kept connected to bags pressurized with heparinized saline solution. A 6 Fr guiding catheter was located at the internal carotid or the afferent vertebral to the AVM. Then we proceeded to navigate the AVM afferent vessels with a Magic 1.5 microcatheter and a 0,009" microguide wire to catheterize the malformation pedicle and place the microcatheter in a wedge position at the entrance or within the nest. Subsequently, superselective angiography was performed using the microcatheter to verify its position in relation to the nest, followed by a superselective test with Propofol. If no changes were found in the neurological test, embolization with n-BCA (Braun Histoacryl) was carried out.

In a first period, extensive devascularization (>40-60% per session) was carried out, embolizing multiple arterial pedicles, without post-procedure hemodynamic control. Following the appearance of hemorrhagic complications, it was decided to limit devascularization to 25-30% per session, establishing strict post-embolization hemodynamic control to achieve a 20% reduction of MAP with respect to basal values, keeping it typically in the 65-75 mm Hg range for 24 hours.

Statistical Analysis

A univariate analysis was carried out to describe the effect of demographic factors, presentation symptoms, pre-embolization neurological condition, morphological parameters, number of embolization sessions, percentage devascularization per session, number of pedicles embolized and hemodynamic control on the risk of post-embolization hemorrhage.

The predictive factors and all the variables

showing a significant relationship in the univariate analysis ($P < 0.05$) or according to experts' criteria were included in the multiple logistic regression model to evaluate their independent association with post-embolization hemorrhage, keeping track of sex and age. Spetzler & Martin's general score and its components were included in the analysis. These studies were carried out using Stata 9.2 statistical software (StataCorp, College Station, TX, 10th release, 2007).

Results

During the follow-up period, 31.1 ± 17.5 months (mean $\pm$ SD), 71 patients who had 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 embolized. The clinical, demographic, morphological and general characteristics of the treatment of AVMs in the studied series are shown in Table 1.

In the series, six patients showed post-embolization hemorrhage (8.5% of the patients and 4.1% of the procedures). One of the most important factors to consider was the impact of extensive devascularization in a single embolization session. The six post-embolization hemorrhages occurred in sessions with devascularization above 40%, while in only 20% of the sessions without post-embolization hemorrhage was devascularization of such a magnitude carried out.

Other factors to be considered hemorrhage predictors are: the lack of post-procedure hypotension, which occurred in five of the six patients presenting this complication; the influence of the AVM nidus size, since hemorrhagic complications arose in 16.7% of the AVMs less than 3 cm in diameter, in 6% of the 3-6 cm AVMs and in 10% of those exceeding 6 cm; the presence of associated aneurysms; the occlusion of drainage veins; Spetzler & Martin's grading and its components and other morphologic characteristics. Special attention was paid in this study to the effect of the combination of extensive devascularization and the absence of post-procedure hypotension as a risk factor for the occurrence of hemorrhagic complications.

In the univariate analysis (Table 2), the risk of post-embolization hemorrhage was associated with: intranidal aneurysms (OR=6.55; CI=1.07-40.23; $P=0.04$); supratentorial location (OR=1.43; CI=1.2-2.07; $P=0.056$); AVM size

under 3 cm (OR=1.81; CI=0.20-16.7; $P=0.598$); deep venous drainage (OR=3.22; CI=0.57-18.2; $P=0.185$); the absence of post-procedure hypotension (OR=4.41; CI=0.78-24.98; $P=0.094$); the occlusion of drainage veins (OR=70; CI=5.21-940.6; $P=0.001$) and devascularization larger than 40% of the AVM per session (OR=18.5; CI=2.08-32.4; $P=0.007$).

The multiple logistic regression analysis, when evaluating the risk of post-procedure hemorrhage in connection with statistically significant morphologic and treatment parameters in the univariate analysis, or with those included according to experts' criteria, showed that the following are predictive factors of post-procedure hemorrhage: AVM devascularization in excess of 40% per session, with OR=32.4 (CI=3.142-518.6; $P=0.009$). This means that the risk of hemorrhage is 32 times greater when devascularization exceeds 40% per session; AVM nidus diameter under 3 cm, with OR=45.02 (CI=1.17-203.79; $P=0.005$); deep venous drainage (OR=20.34; CI=1.05-392.5; $P=0.046$); the absence of post-procedure hypotension, with OR=16.51 (CI=1.81-324.4; $P=0.049$) and the presence of intranidal aneurysms, with OR=7.5 (CI=1.19-341.3; $P=0.041$) (Table 3).

Other factors, such as location and morphology of the AVMs, more than two afferent vessels of the Willis polygon, or high flow arteriopathies or venous angiopathies were not found to be hemorrhage predictors. The occlusion of drainage veins in two cases with post-procedure hemorrhage and in only one case without this complication, although showing OR=41.6, did not show a statistically significant relationship. None of the components of Spetzler & Martin's grading, or its general score, showed a statistically significant association with post-procedure hemorrhage in the multiple logistic regression analysis restricted to these components and their grading.

It is interesting to note that all the hemorrhagic complications in our series (six hemorrhages in 42 sessions) took place in an initial period when devascularization in the 40-60% range per session was practised, lacking the induction of post-procedure hypotension. In contrast, the implementation (subsequent to the hemorrhagic complications described) of changes in our methodology characterized by embolizations with restricted devascularization (25-30%) and induced post-procedure hypotension for 24 hours, with a 20% reduction of the basal MAP (to 65-75 mm Hg) resulted in the

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

Mean age±SD (range)		30.4±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 crisis	8 (11.3)
	Cephalalgia	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 ± SD (range), mm)		41 ± 18 (7 - 90)
Maximum volume of AVM (mean ± SD (range), ml)		22 ± 38 (0.5 - 180)
Deep arterial afferences, n (%)		8 (11.3)
Coroideal afferences, n (%)		1 (1.4)
Afferences of more than two vessels of the Willis polygon, n (%)		32 (45.1)
Associated aneurisms, 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 ± SD (range))		147: 2.07 ± 1.09 (1-6)
Final devascularization percentage, mean ± SD (range)		69.2 ± 26.7 (10-100)
Embolized pedicles, n: mean ± SD (range)		174: 2-28 ± 1-17 (1-6)
Follow-up time, months, mean ± SD)		31-1 ± 17-5
Vascular microsurgery after embolization, n (%)		12 (16-9)
Radiosurgery after embolization, n (%)		11 (15-5)

Table 2 Demographic and morphologic factors predicting post-procedure hemorrhage.

Characteristics	No. (%)	OR	CI: 95 %	P
Age (mean±SD)	30.4±12	1.01	0.59–4.23	0.934
Female (n=71)	30 (42.3)	1.01	0.35–2.92	0.982
Male (n=71)	41 (57.7)	0.88	0.26–2.94	0.832
Racial morphotype, black/ mixed race (n=71)	26 (36.7)	2.13	0.41–10.99	0.365
More than 3 embolization sessions (n=71)	24 (33.8)	1.28	0.14–11.6	0.824
Absence of pre-procedure neurologic deficit (n=71)	63 (45.6)	1.65	0.19–14.6	0.652
Initial presentation (n=71)				
Hemorrhage	41 (57.7)	0.63	0.12–3.22	0.577
Epileptic seizure	8 (11.3)	1.46	0.16–13.2	0.737
Convulsions	13 (18.3)	3.86	0.74–20.14	0.109
Cephalalgia	51 (71.8)	0.48	0.94–2.49	0.582
Focal neurologic deficit (n=71)	20 (28.2)	0.54	0.61–4.79	0.582
Supratentorial Location (n=71)	63 (88.7)	1.43	1.2–2.07	0.056
Deep afferences (n=71)	8 (11.3)	–	–	–
Associated aneurysms (n=71)				
Any of the abovementioned	9 (12.7)	3.91	0.66–23.1	0.133
Flow-related	–	–	–	–
Intranidal	5 (7.0)	6.55	1.07–40.23	0.042
Spetzler & Martin's components (n=71)				
Small AVM (<3cm)	12 (16.9)	1.81	0.20–16.7	0.598
Average AVM (3–6cm)	50 (70.4)	0.76	0.13–4.34	0.762
Large AVM (>6cm)	9 (12.7)	0.84	0.09–7.53	0.880
Deep venous drainage	25 (35.2)	3.22	0.57–18.2	0.185
Location in eloquent area	48 (67.6)	0.21	0.04–1.16	0.074
Spetzler & Martin's grades (n=71)				
Grade 1	2 (2.8)	–	–	–
Grade 2	13 (18.3)	1.37	0.15–12.37	0.781
Grade 3	42 (59.2)	1.4	0.25–7.88	0.705
Grade 4	12 (16.9)	0.74	0.83–6.58	0.787
Grade 5	2 (2.8)	–	–	–
Absence of post-procedure hypotension (n=147)	48 (32.7)	4.41	0.78–24.98	0.094
Post-procedure hypotension (n=147)	99 (67.3)	0.23	0.04–1.28	0.094
Neurologic deficit preembolization (n=71)	18 (25.4)	0.61	0.07–5.36	0.652
Occlusion of drainage veins (n=71)	3 (2.8)	70	5.21–940.6	0.001
Devascularization in 40 - 100 % range (n=147)	35 (23.7)	18.5	2.08–32.4	0.007
More than one pedicle per session (n=147)	19 (13)	1.37	0.15–12.4	0.781
Afference of more than two major vessels of the Willis polygon (n=71)	32 (45.1)	5.85	0.67–51.3	0.111

Table 3 Association between demographic and morphologic parameters and post-procedure hemorrhage; multiple logistic regression analysis.

Parameters	OR	CI: 95 %	P
Absence of pre-procedure neurologic deficit	2.05	0.08–53.19	0.666
Nidus diameter < 3 cm	45.02	1.17–203.79	0.005
Deep venous drainage	20.34	1.05–392.5	0.046
Absence of post-procedure hypotension	16.5	1.81–324.4	0.049
Intranidal aneurisms	7.5	1.19–341.3	0.041
Devascularization > 40% per session	32.4	3.142–518.6	0.009
Occlusion of drainage veins	41.6	0.37–464.4	0.121

Table 4 Univariate analysis showing the risk of post-procedure hemorrhage with and without the induction of post-procedure hypotension and percentage devascularization.

Groups	OR	CI: 95 %	P
Desvasc >40 % without hypotension	29.3	4.72–182.3	0.000
Desvasc >40 % with hypotension	1.14	0.13–10.3	0.905
Desvasc <40 % without hypotension	–	–	–
Desvasc <40 % with hypotension	0.17	0.019–0.97	0.002

Note: In the multiple logistic regression model devascularization in excess of 40 % lacking the application of hypotension showed OR=36.4 (CI=95 % 3.67-362.4;P=0.002)

total elimination of hemorrhagic complications (no hemorrhage in 103 sessions).

The incidence rate ratio (IRR), of post-embolization hemorrhage, determined by means of Poisson's regression, was 14.8 (CI 95%: 1.7-126.7) for patients subjected to devascularization above 40%, whereas for those who underwent devascularization below 40% the IRR was 0.07 (CI 95%: 0.008-0.581). The IRR of post-procedure hemorrhage was 3.5 (CI 95%: 0.65-19.4) in the absence of post-procedure hypotension, while it was 0.28 (CI 95%: 0.051-1.54) for the group that benefited from induced post-procedure hypotension.

The group of patients under study was divided into four subgroups by combining devascularization above or below 40% with the application of post-procedure hypotension or lack of it. Univariate analysis showed OR=29.3 (CI=4.72-182.3; P=0.000) for the subgroup in which devascularization above 40% per session was carried out without post-procedure hypotension (roughly a 30-fold increase in the risk of post-embolization hemorrhage). In contrast, the combination of devascularization under 40% per session with post-procedure hypotension behaved as a protective factor against the occurrence of post-embolization hemorrhage, with OR=0.17

(CI=0.019-0.97; P=0.002) (Table 4). Applying the multiple logistic regression model to evaluate the risk of post-procedure hemorrhage to those four subgroups, only devascularization above 40% lacking post-procedure hypotension showed a statistically significant difference, with OR=36.4 (CI=3.67-362.4;P=0.002). This supports the hypothesis that extensive devascularization and the lack of strict BP control produce hemorrhagic complications.

Discussion

The analysis of our series to determine predictive factors of post-embolization hemorrhage is based on the observation of the large incidence of this complication initially, when extensive devascularization (in excess of 40% per session) was carried out without strict post-embolization monitoring and hemodynamic control. The latter is confirmed by the fact that out of six post-embolization hemorrhages that occurred in sessions with devascularization over 40%, five lacked the application of post-procedure hypotension.

This motivated a revision of our methodology, and the setting-up of a less aggressive treatment,

with devascularization limited to 25-30% per session and the establishment of strict post-procedure monitoring, along with a 20% reduction of the basal MAP, to 65-75 mm Hg. Implementation of these measures put an end to post-embolization hemorrhagic complications. These results supported our initial claim, presented in a previous paper, that extensive devascularization and deficient hemodynamic control increase the risk of post-embolization hemorrhage. These results can be related to one of the important physiological causes of post-embolization hemorrhage described, the phenomenon of "normal perfusion pressure breakthrough" described by Spetzler et al.^{24,25}. However, Spetzler et al. found that this phenomenon was associated with extensive high flow AVMs, angiographically poor filling of the normal cerebral arteries, extensive collateral flow, the stealing phenomenon, afferences through the external carotid and progressive or fluctuating neurological deficit²⁴.

An impending task involves explaining how the hemorrhagic complications arose in 16.7% of the AVMs smaller than 3 cm in diameter; in 6% of the 3-6 cm AVMs and in 10% of the AVMs larger than 6 cm. That is, post-embolization hemorrhage prevailed in AVMs less than 3 cm in diameter.

A simple explanation would be a random presentation of the complications, which is contradicted by the results of the multiple logistic regression analysis, with OR=45.02 (CI=1.17-203.79; P=0.005) for AVMs smaller than 3 cm.

Another explanation is the fact, illustrated in the literature, that extensive embolization can produce a marked flow reduction through the fistulous nidus, causing stagnation in the drainage veins resulting in their thrombosis, nidus congestion and retarded hemorrhage or venous infarction^{5,13,21,16,26,27}. But this would not explain how post-procedure hypotension prevented the post-embolization hemorrhage in our series. It would rather contribute to flow reduction through the nidus, followed by augmented stasis of the drainage veins, venous thrombosis and an increased risk of hemorrhage.

Our working group's assumption is that extensive devascularization abruptly decreases the AVM shunt, with subsequent flow redistribution in the remaining afferent arteries feeding the AVM nidus, which are morphologically abnormal and adapted to cope with chronically low arterial pressures. Thus, they undergo a sudden BP rise that causes rupture of the remaining nidus vessels, so that "rupture at normal arterial

pressure" of the afferent arteries and/or the nidus remains occurs. This would explain how partial devascularization combined with post-procedure hypotension reduce the arterial pressure increase sustained by the afferent arteries and the remains of the nidus, preventing the post-embolization hemorrhage caused by the rupture of afferent arteries that feed the AVM nidus.

This is in agreement with a report by Picard et al.²¹ describing an increase in the hemorrhage rate after extensive devascularization. They explained that occurrence on the basis of the above-mentioned and frequently cited pressure increase in the afferent arteries after intranidal embolization with liquid embolizing agents, that carries the risk of arterial or intranidal vascular rupture^{15,22,28-31}.

The increased risk of hemorrhage in AVMs smaller than 3 cm in diameter is in full agreement with a report by Heidenreich et al.²². Logically, the relative obliteration rate in a session is markedly larger for small AVMs. The same is true for the flow reduction attainable in a session, even without extensive embolization, which increases the risk of reactive pressure rise, as previously described²².

The different hypotheses dealt with in the literature as causes of post-embolization hemorrhage, listed by Picard et al.²¹, help explain the hemorrhages in our series and correlate well with the predictors of hemorrhage found in our statistical analysis: improper venous occlusion of a partially embolized AVM; pressure increase in afferent arteries as a consequence of embolization; rupture phenomenon at normal perfusion pressure, with hyperemia of the normal brain or distribution of blood flow in adjacent areas of the brain; secondary venous thrombosis secondary to the stasis caused by substantial obliteration of the AVM and inflammatory reaction or wall necrosis induced by the emboligenous agent; and intranidal rupture of an aneurysm.

In connection with the proportion of devascularization per session, Weigele et al.⁵ reported a maximum occlusion of 33% of the AVM nidus during a session, with the purpose of minimizing the risk of hemorrhage provoked by rupture at the normal perfusion pressure²⁴. Other authors claim they did not perform occlusions exceeding 30-40%¹². Heidenreich et al.²² reported that extensive devascularization, above 60% per session, increases the risk of post-procedure hemorrhage, constituting a risk factor for hemorrhage (OR=18.8; IC:95%).

Heros³² recommends gradual embolization,

since extensive devascularization is a risk factor for hemorrhage, while Taylor³³ claims to have reduced the percentage embolization in each session to decrease the risk of hemorrhage.

Massoud et al.³⁴, using a theoretical model, concluded that the induction of systemic hypotension during and after embolization of AVMs seemed to have a potential benefit theoretically in preventing hemorrhage from the AVM nidus³⁴. To minimize the possibility of rupture at the normal perfusion pressure and reduce the risk of post-embolization hemorrhage, Debrun et al.²⁰ suggest maintaining MAP 10-15% below the basal value 24 hours after embolization. For their part, Picard et al.²¹ recommend keeping the MAP 10-20% under the basal value for 72 h.

Weigle et al.⁵ suggest monitoring the patients in a neuro-intensive care unit for 24 hours post-procedure, maintaining slight hypotension, 90% of the normal MAP. Jayaraman et al.¹² report only 1.6% of hemorrhagic complications with the implementation of a similar protocol, specifying that the parameters were adjusted taking into consideration the basal perfusion pressure of each patient, the extent of embolization, angiographic characteristics such as arterial or venous slow flow and maintaining an intensive blood pressure monitoring for 24-48 hours, with MAP of 65-75 mm Hg, which in their opinion minimizes the abrupt elevation of the post-embolization systolic arterial pressure and may reduce the risk of post-embolization hemorrhage¹².

Heidenreich et al.²² reported better results in patients treated in postoperative intensive care units than in those looked after in intensive medical care units or in stroke units, which they consider is due to better control of post-procedure arterial pressure.

It is seemingly a proven fact that the risk of post-embolization bleeding increases with extensive devascularization and faulty hemodynamic control. In this series other aforementioned pre-

dictors of hemorrhagic complications did not prove significant in the multivariate analysis, except for the presence of intranidal aneurysms whose rupture is one of the mechanisms of hemorrhage described^{21,35}, possibly due to the hemodynamic stress produced by the blood pressure increase on an angio-architecturally weak spot and the presence of deep venous drainage. The increased risk of hemorrhage by accidental venous occlusion observed in the univariate analysis did not show a significant association in the multiple logistic regression analysis. The embolizing agent's entry into the drainage veins, with consequent venous obstruction or thrombosis, is a risk factor for post-embolization bleeding^{3,15,20,35}. However, in practice embolization of the drainage veins is not always accompanied by complications. This can be significant or not, depending on the size and dynamic importance of the embolized vein, of flow changes through the nidus and whether or not venous drainage from the AVM through other veins is adequate^{21,22}.

Conclusions

In this series, the predictive factors of post-embolization hemorrhage were devascularization exceeding 40%, the absence of post-procedure hypotension, AVM diameter under 3 cm, deep venous drainage, and intranidal aneurysms. A considerable reduction of AVM size increases the risk of hemorrhage, while the induction of strict hypotension post-procedure decreases it. Therefore, we suggest distributing the intervention in partial, 25-30%, devascularization per session and the application of strict hypotension post-procedure, with a 20% decrease of the basal MAP. However, given the size of this series and the magnitude of the intervals of confidence, our results and recommendations should be considered with caution.

References

- 1 Viñuela F, Dion JE, Duckwiler G, et al. Combined endovascular embolization and surgery in the management of cerebral arteriovenous malformations: experience with 101 cases. *J Neurosurg.* 1991; 75 (6): 856-864. doi: 10.3171/jns.1991.75.6.856.
- 2 Pasqualin A, Scienza R, Cioffi F, et al. Treatment of cerebral arteriovenous malformations with a combination of preoperative embolization and surgery. *Neurosurg.* 1991; 29 (3): 358-368. doi: 10.1227/00006123-199109000-00004.
- 3 Deruty R, Pelissou-Guyotat I, Mottolese C, et al. Therapeutic risk in multidisciplinary approach of cerebral arteriovenous malformations. *Neurochirurgie.* 1996; 42 (1): 35-43.
- 4 Wikholm G. Occlusion of cerebral arteriovenous malformations with N-butyl cyano-acrylate is permanent. *Am J Neuroradiol.* 1995; 16: 479-482.
- 5 Weigle JB, Hurst RW, Al-Okaili RN. Endovascular management of brain arteriovenous malformations. In: Hurst RW, Rosenwasser RH, eds. *Interventional Neuro-*

- radiology, 1st ed. New York: Informa Healthcare; 2008. p. 275-303.
- 6 Hartmann A, Pile-Spellman J, Stapf C, et al. The risk of endovascular treatment of brain arteriovenous malformations. *Stroke*. 2002; 33 (7): 1816-1820. doi: 10.1161/01.STR.0000020123.80940.B2.
- 7 Taylor CL, Dutton K, Rappard G, et al. Complications of preoperative embolization of cerebral arteriovenous malformations. *J Neurosurg*. 2004; 100 (5): 810-812. doi: 10.3171/jns.2004.100.5.0810.
- 8 Ledezma CJ, Hoh BL, Carter BS et al. Complications of cerebral arteriovenous malformation embolization: multivariate analysis of predictive factors. *Neurosurgery*. 2006; 58: 602-11. doi: 10.1227/01.NEU.0000204103.91793.77.
- 9 Kim LJ, Albuquerque FC, Spetzler RF, et al. Post-embolization neurological deficits in cerebral arteriovenous malformations: stratification by arteriovenous malformation grade. *Neurosurgery*. 2006; 59: 53-59. doi: 10.1227/01.NEU.0000219219.97287.91.
- 10 Mounayer C, Hammami N, Pötin M, et al. Nidal embolization of brain arteriovenous malformations using Onyx in 94 patients. *Am J Neuroradiol*. 2007; 28: 518-523.
- 11 Katsaridis V, Papagiannaki C, Aimar E. Curative embolization of cerebral arteriovenous malformations (AVMs) with Onyx in 101 patients. *Neuroradiology*. 2008; 50: 589-597. doi: 10.1007/s00234-008-0382-x.
- 12 Jayaraman MV, Marcellus ML, Hamilton S, et al. Neurologic complications of arteriovenous malformation embolization using liquid embolic agents. *Am J Neuroradiol*. 2008; 29: 242-246. doi: 10.3174/ajnr.A0793.
- 13 Haw CS, terBrugge K, Willinsky R, et al. Complications of embolization of arteriovenous malformations of the brain. *J Neurosurg*. 2006; 104 (2): 226-232. doi: 10.3171/jns.2006.104.2.226.
- 14 Picard L, Moret J, Lepoie J, et al. Endovascular treatment of intracerebral arteriovenous angiomas: technique, indications and results. *J Neuroradiol*. 1984; 11: 9-28.
- 15 Merland JJ, Rufenacht D, Laurent A, et al. Endovascular treatment with isobutyl cyanoacrylate in patients with arteriovenous malformation of the brain: indications, results and complications. *Acta Radiol Suppl*. 1986; 369: 621-622.
- 16 Purdy PD, Batjer HH, Samson D. Management of hemorrhagic complications from preoperative embolization of arteriovenous malformations. *J Neurosurg*. 1991; 74: 205-211. doi: 10.3171/jns.1991.74.2.0205.
- 17 Fournier D, terBrugge KG, Willinsky R, et al. Endovascular treatment of intracerebral arteriovenous malformations: experience in 49 cases. *J Neurosurg*. 1991; 75: 228-233. doi: 10.3171/jns.1991.75.2.0228.
- 18 Jafar JJ, Davis AJ, Berenstein A, et al. The effect of embolization with N-butyl cyanoacrylate prior to surgical resection of cerebral arteriovenous malformations. *J Neurosurg*. 1993; 78: 60-69. doi: 10.3171/jns.1993.78.1.0060.
- 19 Wallace RC, Flom RA, Khayata MH, et al. The safety and effectiveness of brain arteriovenous malformation embolization using acrylic and particles: the experiences of a single institution. *Neurosurgery*. 1995; 37: 606-615; discussion: 615-618. doi: 10.1227/00006123-199510000-00002.
- 20 Debrun GM, Aletich V, Ausman JI, et al. Embolization of the nidus of brain arteriovenous malformations with N-butyl cyanoacrylate. *Neurosurgery*. 1997; 40: 112-120. doi: 10.1227/00006123-199701000-00026.
- 21 Picard L, Da Costa E, Anxionnat R, et al. Acute spontaneous hemorrhage after embolization of brain arteriovenous malformation with N-butyl cyanoacrylate. *J Neuroradiol*. 2001; 28: 147-165.
- 22 Heidenreich JO, Hartlieb S, Stendel R, et al. Bleeding complications after endovascular therapy of cerebral arteriovenous malformations. *Am J Neuroradiol*. 2006; 27: 313-316.
- 23 Starke RM, Komotar RJ, Otten ML, et al. Adjuvant embolization with n-butyl cyanoacrylate in the treatment of cerebral arteriovenous malformations. Outcomes, complications, and predictors of neurologic deficits. *Stroke*. 2009; 40: 2783-2790. doi: 10.1161/STROKEAHA.108.539775.
- 24 Spetzler RF, Wilson CB, Weinstein P, et al. Normal perfusion pressure breakthrough theory. *Clin Neurosurg*. 1978; 25: 651-672.
- 25 Martin NA, Khanna R, Doberstein C, et al. Therapeutic embolization of arteriovenous malformations: the case for and against. *Clin Neurosurg*. 2000; 46: 295-318.
- 26 Fox JL, AL-Mefty O. Embolization of an arteriovenous malformation of the brain stem. *Surg Neurol*. 1977; 8: 7-9.
- 27 Duckwiler GR, Dion JE, Viñuela F, et al. Delayed venous occlusion following embolotherapy of vascular malformations in the brain. *Am J Neuroradiol*. 1992; 13 (6): 1571-1579.
- 28 Sorimachi T, Takeuchi S, Koike T, et al. Blood pressure monitoring in feeding arteries of cerebral arteriovenous malformations during embolization: a preventive role in hemodynamic complications. *Neurosurgery*. 1995; 37: 1041-1047. doi: 10.1227/00006123-199512000-00002.
- 29 Handa T, Negoro M, Miyachi S, et al. Evaluation of pressure changes in feeding arteries during embolization of intracerebral arteriovenous malformations. *J Neurosurg*. 1993; 79: 383-389. doi: 10.3171/jns.1993.79.3.0383.
- 30 Jungreis CA, Horton JA, Hecht ST. Blood pressure changes in feeders to cerebral arteriovenous malformations during therapeutic embolization. *Am J Neuroradiol*. 1989; 10: 575-577.
- 31 Debrun G, Viñuela F, Fox A, et al. Embolization of cerebral arteriovenous malformations with bucrylate. *J Neurosurg*. 1982; 56 (5): 615-627. doi: 10.3171/jns.1982.56.5.0615.
- 32 Heros RC. Embolization of arteriovenous malformations. *J Neurosurg*. 2004; 100: 807-809. doi: 10.3171/jns.2004.100.5.0807.
- 33 Taylor CL. Comment on Editorial of Heros RC. Embolization of arteriovenous malformations. *J Neurosurg*. 2004; 100: 809.
- 34 Massoud TF, Hademenos GJ, Young W L, et al. Can induction of systemic hypotension help prevent nidus rupture complicating arteriovenous malformation embolization? Analysis of underlying mechanisms achieved using a theoretical model. *Am J Neuroradiol*. 2000; 21: 1255-1267.
- 35 Viñuela F, Duckwiler G, Guglielmi G. Intravascular embolization of brain arteriovenous malformation. In: Maciunas RJ, ed. *Endovascular neurologic intervention*. Illinois: American Association of Neurological Surgeons; 1995. p. 189-199.

Dr José A Jordan, MD
Jefe Departamento
Department of Radiology
Centro de Investigaciones Médico Quirúrgicas
216 Avenue, Esq 11b, Siboney Playa
La Habana, 10400 Cuba
E-mail: jjordan@infomed.sld.cu