

Functional Outcome and Rate of Recovery in Endovascular Treatment of Brain Arteriovenous Malformations: analysis of a single-center cohort of 66 cases

Evolución y Tasa de Recuperación en el Tratamiento Endovascular de las Malformaciones Arteriovenosas Cerebrales: análisis de una cohorte de 66 casos procedentes de un solo centro

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ABSTRACT

Introduction: We report our experience with endovascular approach to brain arteriovenous malformations. **Objective:** We emphasize the good safety profile of this approach and its potential for anatomical cure. **Materials and Methods:** This cohort study includes all patients diagnosed with a brain arteriovenous malformation who underwent therapeutic embolization in the 4-year period, from January 2015 to December 2018 at the Endovascular Neurologic Center (CEN) of Médica Uruguaya, Montevideo Uruguay. Data were collected from clinical records and computerized databases, as well as from clinical examinations to define current neurological and functional status according to the modified Rankin scale results. **Results:** 66 patients were reviewed, ranging from ages 1 to 73, 28 patients had previous bleeding, 18 had seizures, 9 were incidentally diagnosed and the remaining had minor headaches and neurological deficits. Only 3 patients underwent other therapies (2 had neurosurgery and 1 radiosurgery). Clinical results can be considered as very good, an overall 27% of anatomic cures; the treatment-related morbidity was very low, mRS 0-2 97% and mRS 3 in 3%. There were no patients with mRS 4-6. Clinical improvement was noted in 77.6% of patients. **Conclusion:** In our experience, endovascular therapy as a treatment of arteriovenous malformations is safe, can achieve control of the disease with no changes in quality of life and can be potentially curative in certain cases.

Keywords: Brain arteriovenous malformation; Embolization; Endovascular treatment; Anatomical cure

RESUMEN

Introducción: Informamos de nuestra experiencia sobre el tratamiento endovascular de las malformaciones arteriovenosas. **Objetivo:** Deseamos enfatizar el buen perfil de seguridad de este tratamiento y su potencial para la cura anatómica. **Materiales y métodos:** Este estudio de cohorte comprende todos los pacientes cuyas malformaciones arteriovenosas encefálicas fueron objeto de embolización terapéutica en un periodo de 4 años, desde enero del 2015 hasta diciembre del 2018, en el Centro Endovascular Neurológico de la Médica Uruguaya, en Montevideo, Uruguay. Se realizó la recolección de datos a partir de historias clínicas y bases de datos digitalizadas, así como de exámenes clínicos a fin de definir la evolución del estado neurológico y funcional según la escala de Rankin modificada. **Resultados:** Fueron analizados 66 pacientes, de 1 a 73 años de edad, de los cuales 28 tenían antecedentes de sangrado, 18 habían tenido convulsiones y 9 fueron diagnosticados casualmente en el curso de un estudio, mientras que los restantes presentaban cefaleas menores y déficits neurológicos. Solamente 3 pacientes fueron tratados por otros métodos (neurocirugía en 2 casos, radiocirugía en 1). Los resultados clínicos pueden ser considerados muy buenos, ya que hubo un 27% de curas anatómicas en general. La morbilidad en relación con el tratamiento fue muy baja, la valoración según la mRS fue de 0-2 en el 97% de los casos, y de 3 en el 3%. No hubo pacientes con cifras de mRS de 4-6. En el 77,6% de los pacientes se notó mejoría clínica. **Conclusiones:** En nuestra experiencia, el tratamiento endovascular de las malformaciones arteriovenosas es un método seguro, que puede lograr el control de la enfermedad sin alterar la calidad de vida y es potencialmente curativo en ciertos casos.

Palabras clave: Malformación arteriovenosa encefálica; Embolización; Tratamiento endovascular; Cura anatómica

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INTRODUCTION

The therapeutic approach to brain arteriovenous malformations (bAVMS) still represents a challenge. This issue remains controversial, because strategies on how to proceed have not been clearly standardized yet, on account of given the low prevalence of these malformations and their uncertain natural history¹⁻⁸. The final treatment is often decided according to the preference of the professional on duty.⁸

Recently, randomized studies (ARUBA trial: A Randomized Trial of Unruptured bAVMs) have shown as primary results a three-fold increase morbidity and mortality in the multimodal treatment arm, as compared with the medical arm. In light of these results, certain doubts come up about the role of treatment⁹.

On the other hand, perhaps no subspecialty within neurosurgery has seen such advances over a relatively short period of time as the endovascular field^{10,12}. This progress has enabled the embolization of bAVM to be performed as the only therapeutic option with great curative potential. And in those cases in which this objective is not possible, it can achieve disease control treating risk factors for bleeding, without significant changes in the quality of life of patients^{11,13-20,22}.

In this sense we are encouraged to analyze the role of endovascular embolization, mostly as a single treatment, emphasizing its results in terms of functional outcome and angiographic cure, in this presentation of our cohort study.

MATERIALS AND METHODS

The cohort includes all patients diagnosed and treated by embolization of a bAVM from January 2015 to December 2018 at the Neurosurgical and Endovascular Center (CEN) at Médica Uruguaya, Montevideo, Uruguay.

The only exclusion criteria were Vein of Galen malformations. Data were retrospectively collected from several sources:

clinical records, computerized MRI and CT scans and angiography studies. Once all the information was gathered all patients were interviewed by an independent observer to define neurological and functional outcome (at least 6 months follow-up).

Each malformation was classified according to the topographic criterion of Yasargil, Valavanis, and Lasjaunias^{1,4}, based on the evolution of the brain and the vascular system, and taking into account intrinsic arterial supply and pattern of venous drainage.

In order to unify data information was also classified according to the Spetzler and Martin scale²⁴, although it did not prove to be useful for the analysis and choice of intervention.

The primary goal was to determine the functional outcome after performing endovascular treatment, both for patients with angiographic cure and in process.

With this purpose in mind, patient disability scores according to the modified Rankin scale were determined. No disability was rated 0, minimum disability 1-2, moderate disability 3 and severe disability 4-5²⁵. The score prior to the treatment was plotted against the current one, after at least six months follow-up.

We also quantified the number of patients with improvement of headache, seizures, or neurological deficit, specifying which item had improved. The secondary goals were to determine the angiographic cure and complications. We define the angiographic cure as the absence of nidus with normalization of hemodynamics.

All patients considered to be angiographically cured have had at least a 6-month follow-up and 2 control angiographies that showed a stable result (Figs. 1 and 2).

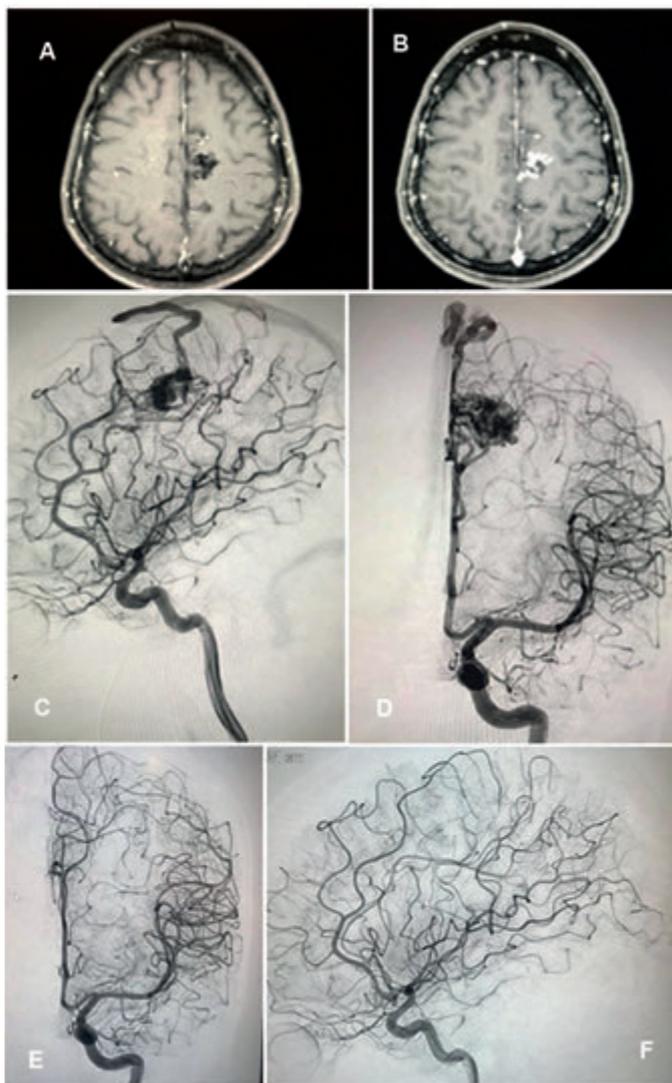


Figure 1. 37-year-old female patient with no previous diseases, presented with 36 with epileptic seizures. Imaging diagnosed a cortical-subcortical arteriovenous malformation on the left frontal lobe, fed by four arteries originating from the left pericallosal artery. This malformation was drained by a single vein that emptied into the superior sagittal sinus. Two embolization sessions were necessary to achieve an anatomical cure. **A-D.** Before treatment. **E-F.** After treatment.

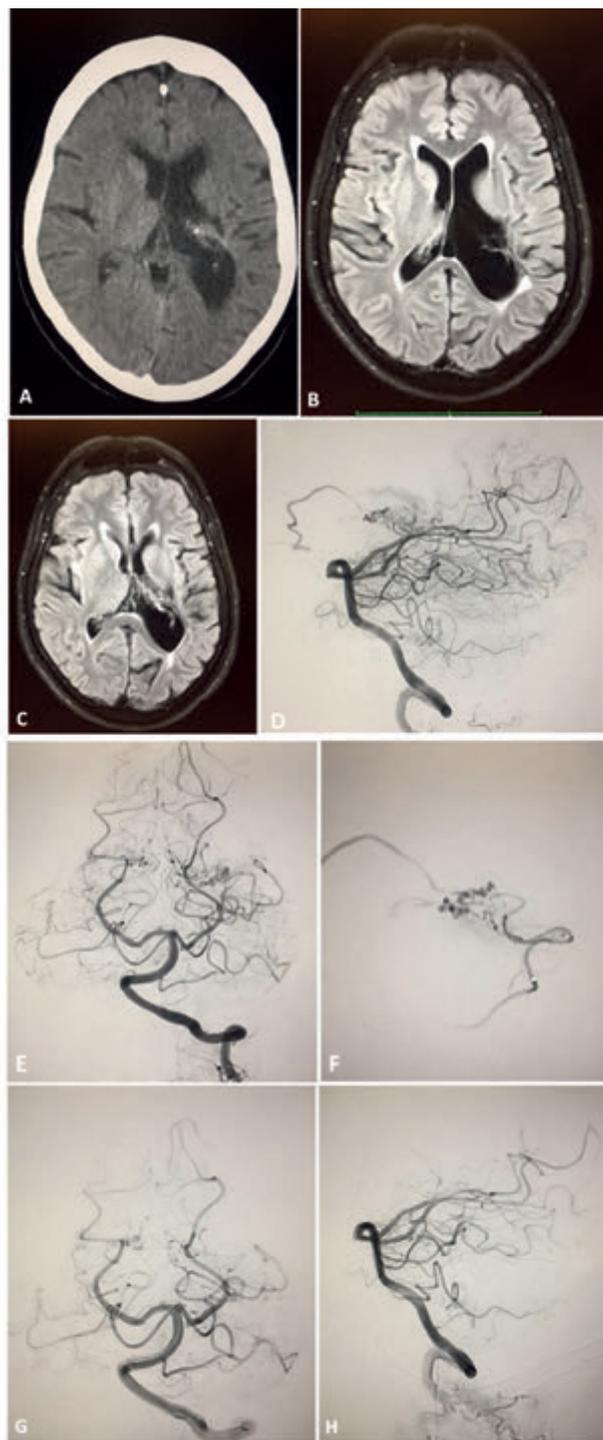


Figure 2. 42-year-old male patient, suffering from frequent headaches. Investigation led to imaging, which demonstrated a left choroidal arteriovenous malformation. It had two feeding arteries originating from the posteromedial choroidal arteries and drained into deep veins of the brain. Treatment was completed in one session. **A-F.** Before treatment. **G-H.** After treatment.

Finally, complications were analyzed. Any adverse event that might have been pathophysiologically linked to the intervention and happened either at the time of puncture or during the subsequent 30 days was considered to be a complication.

RESULTS

A total of 66 patients were included representing 181 procedures and more than 250 intracranial catheterizations.

Patient distribution was as follows: 46 males, ranging in age from 1 to 73, mean age 33.1 years; 20 females in the 6-59 age range, mean age 25.5. Clinical presentation was hemorrhage in 28 patients (42.4%), seizures in 19 (27.3%), headaches in 7 (10.6%), neurological deficit in 5 (7, 6%), while in the remaining 9 patients (13, 6%) the bAVM was an incidental finding.

Table 1. Patients and AVM characteristics

	Purely Cortical	Cortical and ventricular
Patients (n)	36	13
Male	26	9
Female	11	4
Age at presentation	33.1	25.5
Location		
Frontal (and rolandic)	18	4
Temporal	2	2
Parietal (and rolandic)	10	6
Occipital	7	0
Corpus callosum	-	1
Symptoms		
Hemorrhage	11	6
Seizures	17	2
Deficit	2	0
Headaches	3	3
Incidental	4	2
Spetzler Martin Score		
1	2	0
2	18	2
3	11	4
4	4	5
5	2	2

According to the topography 38 malformations were purely cortical (54.5%), 13 were cortical and ventricular (19.7%), 11 gangliobasal (16.7%) and 6 were located in the posterior fossa (9%).

Table 2. Patients and AVM characteristics

	Gangliobasal	Posterior Fossa
Patients (n)	11	6
Symptoms		
Hemorrhage	7	3
Neurologic deficit	2	1
Incidental	2	1
Headache	0	1
Spetzler Martin Score		
2	1	2
3	6	3
4	4	1

Table 3. Overall results

	mRS PRE TT	mRS 6 MOS POST TT
0	25	57
1-2	31	8
3	7	2
4-5	4	0
Clinical improvement	52/67	— 77.6%
Unchanged	13/67	— 19.4%
Transient Deficit	1/67	— 1.5%
Permanent Deficit	2/66	— 3%
Anatomical cure	18/67	— 27%

The mRS score prior to treatment was 0 in 25 patients, 1-2 in 31 patients, 3 in 7 patients, 4-5 in the remaining 4.

The mRS at the 6-month follow-up was 0 in 56 patients (83%), 1-2 in 8 patients (12%), 3 in 2 patients (3%)*.

There were neither patients with severe disability mRS 4-5 nor death in this series. Clinical improvement

was noted in 52 patients (77.6%), while 13 patients remained unchanged (19.4%), 1 patient had a transient deficit and 2 were left with a permanent deficit*.

*One of these patients had underwent a complication; the other evidenced the deficit after open surgery.

Table 4. Anatomical cure

	Age	Present.	Topography	Feeders (direct)	SM Grade	Risk factors	SES	Follow-up (month)
M	39	Seizures	Left temporal gyral	3	3		2	40
F	40	Hematoma	Left parasagittal gyral	4	2		3	36
M	39	Seizures	Left frontal sulcal	1	1		2	39
M	7	ND	Deep-seated	2	4		4	31
F	44	Hematoma	Posterior fossa	2	3	Flow aneurysm	2	32
M	20	Hematoma	Left sulcal occipital	1	2		3	16
M	53	Deep hematoma	Diencephalic	2	3		2	19
F	29	Hematoma	Right occipital sulcal	4	2		3	21
M	30	Hematoma	Right parietal sulcal	2	3	Intranidal aneurysm	1	29
M	26	Hematoma	Right thalamic	4	2	Intranidal aneurysm	1	16
M	35	Hematoma	Left parietal mixed sulcal-gyral	2	2		2	19
F	41	Headache	Right frontal sulcal	4	2		2	16
M	52	ND	Posterior fossa	2	2		2	9
M	67	ND	Frontal mixed sulcal-gyral	3	2		1	11
M	38	Incidental	Right frontorolandic sulcal	3	2	Intranidal aneurysm, venous ectasia	2	12
M	48	Hematoma	Right frontal sulcal	3	2		2	7

Legend: ND – Neurologic Deficit

Table 5. Complications

	Age	Present.	Topography	SM Grade	Complication	Deficit	mRS Follow-up
F	60	Hematoma	P-O sulcal MAV	3	Partial thrombosis of sagittal sinus, hemorrhagic stroke	Permanent	3
M	38	Hematoma	F-O cortical and ventricular	4	Sylvian feeder dissection	Previous*	2
F	44	Hematoma	Deep-seated	3	Ischemic Stroke	Transient	0
F	41	Headache	Right frontal sulcal	2	Ischemic Stroke	None	0

*The patient with the Sylvian feeder dissection complication had a previous hemiparesia due to microneurosurgery when he was 18 years old.

DISCUSSION

Therapeutic strategy

In all cases, the primary goal was to eliminate the hemorrhagic risk of the bAVM. We attempted a curative treatment when feasible and achieved an ‘anatomical cure’. In those cases when that was not possible due to AVM’s characteristics, the objective was to treat the risk factors and to improve hemodynamics in that way.

We did not take into account the Spetzler and Martin classification in our therapeutic decision because it fails to consider the specific angioarchitecture and hemodynamic features and cannot be used as a reference to the assumed natural history of all AVMs as a group^{1,4}.

We performed in all patients transarterial embolization by the femoral approach; this approach is widely regarded as a key point for atraumatic super selective microcatheterization^{1,4,29}. All locations were regarded as eloquent⁴. The embolic material used was N-butyl-cyanoacrylate (NBCA) Histoacryl® and/or Onyx® Liquid embolic system, Micro Therapeutics Inc USA and/or SQUID Emboflu, Switzerland. A multistaged treatment was performed, with a median of 3 sessions/patient, depending on the case.

Morbidity and functional outcome

Comparing functional outcome as measured at follow-up (at least 6 months later) on the basis of mRS score, with the previous one, we found a substantial improvement; particularly in the 0 category, going from 38% to 85% (with a difference of 47%), followed by patients with minor disability going from 45.5% to 12% (a difference of 33.5%); patients with a moderate disability went likewise from 10% to 3%, while in the severe disability group the improvement was 100%. At the present time, there are neither patients with a 3-4 score nor deaths in our series.

In addition, 77% of patients report an improvement in terms of frequency and control of seizures, headache or focal neurological deficit.

According to the results summarized in Table 5, only one case

of permanent neurological deficit with moderate impairment of function was found, the patient with a hemorrhagic stroke due to partial thrombosis of the superior sagittal sinus.

As to the other three patients who suffered complications, one showed transient sensitive symptomatology determined by focal ischemia, and the other two were asymptomatic (Sylvian pedicle dissection and minor ischemic stroke).

Two patients had a delayed hemorrhagic stroke at least 3 months after the last treatment; none of them caused severe disability or death.

Based on the data analyzed above, we found a permanent morbidity of 1.5% and a mortality rate of 0% in this series.

In light of the ARUBA trial (a randomized trial of unruptured bAVMs) showing a three-fold increase in morbidity and mortality in the multimodal interventional arm compared with medical arm (30.7 vs 10.1), the opportunity of treatment of unruptured bAVMs⁹ must be carefully assessed.

Many concerns and criticisms have emerged. Selection criteria resulted in a heterogeneous population of patients, with a very low proportion of randomized cases versus screened patients (226/1740 – 13%), which limits external validity and its applicability^{29, 32-37}. A wrong sided trial hypothesis^{29,37} was established, with inappropriate endpoints (both primary and secondary) based on incomplete and unclear criteria³³⁻³⁵. The treatment arm was not standardized^{32,36}. Subgroup analysis should not have been conducted, on account of the design of the trial and the relatively small size of the population under study.

On the other hand *'treatments must be individually validated as beneficial on their own merits. By grouping all management alternatives on the other side of the comparison, without stratification, the ARUBA trial could only test and verify that medical management was best'*²⁹, which can lead to a contentious interpretation of results.

The follow-up period, with a mean time of 33 months, is likewise debatable, because the goal of any interventional

treatment is to prevent the risk of rupture for a lifetime³². *'We ended up testing the single option that in the absence of evidence did not need to be tested. Combined with a choice of analyses that could not measure the promised longterm outcomes, the trial was, in a sense, unfair.'*²⁹.

So we conclude that the usefulness of this trial lies in its being both a turning point and a point of departure for future trials. Our results are comparable to many international series¹⁵⁻¹⁹.

Anatomical obliteration

As shown in Table 4, an anatomical obliteration was obtained in eighteen out of 67 bAVMs (27%), with at least two control angiographies and follow-up period ranging from six to forty months, supporting a stable result.

CONCLUSIONS

In our experience a complete cure of bAVMs by embolization alone is not an uncommon occurrence, with a 24% cure rate, the angiographic follow-up period ranging from 3 to 40 months. An excellent safety profile is supported by these facts: 85% of patients became asymptomatic, only one patient was left with a permanent neurologic deficit, no patients presented severe disability and there were no deaths. This translates into a permanent morbidity of 1.5% and a mortality rate of 0%. When total obliteration of a bAVMs is not possible, embolization seems to be very useful to reduce both the flow and size of bAVMs and to identify and treat risk factors. This is proved by symptomatic improvement in 77% of patients and a low rate of repeat bleeding events in the long term. Note that none of these bleeding events determined severe disability or death in our series. Long-term follow-up of patients treated by embolization is mandatory and essential to determine stability and long-term safety.

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