

Safety and Efficacy of Transarterial Embolization of Intracranial Arteriovenous Malformations

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ABSTRACT

Background: The development of new technology in neurosurgery, interventional neurovascular techniques, and gamma knife surgery (GKS) has dramatically changed the therapeutic alternatives for brain arteriovenous malformations (AVMs). The purpose of this study is to report the safety and efficacy of transarterial embolization of intracranial arteriovenous malformations treated with N-Butyl Cyanoacrylate (Histoacryl). **Patients & Methods:** We present a prospective analysis of 42 consecutive patients with brain AVMs treated in Ain Shams University from June 2005 to January 2007, (30 men, 12 women). The patients' average age was 30.5 years. Seizures was the presenting symptom in 24 patients. The average Spetzlar – Martin grade at presentation was grade 3. The AVMs Nidus volume ranged from 2 cm³ to 90 cm³. Embolization of the AVMs by N-Butyl Cyanoacrylate was done in 42 patients. All patients were treated with the ultimate goal of complete AVMs obliteration. AVMs that are not totally obliterated were embolized to reduce the size and referred to gamma knife treatment. The course of treatment for each patient was reviewed. The effectiveness at the end of treatment was analyzed if not totally occluded, and the ability to reduce the AVMs to radiation size is assessed. Additionally, the safety of each embolization technique was evaluated in terms of the safety of the procedure itself, and the outcome at the end of the treatment. **Results:** One hundred and four procedures were done in 42 patients. The number of sessions varied from 1 to 6 sessions. The percentage of volume reduction ranged from 100% to 78.2%. Total occlusion (cured by embolization only) was achieved in ten patients (23.8%), reduction to a volume less than 4 cm³ (suitable for radiosurgery) was achieved in 30 patients (71.4%), while in two patients (4.8%) reduction to a volume between 4-10 cm³ was achieved. Complications occurred in three patients (7.1%); seizures occurred in two patients; while intracerebral with intraventricular hemorrhage occurred in one patient (2.4%). There was minimal transient morbidity in one patient (2.4%) in the form of temporary decrease in visual acuity. Permanent morbidity related to the procedures observed in one patient (2.4%) in the form hemi-paresis grade 3. There was no mortality in this study. **Conclusion:** Intracranial arteriovenous malformation embolization with N-Butyl Cyanoacrylate (Histoacryl) is a safe and effective technique that permits complete cure of brain AVMs. However, larger AVMs are reduced in volume to be fit for radiosurgery. **Key words:** Embolization, Intracranial arteriovenous malformation; N-Butyl Cyanoacrylate.

INTRODUCTION

Arteriovenous malformations (AVMs) of the brain are congenital lesions most likely developing during the late embryonic life. The primary pathologic lesion consists of one or

more persistent direct connection between the arterial inflow and venous outflow without an intervening capillary bed⁽¹³⁾. The development of new technology in neurosurgery, interventional neurovascular techniques, gamma knife surgery

(GKS) has dramatically changed the therapeutic alternatives for brain arteriovenous malformations^(14,30). Initially, the goal of endovascular embolization was complete occlusion of arteriovenous malformations. However, with the growing experience, it seemed that this goal could be achieved in only a limited number of cases. These include AVMs of small or moderate size which are supplied by a limited number of feeders, less than three feeding vessels. Yet endovascular embolization is useful in combined therapies as it improves surgical and radiosurgical cure rate of arteriovenous malformations by 25%^(8,11,35).

Before radiosurgery, reduction in AVM volume, occlusion of aneurysms, and high-flow fistulae are the desired outcomes of endovascular embolization. A variety of embolic agents are used to induce embolization^(16,29) poly phenyl alcohol (PVA) and coils are commercially available in the United States (i.e., approved by the Food and Drug Administration). Microspheres (precisely calibrated, spherical particles) have been evaluated for embolization of cerebral AVMs^(14,25). The most commonly used embolic agent is the fast polymerizing liquid adhesive *n*-butyl cyanoacrylate (*n*-BCA). The use of *n*-BCA in brain AVMs requires experience and skills, because intranidal flow and polymerization of *n*-BCA are quick and largely unpredictable. Recently, a new liquid embolic agent became available: Onyx liquid embolic system (ev3, Irvine, Calif). Onyx is less adhesive and polymerizes slowly, which seems advantageous over *n*-BCA^(21,25,31). The purpose of this study is to report the safety and efficacy of transarterial embolization of intracranial arteriovenous

malformations treated with N-Butyl Cyanoacrylate (Histoacryl).

PATIENTS & METHODS

A prospective analysis of 42 consecutive patients with brain AVMs treated in Ain Shams University hospitals from June 2005 to January 2007 is carried on. Treatment decision and plane was carried out in a multidisciplinary approach. Assessment of the patient and designing a plan to accomplish the goals of treatment was done after a good understanding of the pre-treatment angiographic studies, clinical picture and apparent influence of the angioarchitecture on the natural history of each individual arteriovenous malformation. A preliminary assessment of the technical possibilities and difficulties was done, as well as a formulation of the reasonable risks, exceptions, and results were done as an initial therapeutic plane. Both inclusion and exclusion criteria are planned.

Aim of Embolization

Initially was complete occlusion of the AVM. If initial total occlusion could not be reached, elimination of a portion of the AVM (or closure of the dural supply) to decrease size before radiosurgery was our target. Also to normalize pressure in pedicles, reduce venous pressure in draining veins, or to eliminate high risk angioarchitectural features, closure of a direct A-V fistula with in the AVM to decrease risk until radiosurgery effect is evident. Also symptomatic relief-either palliative or until radiosurgery effect is evident was aimed.

Inclusion Criteria

Patient not fit for other single modality; high surgical risk; high risk

of gamma knife; patient refusal for treatment by other modality; presence of an appropriate pathway to reach the nidus endovascularly; presence of high risk pathological angioarchitectural features (e.g. intranidal aneurysm); Presence of a clinical indicator for treatment as: reduction of neurologic deficit due to arterial steal or venous hypertension; reduction of severity, reduction duration of frequency of headache; reduction of severity, reduction duration of frequency of seizures; reduction of frequency of hemorrhagic events.

Exclusion Criteria:

Patients declined embolization; old age with poor medical condition that can't withstand multiple sessions; and complicated vascular anatomy.

All patients were subjected to preprocedural, procedural and postprocedural assessment. Preprocedural patients were assessed clinically by: general and neurological examination and data were collected. Radiologically by CT scan (with and without contrast); MRI was used as good diagnostic tool in revealing pathological anatomy, edema and gliosis also may reveal some pathological associated angioarchitecture as venous varix and nidal aneurysm ; MRA and MRV were available in some patient and not in others, where it was replaced by the intra-arterial digital subtraction angiography.

Intra-arterial digital subtraction angiography (IA-DSA) remains the criterion standard for AVM evaluation, angiography was done to 6 vessels: 2 ICA, 2 ECA, 2 VA, in order to detect any dural blood supply, from external carotid arteries and also to detect multiple feeders from other vessels, as missing these points may give false impression about the real dimensions

of the AVM treated. Detailed Arteriovenous Angiographic Data were collected from IA-DSA as regard: nidus location, size, number of arterial feeders, venous drainage, dural supply, associated vascular pathologic conditions as arterial aneurysms (intranidal), venous varices or ectasia, venous stenosis. Also the anatomical access and its feasibility for that IA-DSA were used as the radiologic investigation of choice for: planning treatment, preprocedural data collection, and assessment of treatment efficacy and follow up.

Patients

Forty two patients: 30 men; 12 women. The patients' average age was 30.5 years. In the 42 patients with brain arteriovenous malformation: 24 patients (57.1%) presented with seizures only; eight patients (19.05 %) presented with intracerebral hemorrhage +/- intraventricular hemorrhage; eight (19.05 %) patients presented with headaches and two patients (4.8%) presented with deterioration of visual activity.

Arteriovenous malformation data

Twenty four brain AVMs (57.1%) were left, 18 brain AVMs (42.9%) were right. They were distributed as follows: 13 parietal; 3 deep parietal with intraventricular extension; 3 parieto-occipital; 5 frontal; 5 frontoparietal; 3 posterior temporal; 3 temporo-parietal; 1 thalamic; 2 occipital and 3 cerebellar AVMS. Thirty eight brain AVMs (90.5%) were located in eloquent areas, while only 4 brain AVMs (9.5%) were located in a non-eloquent area. Nidus size was referred to the maximum diameter measured .It varied from 2 cm to 8 cm with a mean of 4.48 ± 1.8 , and was classified into: small if < 3 cm; medium if it is 3-6 cm; large if > 6 cm. Five AVMs (11.9%) were small, 25 AVMs (59.5%) were

medium sized, and 12 AVMs (28.6%) were large in size. Nidus volume ranged from 2 cm³ to 90 cm³. Nidus volume was classified into three groups; group one: which had a volume less than 10 cm³, they were 5 patients (11.9%); group two, which had a volume between 10 and 50 cm³ they were 25 patients (59.5%) and; lastly group three; which had a volume more than 50 cm³, these were 12 patients (28.6%).

Thirty four AVMs (80.9%) had no dural supply, and while eight AVMs (19.1%) had dural supply. Thirty four AVMs (80.9%) had only superficial

venous drainage; and eight AVMs (19.1%) had also deep venous drainage. Twenty patients (47.6%) had arterial steal phenomena in their 4 vessel digital subtraction angiography prior to embolization, 26 patients (61.9%) had venous ectasias, and 10 patients (23.8%) had intranidal arterial aneurysms.

As regard Spetzlar and Martin classification it ranged from grade 2 to grade 5 [table-1]; with a mean of 3.14 ± 0.85, where: 10 patients (23.8%) were grade 2; 18 patients (42.8%) were grade 3; 12 patients (28.6%) were grade 4; 2 patient (4.8%) was grade 5.

Table (1): Distribution of AVMs as regard Spetzlar and Martin classification

Spetzlar and Martin Grade	Number of patients
Grade 1	
Grade 2	10 (23. 8%)
Grade 3	18 (42. 8 %)
Grade4	12 (28. 6 %)
Grade 5	2 (4,. 8 %)

Technique

All procedures were carried out in the angiography room under general anaesthesia. Once the patient is comfortable on the angiography table, the monitoring equipments is connected and endotracheal anaesthesia is induced. Both groin areas are prepared and draped in a sterile manner. With the percutaneous cannulation technique, the skin is punctured three finger breadth below an imaginary line connecting the superior iliac crest and the pubic symphysis, with an 16-gauge needle (Seldinger's needle, Cordis Neurovascular, Miami Lakes, FL, USA) aiming for the femoral artery. The site is punctured over the femoral head to allow effective compression at

the end of the procedure. A J-wire (Terumo 0.035-inch guiding wire) is passed through the needle, which is then removed, and a 6F sheath (Cordis Neurovascular, Miami Lakes, FL, USA) is passed over the wire. The guiding catheter mostly 6F Envoy (Cordis Neurovascular, Miami Lakes, FL, USA), or a 6F Guider softip (Target Therapeutics-Boston scientific, Fremont, CA USA) is than navigated under fluoroscopic guidance over the guide wire into the vessel that provides access to the arteriovenous malformation. The sheath and guiding catheter are connected to saline solution, where a rotating haemostatic adapter (pump) is applied to allow continuous flushing to avoid thrombus formation in the system. Special

attention was given to air bubbles, wire and catheter cleanness and continuous irrigation of catheter with saline solution. Also attention was paid to the size of target vessel, as smaller vessels may not accommodate 6F catheter and need a 5F catheter, and for atherosclerotic patients to prevent emboli related to scraping of atheromatous plaques

Flow directed microcatheters (magic microcatheters of Balt extrusion, Montmorency, France, size; 1.2, 1.5, 1.8 French) were used to reach the AVM nidus depending on flow control. In some cases where there was a difficulty in vascular negotiations to access the AVM nidus microguide wire hydrophilic 0.007, 0.008 and 0.009 inch were used (Steel 0.007, 0.009, Balt extrusion, Montmorency, France and Mirage 0.008, Micro Therapeutics, Inc., Irvine, CA, USA).

Size of the catheter was determined according to the diameter size of the feeder. No functional test was done before embolization of the AVM even in AVM in eloquent areas, as injection by embolic agents wasn't done unless the microcatheter is in an ideal position, and is wedged within the AVM nidus without proximal reflux of contrast during pre-embolization test by dye injection. Once in appropriate place for embolization, the dead space of the magic microcatheter is flushed with 5% dextrose by a 3 ml syringe. The patient is kept in a hypotensive state throughout the procedure to prevent migration of the embolic material to the venous side and also prevent rapid distribution of the embolic agent to a large territory of the AVM nidus, and this may lead to normal perfusion pressure breakthrough and AVM nidus bleeding. So the patient's mean arterial blood pressure is kept between 60 to

80 mmHg. A mixture of N-Butyl Cyanoacrylate (Histoacryl, Balt extrusion, Montmorency, France), or (Cordis neurovascular, Miami Lakes FL. USA) and lipidol is prepared. Typically the mixture ranges from 1:1 (Histoacryl: lipidol) in high flow AVM to 1:3 in low flow AVM, as the ratio increases the Histoacryl is more diluted and takes a longer time before being polymerized with blood, so allowing the embolic mixture to spread and close a larger territory in the AVM nidus without gluing of the microcatheter in place inside the AVM nidus.

The N-Butyl Cyanoacrylate glue (Histoacryl-lipidol) mixture is injected slowly using live road mapping to allow clear visualization of glue progression through the AVM. The end point of injection is reached only when there is no further progression of the Histoacryl glue into the nidus of the AVM can be detected, or when reflux of the Histoacryl glue proximal the microcatheter's tip is observed. Once the end point of injection is reached (when: there is no further progression of the Histoacryl glue into the nidus of the AVM can be detected; or when reflux of the Histoacryl glue proximal the microcatheter's tip is observed), we aspirate the injecting syringe and pull the microcatheter rapidly out from the guiding catheter.

If there will be another injection of another pedicle in the same session, the steps are repeated again. By the end of the session, complete angiography study is done to assess changes from baseline preprocedural angiography and to plane further treatment strategy.

By the end of the session, after the patient awakes from general anaesthesia, a complete neurological examination is done to assess changes from baseline. The patient is then

transferred to the neurointensive care unit for monitoring. The mean arterial blood pressure is maintained approximately 10% below baseline (60-80 mmHg), during the postprocedural care, this is done in order to minimize the controversial phenomenon of normal pressure breakthrough and decreases the risk of postembolization delayed haemorrhage, in which partial venous outlet occlusion has occurred, which is thought to be the most significant cause of haemorrhage. All patients were kept in neurointensive care unit for 24 hours, and then transferred to the ward for close observation to be discharged within 48 hr, a delay may occur in patients' discharge according to presence of complications and their neurological condition. If a large portion of the AVM was occluded in one session those patients are kept under anaesthesia over night with gradual recovery by the next day.

Five thousand units of heparin are administered intravenously, and then 1000 unit/hour are given during the procedure, if the nidus of AVM was less than 3 cm in diameter and had few feeders, where as heparinization was not considered to be necessary when the nidus of the AVM was larger than 3 cm in diameter and has multiple feeders from two or three major trunks (e.g. MCA, ACA, and PCA). All catheters used and the sheath were connected to haemostatic adaptor (pump) for continuous flushing to guard against formation of micro emboli in the catheter system.

For all patients with seizures, or on anticonvulsant therapy they received preprocedural intravenous loading dose of anticonvulsant, with postprocedural maintenance dose for the first 48 hours. Steroids were preserved for patients, that had embolization that led

to closure of a large portion of the nidus in one session, or patients with changes in the brain perfusion due to reperfusion of ischemic areas of the brain due to a decrease in arterial steel, and also in patient with evident brain edema postprocedural.

All patients were subjected to postprocedural CT scan without contrast after the end of each session to exclude hemorrhage or brain edema.

RESULTS

One hundred and four procedures were done in 42 patients. The number of sessions varied from 1 to 6 sessions.

Anatomical outcome

The percentage of volume reduction ranged from 100% to 78.2%, total occlusion (cured by embolization only) occurred in 10 patients (23.8%) [Figure 1,2,3], reduction to a volume less than 4 cm³ (suitable for radiosurgery) occurred in 30 patients (71.4%) [Figure 5] and in 2 patients (4.8%) reduction to a volume between 4-10 cm³

Postembolization changes in angioarchitectural characteristics

In the eight AVMs with dural supply, the dural supply was embolized in all the eight AVMs. Twenty AVMs had arterial steel, in six (30%) no improvement was achieved, in 14 (70%) arterial steel improved [Figure 3]. In 26 AVMs with venous ectasias in six patients (23%) there was no change, in ten patients (38.5%) venous ectasias showed decrease in size, , and in ten patients (38.5%) venous ectasias disappeared [Figure 5]. In ten AVMs with intranidal aneurysms, all intranidal aneurysms were initially embolized to prevent further rupture of such aneurysms.

Radiological follow up

Radiological follow up was done by 6 vessels digital subtraction angiography with external carotid arteries study for all cases at six

months duration. Stable embolization was achieved in 41 cases, while progressive thrombosis to complete obliteration was observed in one case [Figure 4].

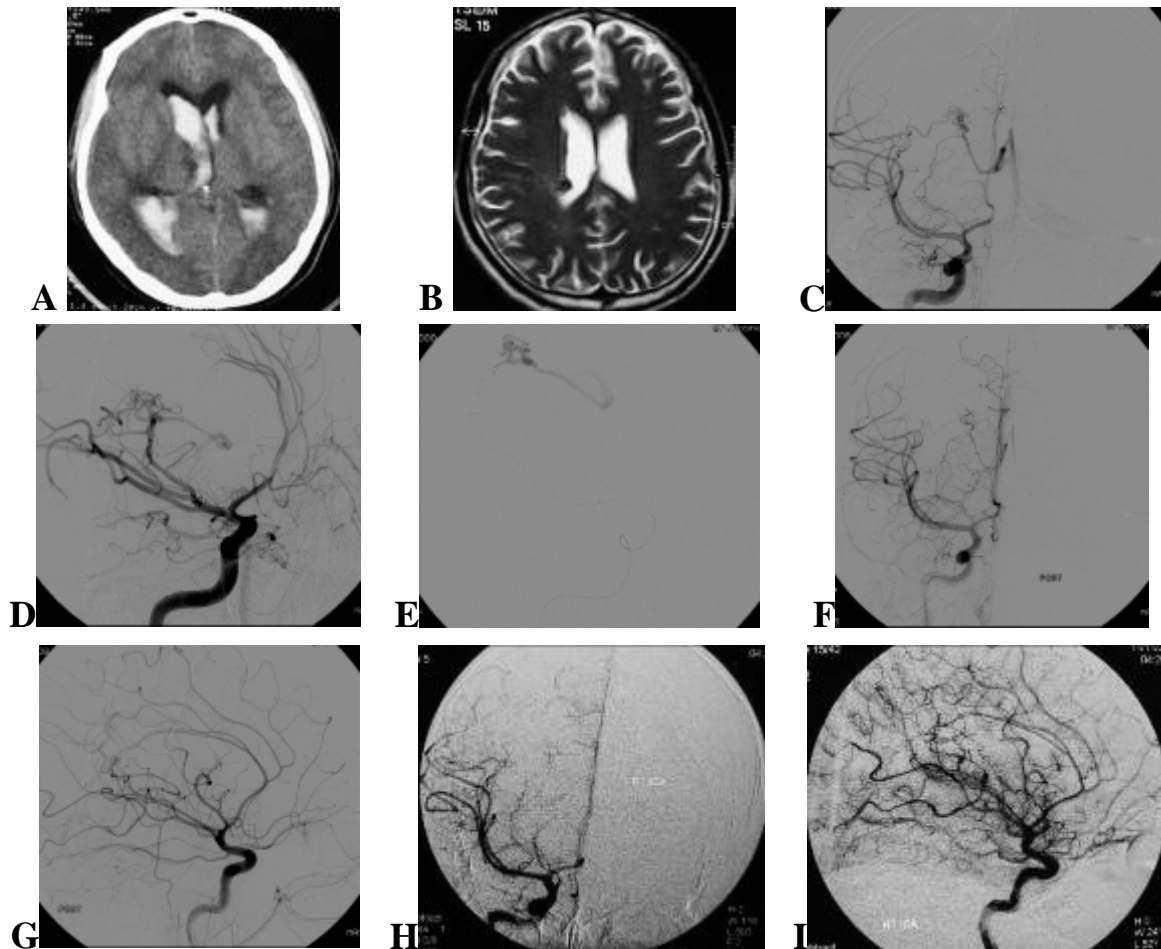


Figure 1: Case 1, Twenty six years old male, who presented with intraventricular haemorrhage. **A**, CT scan without contrast showing intraventricular haemorrhage. **B** MRI scan of the brain (axial T2W) showing a micro AVM in the lateral wall of the lateral ventricle on the right side. **C, D** towne's and lateral views DSA of the right internal carotid artery demonstrating right periventricular micro-AVM, supplied by branches of the right middle cerebral artery. **E**, DSA showing superselective injection of the AVM by the microcatheter. **F, G** towne's and lateral views DSA of the right internal carotid artery after embolization of the AVM by Histoacryl, showing total occlusion of the AVM in one session. **H, I** towne's and lateral views DSA of the right internal carotid artery after 6month follow up with stable embolization and no recurrence.

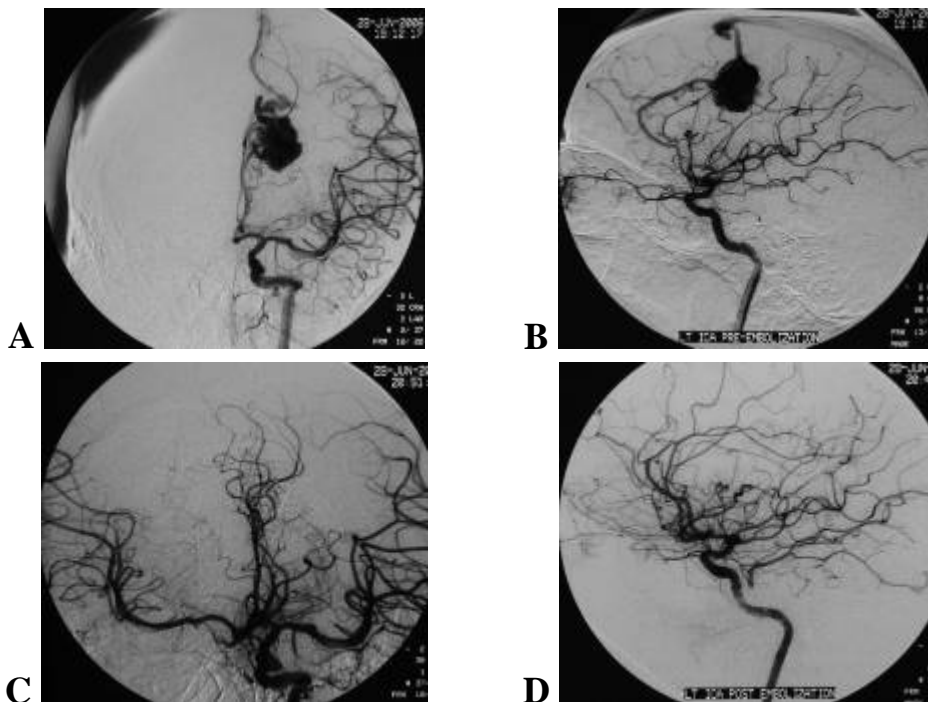


Figure 2: Case 2, Eighteen years old male, who presented with seizures. **A,B** Towne's and lateral views DSA of the left internal carotid artery demonstrating left parasagittal AVM, supplied by branches of the left anterior cerebral artery. **C,D**, same views in after embolization of the AVM by Histoacryl, showing total occlusion of the AVM, with cross filling of the other hemisphere via the anterior communicating artery.

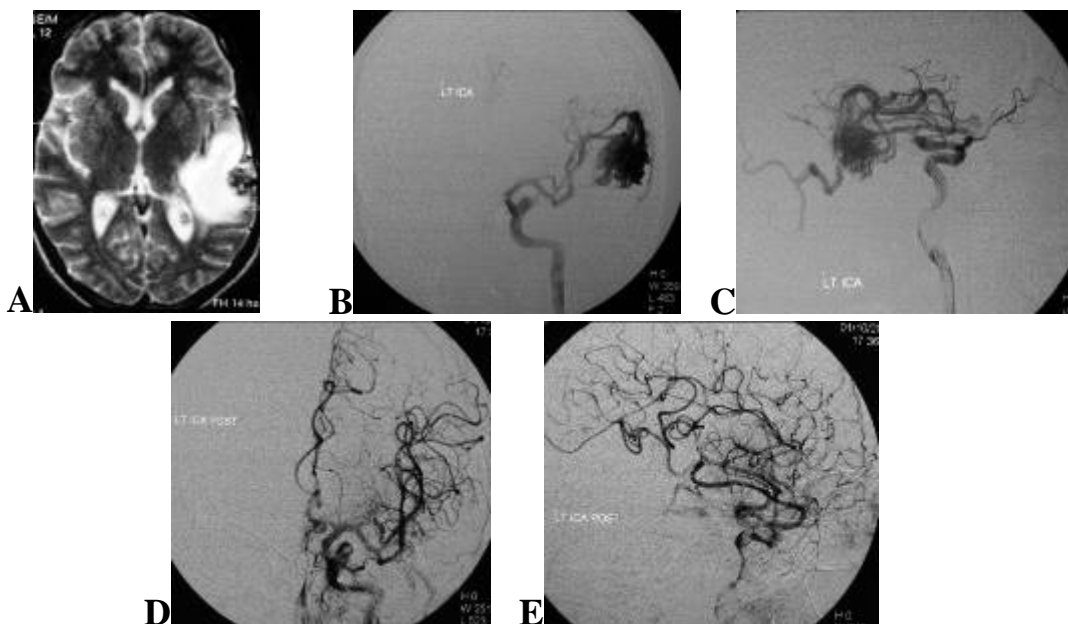


Figure 3: Case 3, Thirty three years old male who presented with intractable seizures. **A**, MRI scan of the brain (axial T2W) shows the AVM in the left parietal lobe. **B, C** anteroposterior and lateral DSA, demonstrating plexiform AVM filled by branches of the left middle cerebral artery with arterial steal of the left anterior cerebral artery. **D, E**, same views of B, C after total embolization of the AVM by Histoacryl, with improvement of the arterial steal of the anterior cerebral artery.

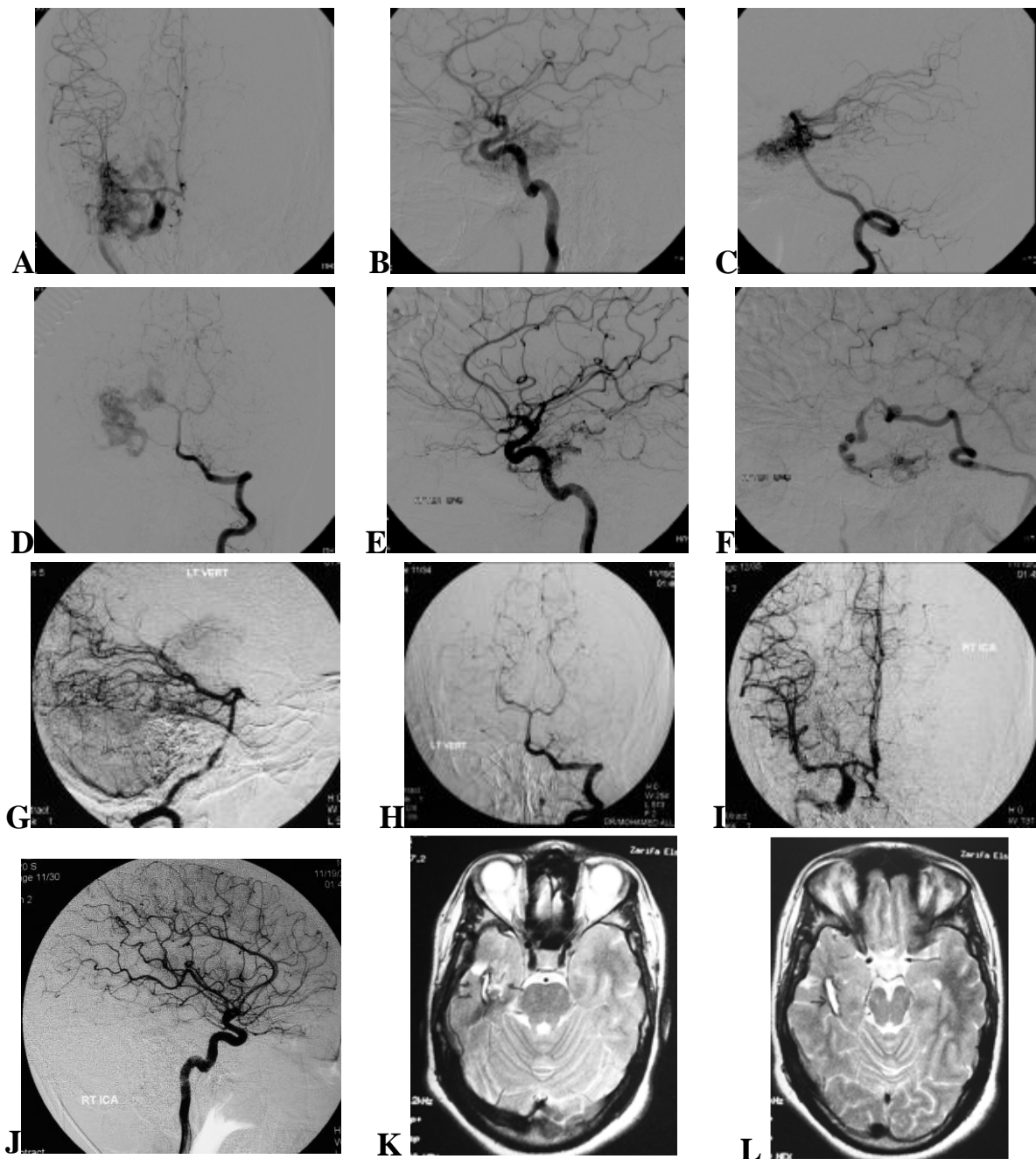


Figure 4: Case, Twenty nine years old female who presented with intractable seizures. **A, B** towne's and lateral views DSA of the right internal carotid artery demonstrating right temporal AVM, supplied by branches of the left anterior. **C, D**, lateral and towne's views DSA of the left vertebral artery showing the same AVM. **E, F** lateral view DSA of the right internal carotid artery, arterial and venous phase after 1st session of embolization. **G, H** lateral and towne's views DSA of the left vertebral artery 3 month later showing complete occlusion of the AVM by spontaneous progression of thrombosis without further embolization. **I, J** towne's and lateral views DSA of the right internal carotid artery demonstrating total occlusion of the AVM. **K, L** MRI scan of the brain (axial T2W) shows total resolution of the AVM in the right temporal lobe.

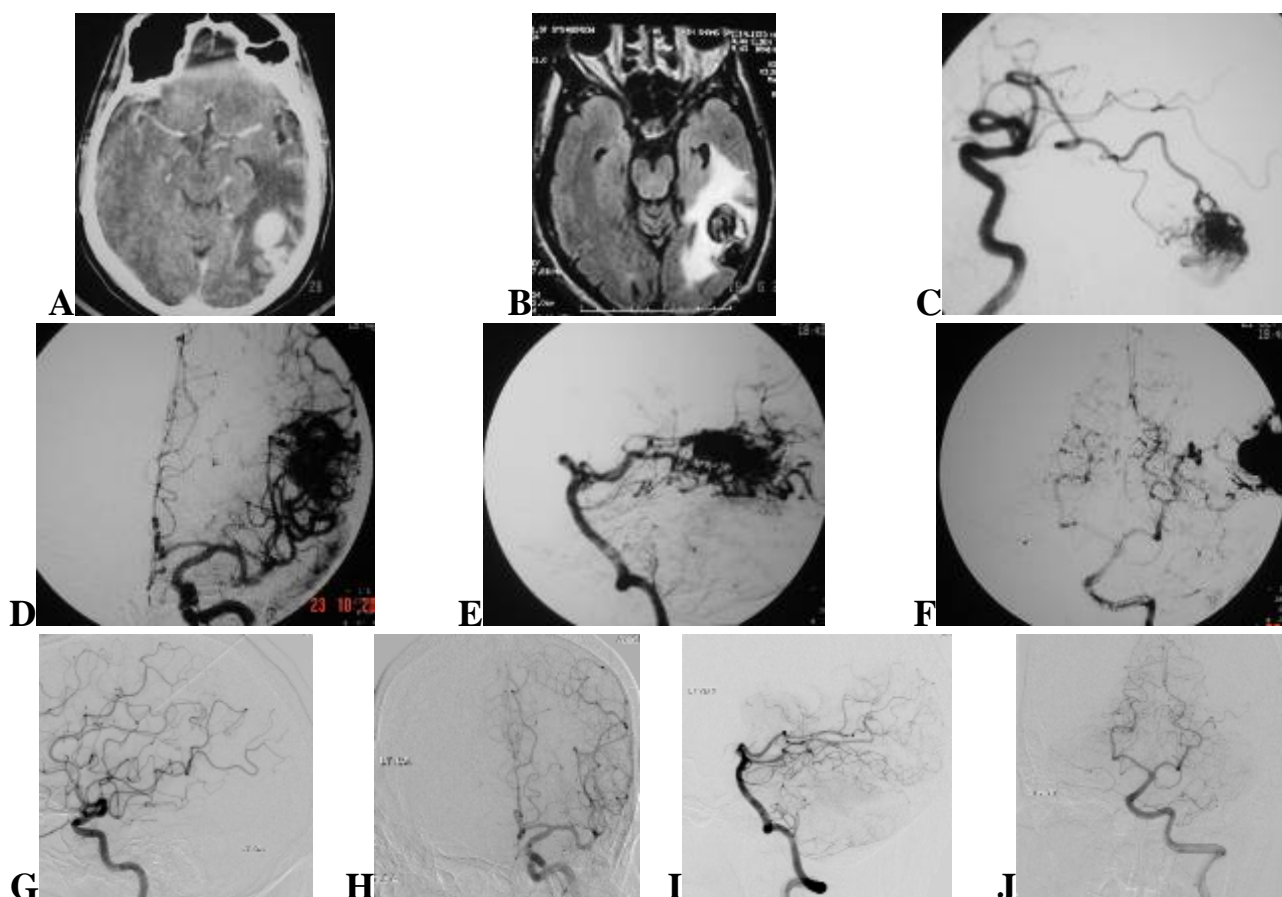


Figure 5: Case 5, Forty three years old male who presented with intractable seizures. **A,** CT scan without contrast showing parieto-occipital AVM with evident venous ectasia. **B** MRI scan of the brain (axial T2W) parieto-occipital AVM with evident venous ectasia. **C,D** lateral and towne's view DSA, left internal carotid artery demonstrating left parieto-occipital AVM filling by branches of the left middle cerebral artery. **E,F,** lateral and towne's view DSA, left vertebral artery demonstrating left parieto-occipital AVM filling by branches of the left posterior cerebral artery. **G,H,I,J,** same views of **C,D,E,F** after partial embolization of the AVM by Histoacryl in 2 sessions and, 1and half year after having Gamma knife of the residual of the AVM. There is total resolution of the AVM with disappearance of the evident venous ectasia.

Clinical outcome

Clinical outcome was assessed after the procedures by GOS: the 41 patients were all GOS grade 5 and in one patient was grade 4.

Symptomatic improvement

In patients who had seizures before starting treatment; 12 patients (50%) had controlled seizures; six patients (25%) had decrease in seizure frequency and six patients (25%) had same frequency of seizures. In the eight patients who had headaches

before starting treatment: seven patients (87.5%) had headaches controlled, and one patient (12.5%) had no change. In the all patients who presented with intracerebral +/- intraventricular hemorrhage, no one of them had any attacks of hemorrhage after embolization. With no other patients presented with bleeding.

Safety

Periprocedural problems occurred in three patients from the 42 patients (7.1%): dissection of PComA during

Histoacryl injection occurred in one patient; migration of Histoacryl to venous sinuses during embolization occurred in two patients. Complications occurred in three patients (7.1%): Seizures occurred in two patients; Intracerebral with intraventricular hemorrhage occurred in only one patient (2.4%).

Morbidity and mortality related to the procedures

There was minimal transient morbidity in one patient (2.4%) in the form of temporary decrease in visual acuity. There was permanent morbidity related to the procedures done in one patient (2.4%) in the form hemi-paresis grade 3. There was no mortality in this study of patients.

DISCUSSION

Current treatment of AVM of the brain complies three well established options: radiosurgery, endovascular therapy (embolization) and microsurgical resection. Radiosurgery is the simplest and least invasive, but 2 to 3 years are required to achieve total obliteration, and throughout this time there is the risk of bleeding, its use is limited to small AVMs. Embolization today plays a fundamental role more as an adjunct, rather than a single modality of treatment. Microsurgery has the advantage of being the only mode of therapy that offers a degree of immediate angiographic obliteration of almost 100% and is still the most widely employed, despite its morbidity rate also being highest. AVM management is an algorithm in which, according to size and localization, the three therapeutic options should be used alone or in combination. The management of these lesions requires a combined effort of all the factors that

can be of any help in the solution, and these modes are more complementary than competitive in situations in which they are all valid therapeutic options^(10,11,32). Endovascular embolization of intracranial AVMs can serve as a primary treatment (complete angiographic occlusion, staged angiographic occlusion, and/or occlusion of a nidus or pedicle aneurysm); adjuvant treatment (in preparation for surgery, in preparation for radiosurgery, intraoperative embolization); and palliative treatment (to reduce arterial steal phenomenon or progressive neurologic deficit, to reduce venous hypertension effects, to reduce headache, to reduce intractable seizures, to reduce high output cardiac failure). Efficacy indicators of AVM embolization include clinical and technical indicators. Clinical indicators are reduction of neurologic deficit; reduction of severity, duration, or frequency of headaches; reduction of severity, duration, or frequency of seizures; reduction of signs and symptoms of high output cardiac failure; and reduction of frequency of hemorrhagic events. Technical indicators are complete angiographic occlusion of the AVM, obliteration of the nidus or pedicle aneurysm, occlusion of targeted portion of the AVM, occlusion of the targeted feeding artery, and to diminished flow through the AVM^(1,30,32).

The successful treatment of arteriovenous malformations is a challenge for neurosurgeons, where a lot of AVMs may be considered untreatable on the basis of their size and location⁽⁴⁾.

In 1960, the first modern report on embolization of cerebral arteriovenous malformations (AVMs) appeared in the literature⁽²⁷⁾. There has been continuing development since then. The progress

has concerned materials and techniques as well as increased understanding of the lesions. The agents used for embolization have changed from materials like muscle, dura mater, silicon beads, polyene threads, and concentrated alcohol to the polyvinyl alcohol (PVA), mainly for preoperative embolization^(15,25).

More recently the Food and Drug Administration has approved N-butyl Cyanoacrylate (NBCA, Cordis Neurovascular, Inc., Miami, FL) for the treatment of cerebral AVMs (23, 25). The Onyx, (micro therapeutics, Inc., Irvine, CA) is a new, nonadhesive liquid embolic agent that is currently being evaluated, for embolization of intracranial arteriovenous malformations and aneurysms^(21,30).

Improved delivery devices have led to a change from surgical exposure, via balloons with calibrated leaks, to guidewire guided microcatheters like Tracker (Target Therapeutics, Fremont, CA) and flow-guided catheters like Minitorquer (Nycomed-Ingenor, Paris, France) and Magic (Balt, Montmorency, France). The improved devices have decreased the risk of vascular damage and increased access to the lesion^(15,25).

The endovascular treatment of cerebral arteriovenous malformations (AVMs) is a controversial topic because of the availability of alternative therapeutic options (surgery and radiosurgery), absence of standardized credentialing for the endovascular therapist, lack of uniformity of opinion regarding goals of therapy for individual patients, and variety of available interventional techniques and embolic agents. Moreover, the presence of an AVM confers the risk of death or permanent neurologic deficit to the patient, and endovascular therapy carries similar

significant risks. Choice of treatment method typically depends on clinical presentation; size, location, and angioarchitectural features of the AVM, and in many instances, the treatment capabilities of the team. The treatment applied should be less risky than the natural history of the disease process, which suggests a hemorrhage rate of approximately 3% per year^(1,30,32).

In this study the percentage of volume reduction ranged from 100% to 78.2% ,total occlusion (cured by embolization only) occurred in 10 patients (23.8%), reduction to a volume less than 4 cm³ (suitable for radiosurgery) occurred in 30 patients (71.4%), and in 2 patients (4.8%) reduction to a volume between 4-10 cm³.

Complete obliteration of AVMs by embolization only has been reported to be possible 16% by Berenstein presented at Val D'isere, in 1989. This statement fails to consider that most patients referred for embolization have very large lesions in difficult locations. If one considers large lesions with supply from multiple sources, (anterior, posterior and middle cerebral arteries and perforators), the incidence of complete obliteration will be zero⁽³⁾.

Many studies reported total occlusion by embolization to be 11.2% and 13%^(14,15) and up to 22% and 35%^(6,35), and size reduction to be suitable for radiosurgery in 63%, 66%, 74.1% and 76.8%^(14,15,21,30), with 4.8% failed treatment, and remaining 7% didn't reach a size suitable for radiosurgery⁽¹⁴⁾. However, in lesions supplied by one or two pedicles regardless of location, complete obliteration can be attained, in over than 95% of single pedicle lesions. With advances of embolization

technique, overall complete occlusion has exceeded 20% in all lesions^(3,35).

In this study, total occlusion rates and rates of size reduction to volumes suitable for radiosurgery is in average with that previously reviewed.

It was reported that small AVMs (volume $<4\text{cm}^3$) treated with stereotactic radiosurgery have a total obliteration rate of 80 to 88% 2 years after radiosurgery. However, equipment geometry and dose limitations diminish the obliteration rate to single stage radiosurgery to 58% for AVM volumes between 4 and 10cm^3 , with obliteration rates for AVM greater than 10cm^3 falling to 28%^(26,32).

Documenting the effect of reducing large AVMs to a manageable size and thereby increasing treatment efficacy Dawson et al.⁽⁶⁾ reported encouraging results in a small group undergoing initial staged embolization before stereotactic radiosurgery when the AVM nidus exceeded 10cm^3 in volume.

Aoyama et al.⁽²⁾ reported that single fraction stereotactic radiosurgery has proved to be effective, especially in AVMs smaller than 2 cm. Lindvall et al.⁽²⁴⁾ reported an overall obliteration rate of 83% in AVM with a mean volume of 11.5cm^3 by hypofractionated stereotactic radiotherapy.

Size reduction of AVMs prior to radiosurgery is very important because all radiosurgical series have reported a strong correlation between the size of the AVM and the rate of obliteration. Many series demonstrated an excellent obliteration rate with no difference between 1 to 4cm^3 and the 4 to 10cm^3 , which represented the majority of our cases. Also different studies demonstrated that, intravascular embolization should be considered

prior to Gamma Knife surgery in an attempt to reduce the hemodynamic stress and there by decrease the risk of hemorrhage. After embolization with Cyanoacrylate, the residual nidus of an AVM can be irradiated with results almost as good as in a native AVM of the same size and that preradiosurgery embolization with Cyanoacrylate allowed the successful irradiation of large AVMs that otherwise would not have been candidates for radiosurgery^(10,14,19,24).

N-butyl Cyanoacrylate embolization was reported to improve post-surgical outcome. The long-term evaluation continued to favour the surgery and embolization combination⁽⁷⁾.

In the eight AVMs with dural supply, the dural supply was embolized in the all eight AVMs.

Twenty AVMs had arterial steal, in six (30%) no improvement was achieved, in 14 (70%) arterial steal improved. In 26 AVMs with venous ectasies, in six patients (23%) there was no change, in ten patients (38.5%) venous ectasies showed decrease in size, , and in 10 patients (38.5%) venous ectasies disappeared. In ten AVMs with intranidal aneurysms, all intranidal aneurysms were initially embolized to prevent further rupture of such aneurysms.

It was reported that in patients with acute spontaneous hemorrhage after embolization of brain arteriovenous malformation with N-butyl Cyanoacrylate the presence of arterial steal phenomena in 87%, and multiple feeding arteries in 100%, and noted that the presence of such angioarchitectural features may be combined with postprocedural hemorrhage⁽³⁾. Stefani et al.⁽³⁴⁾ reported that the presence of venous ectasies were significant associating factor in

AVMs associated with hemorrhagic presentation. Holland et al.⁽¹⁸⁾ noted that perhaps the most significant course of non hemorrhagic neurological deficit is ischemia, where vascular steal may be a cause of.

In the current study, we tried improving the pathological angioarchitectural characteristics that are associated with the AVMs to decrease any risk factor of further complication, also we tried closing the dural supply of the AVMs as it was reported by Soderman et al.⁽³³⁾ that dural supply to an AVM is sometimes overlooked and that this oversight may sometimes lead to erroneous decisions and thus giving unfavourable cure to complication ratio as regard combined endovascular and radiosurgery therapy for AVMs.

Symptomatic improvement

In patients who had seizures before starting treatment: 12 patients (50%) had controlled seizures; six patients (25%) had decrease in seizure frequency and six patients (25%) had same frequency of seizures. In the eight patients who had headaches before starting treatment: seven patients (87.5%) had headaches controlled, and one patient (12.5%) had no change. In all patients who presented with intracerebral +/- intraventricular hemorrhage, no one of them had any attacks of hemorrhage after embolization. With no other patients presented with bleeding.

Many authors noted that there was a significant improvement with respect to headache and epilepsy (62.5% of patients) in patients who received either full or partial embolization^(14,15).

Bernestien et al.⁽³⁾ reported an incidence of rebreeding in 3% of his series. Gobin et al.⁽¹⁴⁾ reported that none of completely embolized AVMs had bled during the follow up period.

This corresponded to a postembolization bleeding rate of 3% per year during the period of follow up with a mean of 38.8 month, in partially embolized AVMs. He also reported that there was no correlation between the postembolization hemorrhage and the size of residual AVM. However all patients who bled postembolization had done so, before embolization. Whereas, no patients with an unruptured AVM bled after embolization.

Various studies of the natural history of AVMs suggest bleeding rates from 2% to 4% per year. It was also found that at 10 years the risk of bleeding from previously ruptured AVMs doubled when compared with unruptured lesions⁽⁵⁾.

Recanalization

Radiological follow up was done by 6 vessels digital subtraction angiography with external carotid arteries study for all cases at 6 month duration, stable embolization was in 41 cases with progressive thrombosis to complete obliteration in one case.

Different series, reported no recanalization in the AVMs embolized totally at follow up period ranging from four to six months^(14,35) and further thrombosis to total occlusion in previously embolized AVM up to 22% (six in 27 patients)⁽³⁵⁾. Yet Berenstein et al.⁽³⁾ reported that less than 2% of their patients had shown recanalization referring it to the presence of a patent shunt, and more to be in temporal and occipital lobes, and in areas with rich leptomenigeal collaterals.

Incidence of rebleeding

In Meisel et al.⁽²⁸⁾ study, it was reported that, the yearly hemorrhage incidence rate at all untreated patients was observed as 0.089%. This rate was 0.052 % in the subgroup of patients

who underwent partial embolization treatment for their AVMs later. He confirmed that the neurointerventional patients under their study show a lower hemorrhage risk established after the start of partial targeted embolization treatment of AVMs in two years.

Crawford et al.⁽⁵⁾ results about intracranial hemorrhage during the natural course show the lowest risk values compared to other published studies. There was a significant difference between his reference data and intracerebral hemorrhage incidence after the start of partial embolization treatment in the neurointerventional populations.

Post embolization morbidity and complications

Periprocedural problems occurred in three patients from the 42 patients (7.1%): dissection of PComA during Histoacryl injection occurred in one patient; migration of Histoacryl to venous sinuses during embolization occurred in two patients. Complications occurred in 3 patients (7.1%): Seizures in occurred two patients; Intracerebral with intraventricular hemorrhage occurred in one patient (2.4%). Different series

reported a rate of complications from 12.8 % complications and up to 39.3%^(14,15,16,17,22). Complications were related to haemorrhage in 9.3%, arterial dissection in 2.6%, vasospasm in 1.3%, thromboembolic events in 3.3%⁽¹⁴⁾.

In the current study, there was minimal transient morbidity in one patient (2.4%) in the form of temporary decrease in visual acuity. There was permanent morbidity related to the procedures done in one patient (2.4%) in the form hemi-paresis grade 3. There was no morbidity in this study of patients.

In a review of 1246 patients in 32 series over a 35 year period, temporary morbidity ranged from 0 to 50% and averaged 10%. Permanent morbidity ranged from 0 to 24% and averaged 8% and mortality ranged from 0 to 6% averaged 1%. Newer technologies had decreased the complication by one third. In the present review, permanent morbidity was 9% in series published before 1990 and 8% in series published since 1990, whereas mortality averaged 2% in series published before 1990 and 1% in series published since 1990.^(12,17,20,22)

Table (2): morbidity and mortality rates in variable studies

	Transient morbidity	Permanent morbidity	Mortality
Gunnar et al. ⁽¹⁵⁾	12.7%	6.7%	1.3%
Jahan et al. ⁽²¹⁾	13%	4%	-
Hartman et al. ⁽¹⁶⁾	14%	2%	2%
Meisel et al. ⁽²⁸⁾	5.3%	2%	-
Dowzenko and Jaworski ⁽⁹⁾	4.85%	2%	2%
Haw et al. ⁽¹⁷⁾			3.9%
Jayaraman et al. ⁽²²⁾	11.5 %		1.6%

CONCLUSION

Endovascular treatment of intracranial arteriovenous malformation is a valuable tool which is safe and efficient in selected cases, although it can lead to definitive treatment in a relatively low percentage, yet it can be used in larger AVMs (>10cm³) which are not candidate for other modalities, to allow successful size reduction to be candidate to other modalities (e.g. Radiosurgery). In addition it can improve clinical symptomatology of the patient and secure high risk angioarchitectural pathological characteristics of AMVs (That may cause failure of treatment or bleeding) during the period of follow up after radiosurgery. Long term follow is needed for patients with embolization and radiosurgery to assess the efficacy of such treatment combination. The decision and the planning of treatment of intracranial arteriovenous malformation must be carried in a multidisciplinary approach, were various neurosurgeon involved (vascular, endovascular, radiosurgery) has to assess the patient and design a plan to accomplish the goals of treatment.

Beside size reduction, endovascular embolization of arteriovenous malformation may be essential for other factors: embolization of dural supply of the AVM, securing high risk angioarchitectural pathological findings that may case bleeding during follow up period, and clinical symptomatic improvement. Further clinical and radiological follow up is essential for patients who will have radiosurgery after embolization of their AVMs, for assessment of the efficacy

and safety of such a treatment combination.

REFERENCES

1. **Accreditation Council on Graduate Medical Education:** Cerebral arteriovenous malformation. *AJNR*, 22: S10-S11, 2001
2. **Aoyama H, Shirato H, Nishioka T, Kagei K, Onimazu R, Suzuki K, Ushikoshis, Houkin K, Kuroda S, Abe H, Miyasaka K:** Treatment outcome of single or hypofractionated single-isocentric stereotactic irradiation (ST1) using a linear accelerator for intracranial arteriovenous malformation. *Radiotherapy oncol*, 59: 323-328, 2001
3. **Berenstein A, Lasjaunias P, Ter Brugge K G:** Cerebral vascular malformations, Goals and Objectives in the management of arteriovenous malformations. In Berenstein A, Lasjaunias P, Ter Brugge K G (eds). *Surgical Neuroangiography, Volume2.2, Clinical and Endovascular Treatment Aspects in Adults*, Springer-Verlag, Berlin Heidelberg; 609-736, 2004
4. **Chang SD, Marcellus ML, Marks MP, Levy RP, DOHM, Steinberg GK:** Multimodality treatment of giant intracranial arteriovenous malformations. *Neurosurgery* 53:1-14, 2003
5. **Crawford PM, West CR, Chadwick DW:** Arteriovenous malformations of the brain: natural history in unoperated patients. *J Neurol, Neurosurgery ,psychiatry*, 49: 1-10, 1986
6. **Dawson RC, Ton RW, Hech ST, et al.:** Treatment of arteriovenous malformations of the brain with combined embolization and sterotactic radiosurgery. *AJNR*, 11: 857-864, 1990
7. **DeMerill JS, Pile-spellman J, Mast H, Moohan N, Lu DC, Young WL,**

- Hacein-Bey L, Mohr JP, Stein BM:** Outcome analysis of preoperative embolization with N-butyl cyanoacrylate in cerebral arteriovenous malformations. *AJNR*, 16: 1801-1807, 1995
8. **Deruty R, Moret C, Turjman F. et al. :** Reflection on the management of cerebral arteriovenous malformations. *Surg. Neural*; 50: 245-256, 1998
9. **Dowzenko A, Jaworski M:** Endovascular embolization of cerebral arteriovenous malformations. *Neurol Neurochir*, 37 (4): 861-870, 2003
10. **Fernandez-Melo R, Lopez-Flores G, Cruz-Garcia O, Jordan-Gonzalez J, Felipe-Moran A, Benavides-Barbosa J, Mosquera-Betancourt G:** Modes of treatment for arteriovenous malformations of the brain. *Rev Neurol.*, 37 (10): 967-975, 2003
11. **Fiorella D, Albuquerque FC, Woo HH, McDougall CG, Rasmussen PA:** The role of Neuroendovascular therapy for the treatment of brain arteriovenous malformations. *Neurosurgery*, 95 (5 Suppl 3):S163-7, 2006
12. **Frizzel R, Tyler R, Wink F:** Cure, morbidity and mortality associated with embolization of brain arteriovenous malformations: A Review of 1246 patients in 32 series over a 35 year period. *Neurosurgery*, 37: 1031-1040, 1995
13. **Garretson HD:** Intracranial arteriovenous malformations. In Wilkins RH, Rengachary SS (eds). *Neurosurgery*, 2nd edition, New York, McGraw-Hill: 2433-2442, 1996
14. **Gobin PY, Laurent A, Merienne L, Schlienger M, Aymard A, Houdart E, Casasco A, Lefkopoulos D, George B, Merland JJ:** Treatment of brain arteriovenous malformation by embolization and surgery. *J Neurosurg*, 85: 19-28, 1996
15. **Gunnar W, Christer L, Paul S:** Transarterial embolization of cerebral arteriovenous malformations: improvement of results with experience. *AJNR*, 16: 1811-1817, 1995
16. **Hartmann A, Pile-Spellman J, Stapt c, Sciacca RR, Faulstich A, Mohr JP, Schumacher HC, Mast H:** Risk of endovascular treatment of brain arteriovenous malformations. *Stroke*, 33 (7): 18169-1820, 2002
17. **Haw CS, terBrugge K, Willinsky R, Tomlinson G:** Complications of embolization of arteriovenous malformations of the brain. *J Neurosurg*, 104(2):227-32, 2006
18. **Holland MC, Martin NA et al.:** Clinical presentation and diagnostic evaluation of intracranial arteriovenous malformation. In the practice of neurosurgery. In Tindal GT, Cooper RP, Barrow DL, (eds). *Practice of Neurosurgery*; 142: 2155-2171, 1997
19. **Inoue HK, Ohye C:** Hemorrhage risks of obliteration rates of arteriovenous malformations after Gamma knife radiosurgery. *J Neurosurg (Suppl 5)* 94: 474-479, 2002
20. **Jafar JJ, Davis AJ, Berenstein A, Choi IS, Kupersmith MJ:** The effect of embolization with N-butyl cyanoacrylate prior to surgical resection of cerebral arteriovenous malformations. *J Neurosurg*, 78: 60-69, 1993
21. **Jahan R, Murayama Y, Gobin YP, Duckwiler GR, Vinters HV, Vinuela F:** Embolization of arteriovenous malformations with Onyx: Clinicopathological experience in 23 patients. *Neurosurgery*, 48: 984-997, 2001
22. **Jayaraman MV, Marcellus ML, Hamilton S, Do HM, Campdell D, Chang SD, Steinberg GK, Marks MP:** Neurologic complications of arteriovenous malformation embolization using liquid embolic agents. *AJNR*, 29(2):242-6, 2008
23. **Kerber CW, Wong W:** Liquid acrylic adhesive agents in interventional Neuroradiology. *Neurosurg Clin N Am*, 11: 58-99, 2000
24. **Lindvall P, Bergstrom P, Lofroth**
-

- PO, Hariz M, Henriksson R, Jonasson P, Bergenheim AT:** Hypofractionated Stereotactic Radiotherapy for Arteriovenous Malformations. *Neurosurgery*, 53: 1-8, 2003
- 25. Linfante I, Wakhloo AK:** Brain aneurysms and arteriovenous malformations: advancements and emerging treatments in endovascular embolization. *Stroke*,38(4) :1411-7, 2007
- 26. Lunsford LD, Kondziolka D, Flickinger JC, et al.:** Stereotactic radiosurgery for arteriovenous malformations of the brain. *J Neurosurg*, 75: 512-514, 1991
- 27. Lussenhop AJ, Spence WT:** Artificial embolization of cerebral arteries: Report of use in a case of arteriovenous malformation. *JAMA*, 172: 1153-1155, 1960
- 28. Meisel HJ, Mansmann U, Alvarez H, Rodesch G, Brok M, Lasjaunias P:** Effect of partial targeted N-butyl cyanoacrylate embolization in Brain AVM. *Acta Neurochirurgica*, 144 (9): 879-888, 2002
- 29. Munoz F, Clavel P, Molet J, Castano C, De Teresa S, Solivera J, De Quintana C, Tresserras P, Rodriguez R, Bartumes F:** Current management of arteriovenous malformations. Retrospective study of 131 cases and literature review. *Neurocirugia*, 18(5):394-405,2007
- 30. Natarajan SK, Ghodke B, Britz GW, Borne DE, Sekhar LN:** Multimodality treatment of brain arteriovenous malformations with microsurgery after embolization with Onyx: single – center experience and technical nuances. *Neurosurgery*, 62:1213-26, 2008
- 31. Pierot L, Januel C, Herbreteau D, et al.:** Endovascular treatment of brain arteriovenous malformation using Onyx: preliminary results of a prospective multicenter study. *Interventional Neuroradiology*;11:159–64, 2005
- 32. Richling B, Killer M, Al-Schameri AR, Ritter L, Agic R, Kern M:** Therapy of brain arteriovenous malformations: multimodality treatment from a balanced standpoint. *Neurosurgery*, 95 (5 Suppl 3):S148-57, 2006
- 33. Soderman M, Rodesch G, Lasjaunias P:** Transdural Blood supply to cerebral arteriovenous malformations adjacent to the dura mater. *AJNR*, 23: 1295-1300, 2002
- 34. Stefani MA, Porter PJ, Ter Brugge KG, Montanera W, Willinsky RA, Wallace MC:** Angioarchitectural factors present in brain arteriovenous malformation associated with hemorrhagic presentation. *Stroke*, 33 (4): 920-924, 2002
- 35. Yu SC, Chan MS, Lam JM, Tam PH, Poon WS:** Complete obliteration of intracranial arteriovenous malformation with endovascular Cyanoacrylate embolization: initial success and rate of permanent cure. *AJNR*, 25(7):1139-43, 2004.
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