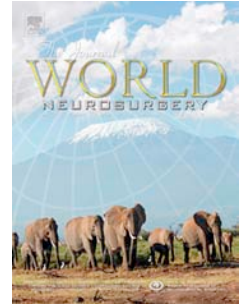


Accepted Manuscript

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PII: S1878-8750(14)00550-6

DOI: [10.1016/j.wneu.2014.05.037](https://doi.org/10.1016/j.wneu.2014.05.037)

Reference: WNEU 2397

To appear in: *World Neurosurgery*

Received Date: 8 August 2013

Revised Date: 20 November 2013

Accepted Date: 3 May 2014

Please cite this article as: D'Aliberti G, Talamonti G, Cenzato M, La camera A, Debernardi A, Valvassori L, Mariangela P, Nichelatti M, Arterial and Venous Aneurysms associated with Arteriovenous Malformations, *World Neurosurgery* (2014), doi: 10.1016/j.wneu.2014.05.037.

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Arterial and Venous Aneurysms associated with Arteriovenous Malformations.

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Abstract

Objective

Basing on the different hemorrhagic risk, this study aims to identify the prioritizations and indications for treatment of the arterial and venous “aneurysms” associated with arteriovenous malformation (AVM-AAV).

Methods

A total of 34 pts (8.5%) with 45 arterial or venous “aneurysms” were extrapolated from a global series of 400 consecutively treated AVMs. These 45 lesions were classified as: unrelated aneurysms (UR-type) = 5 cases (11.); flow-related aneurysms = 18 cases (40%); and intra-postnidal venous lesions (V-type) = 22(49%). The 18 flow-related aneurysms were further divided in remote (FR-type) = 6 cases and adjacent (FA-type) = 12 cases. Fifteen out of 45 AVM-AAs were unruptured with a 5 years mean follow-up.

Various possible risk indicators were considered and measured by univariate and multivariate analyses.

Results

During the follow-up, one of 15 unruptured aneurysms bled and the patient died. A significantly different bleeding incidence was found between UR-type and flow-related aneurysms ($p=0.002$). Moreover, bleeding was significantly less probable in FR-type than in V and FA -types ($p=0.007$). The location of the aneurysm resulted the only true risk factor for bleeding while the other parameters had no influence.

Conclusions

In our series, different subtypes of AVM-AAs had different clinical behaviours. The bleeding risk of the UR-type and the FR-type should be considered almost the same of any else unruptured aneurysm. That means it should be regarded just taking into account the INSUIA parameters

(location, size and morphology). Conversely, the FA-type the V-type present significantly higher hemorrhagic potentials.

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Introduction.

Patients with arteriovenous malformations (AVMs) present higher incidence of intracranial aneurysms than the general population. The aneurysms associated with AVMs (AVM-AAAs) would account for 7% to 23% in large AVM series (22,30,33,38), but the quoted rates could be even higher using superselective catheterization for digital angiography (DA) (10,26,30,39). Several Classifications have been proposed for AVM-AAAs (7,24,31,33). They can be grossly divided in perinidal and intra-postnidal aneurysms. The former are exclusively arterial lesions and may be subdivided in: 1) Flow unrelated type (UR-type), 2) Flow related remote type (FR-type), 3) Flow related adjacent type (FA-type); the latter are exclusively venous lesions (V-type) (Figure1). The natural history of the AVM-AAAs, as well as the proper management strategies are not yet well delineated because the pathophysiology of the different aneurysm types still remains poorly understood. For instance, data are lacking about the real nature of so called “venous aneurysms” and “pseudoaneurysms” (2,3,4,12,21,27,30,33). It is now recognized that AVMs usually bled at the level of the draining veins. These veins frequently present anomalies such as pouches and varices, which may be near or into the nidus of the ruptured AVMs, and which are often inappropriately termed “*venous aneurysms*” (24,32). These venous dilatations are known to carry high potential of rupture. Practically, wrong terminology and misinterpretation of the angiographic findings may lead to the erroneous attribution of elevated bleeding risks to the AVM-AAAs rather than to the intra or perinidal venous dilatations. This can be avoided using superselective angiography which can provide nice differentiation between aneurysms adjacent to the AMN nidus (such as the aneurysms arising on perforators or the “pseudo-aneurysms” originating from the rupture of thin-walled vessels) (31) and intra- or perinidal venous dilatations (32) (Figure 2).

In this paper, from our global series of 400 consecutively treated AVMs, we extrapolated 34 patients harbouring 45 AVM-AAAs. These cases were retrospectively reviewed and the main features, the angiographic patterns, the treatment modalities and the outcomes were analyzed and correlated.

Material and Methods

Clinical data

During the last 15 years, a total of 400 consecutive pts underwent treatment for cerebral AVMs at the Department of Neurosurgery of the Niguarda CA' Granda Hospital, Milan, Italy. In this series (citare il nostro articolo), a total 199 pts (49.7%) presented with hemorrhage, which was related to aneurysm rupture in 30 cases (15%). The global AVM series also included 4 patients (1%) with associated aneurysm but without any history of cerebral hemorrhage. Accordingly, a total of 34 pts (8.5%) with AVM-AAs could be extrapolated from the global series.

These 34 pts represent the core matter of this study. They harboured an overall number of 45 cerebral AVM-AAs. The male/female ratio was 1/1, while age ranged from 6 to 64 years (mean 37.8 years). As aforementioned, the clinical presentation consisted of hemorrhage in 30 cases (88.2%); the 4 pts (11.8%) without hemorrhage presented with seizures. All pts were postoperatively evaluated through the modified Rankin scale (Table 1) (40).

Initial radiological assessment

All pts were studied by Computer Tomography (CT)-scan, Magnetic Resonance Imaging (MRI) and Digital Angiography (DA). The main angiographic features are summarized in Table 2. The AVMs were classified according to the Spetzler and Martin Grading System (35): there were 2 Grade 1 (5.8%), 11 Grade 2 (32.3%), 16 Grade 3 (47%), 5 Grade 4 (14.7%) and no Grade 5. Twenty-five pts (73.5%) harboured a single aneurysm, while 2 and 3 aneurysms were respectively reported in seven (20.5%) and two (5.9%) pts. The aneurysm diameter was less than 10 mm in 41 cases; more than 10 mm in 2 cases; more than 15 mm in 2 cases.

The 45 AVM-AAs could be classified as follows: 5 UR-type (11.1%), 6 FR-type (13.3%); 12 FA-type (26.6%); 22 V-type (48.8%). Using superselective angiographies, we could recognize 3 main types of venous aneurysms: 1) *Venous Pouches*: these were blebs originating on the venules of the nidus and had no defined relationship with the draining veins. They were usually small and multiple

(Figure 2 A and B); 2) *Venous aneurysms*: these resembled true berry aneurysms and were located into or strictly close to the nidus, originating on the first tract of the main AVM drainage (Figure 2 C and D); 3) *Variceal enlargements*: these consisted of wall blebs due to progressive wall wearing, were located more distally on the draining veins and were quite similar to the same venous dilatations that can be met in other organs (Figure 2 E-F-G).. Sometimes, such enlargements were so wide to represent properly termed varices (Figure 2 H-I).

The relationships between bleeding as presenting symptom and the various aneurysm types are reported in Table 3. Two main groups of pts could be considered: *Group 1*: 30 pts with bleeding aneurysms and *Group 2*: 4 pts with unruptured aneurysms.

Group 1. In all these 30 pts, the clinical presentation consisted of cerebral hemorrhage due to the aneurysm rupture. The initial CT-scan showed subarachnoid hemorrhage (SAH) in 5 cases (16.7%), intraventricular hemorrhage (IVH) in 15 cases (50%), and intracerebral hemorrhage (ICH) in the remaining 10 cases (33.3%). All the cases of SAH were caused FA- or FR-types aneurysms; all the cases of IVH and ICH were ascribable to FR- or V-types aneurysms. In other words, the clinical presentation with hemorrhage was ascribable to arterial aneurysms in 12 cases (1 FR-type and 11 FA-type), and to “venous aneurysm” (V-type) in 18 cases.

Group 2. In these 4 pts, the clinical presentation consisted of seizures without any evidence of cerebral hemorrhage. Of course, in these cases, the clinical manifestations were to be related to the AVM rather than to the aneurysms, which were to be considered asymptomatic.

Statistical methods

All variables were analyzed using the usual descriptive methods. Cross-tabulations of categorical variables were checked by the Fisher's exact test, whereas the general linear model (GLM) with logistic link (using the standard, as well as the exact algorithm) was used to evaluate the association between bleeding and all the other variables in univariate and multivariate modeling. All analyses were carried out using the Stata/SE 13.0 package. The statistical significance was assumed for $p < 0.05$.

Treatment

Different therapeutic modalities (surgery, endovascular embolization, radiosurgery, or their combination) were selected basing on the presumed risk of the management. In general, facing with AVMs and aneurysms, the management of the symptomatic lesion was prioritized.

Group 1: Emergency surgery (ventriculostomy) was required only by 10 pts with IVH and acute hydrocephalus. Indeed, 1 pt with massive SAH underwent early clipping and concomitant AVM excision. All the other pts (including those with ICH) could be treated on elective basis. In all cases, treatment prioritization was addressed to the bleeding lesions, that were the aneurysms in all cases. When possible, both aneurysm and AVM were simultaneously managed.

Group 2: In all these cases, the AVM was first managed. Then, 2 pts were conservatively managed, whereas 2 underwent aneurysm embolization. One of these 2 pts harboured 2 V-type aneurysm: one was endovascularly treated, the other was left untouched waiting for AVM radiosurgery. Unfortunately, 6 months after embolization, lethal hemorrhage occurred.

Treated and not treated aneurysms are reported in Table 4.

In general, the 34 AVMs were treated as follows: 14 pts underwent embolization plus radiosurgery; 8 pts embolization followed by microsurgery; 7 pts direct microsurgery; 3 pts embolization only; 2 pts radiosurgery only. All the 30 aneurysms presenting with hemorrhage were treated: 7 by clipping

and 23 by coiling; conversely, only one of the 15 unruptured aneurysms underwent endovascular treatment, whereas 14 were conservatively managed.

The follow-up ranged between 6 months and 12 years (mean = 5 years).

Results

Clinical Outcome and Follow up

The overall results are summarized in Table 1: Rankin 0-1 was reported in 24 pts (70.6%), Rankin 2-3 in 7 pts (20.6%), and Rankin 4-5 in 2 pts (5.9%).

There was 1 case of mortality (2.9%). This is the aforementioned pt who died because of the rupture of a residual V-type aneurysm while she was waiting for radiosurgery. Severe morbidity was reported in 2 pts (5.9%), and consisted of treatment-related hemorrhages in both cases: one case of postoperative hemorrhage requiring reoperation, but not affecting the final neurological outcome; one case of embolization-related hemorrhage requiring clot removal and concomitant AVM excision which was responsible of permanent disability (Rankin 3). Moderate disability was reported in an overall number of 7 pts (20.6%) and **was mainly related to the initial hemorrhage.**

Statistical analysis

These series included an overall number of 31 pts who experienced cerebral hemorrhage due to the rupture of AVM-AAs. In 30 cases, the hemorrhage represented the presenting symptom, while in 1 case, an initially unruptured V-type aneurysm bled 6 months after the treatment of another analogous V-type aneurysm. The total time at risk for the whole cohort was 70.5 patient-year.

As to the different types of AVM-AAs, the 5 UR-type aneurysms were responsible for no hemorrhage (0/5 cases); conversely, the 40 flow related aneurysms were responsible for 31 cases of hemorrhage (77.5%). This difference in bleeding frequency between the UR-type and the flow related types was significant (Fisher's exact test: $p = 0.002$). As to the subtypes of flow related lesions, the crude percentage of bleeding was 16.7% in FR-type aneurysms (1/6 cases), was 91.7% in FA-type aneurysms (11/12 cases), and was 81.8% in V-type aneurysms (18/22 cases). The

logistic model with exact algorithm shows that bleeding was significantly less probable in FR- and UR-types aneurysms than in V-type ($p = 0.0132$ and $p = 0.0031$, respectively) (Table 5). Also, the logistic model shows that bleeding was significantly less probable in FR and UR-types aneurysms than in V- and FA-types ($p = 0.0040$ and $p = 0.0009$, respectively). **In particular, the probability of bleeding of FR-type versus V- and FA-types was only 3.78%, while the probability of UR-type vs V- and FA-type was 3.12%.**

Fitting a multivariate logistic model containing aneurysm type, grade, size, drainage, Rankin scale and recruitment of cortical veins, we saw that the only significant variable affecting the bleeding was the presence of a FR-type versus V- and FA types ($p = 0.007$) (Table 6). This clearly means that – even if our sample size is small – the only factor apparently involving bleeding is the topographic position of the aneurysm, and not the other parameters.

Illustrative cases

Case 1

A neurologically intact 45-year-old woman was referred to us with acute onset of severe headache. Emergency CT scan of the brain showed a basal cistern SAH (Figure 3A). The initial DA with 3-D reconstructions (Figure 3 B,C,D) showed a large ruptured left middle cerebral artery. This proximal aneurysm was on a main feeder of a grade II (35) temporal AVM and was **classifiable as a FR-type aneurysm**. The patient underwent immediate surgery with direct aneurysm clipping and AVM excision. The post-operative DA documented the cure of both lesions (Figure 3E). Fifteen days after surgery, the patient was discharged without any neurological deficits. Nine years later, she was neurologically intact and MRI showed no ischemic lesions (Figure 3F).

Case 2

A 60-year-old man was admitted to our department with a slight frontal syndrome. Six months before, he had complained for IVH. On MRI, a cavity was evident at the margin of the area of the previous IVH (Figure 4A). DA (Figure 4 B) showed a **paraventricular** grade III (35) AVM fed by perforators of the middle cerebral and anterior choroidal arteries associated with a “venous aneurysms” on the draining thalamo-striatal vein (V-type aneurysm). This patient underwent direct surgery through a right transcalsal trans-ventricular approach. Intraoperative findings confirmed the presence of a venous aneurysm at the origin of the venous drainage (Figure 4C). The AVM was excised and the drainage obliterated. Post-operatively, the frontal syndrome transiently worsened but returned to the preoperative level within 10 days. Control DA documented the cure of both the malformations a (Figure 4D). The patient remained well for 15 years but ultimately died for a pancreatic cancer.

Discussion.

Pathophysiology of the AVM-AAAs

The term aneurysm correctly refers just to a circumscribed dilatation of an artery. In fact, the definition “venous aneurysm” is not nosologically correct and merely refers to a venous varix. However, the term “venous aneurysm” entered the common medical jargon and is commonly used in clinical practice (10,24,32).

The AVM pathogenesis is not yet completely understood particularly for what concerns the associated aneurysms. A role is likely played by the vessel stress due to the overload caused by the arteriovenous shunt. Three particular items about the AVM pathogenesis should be considered. First: surgical findings and pathological studies clearly demonstrated that the excised AVM nidus is

a conglomerate of venous tangles and loops (14). That means the venous drainage begins at the nidus level with the arterial vessels ending just before, so that the arteriovenous shunt would occur a little bit proximal to the nidus. Second: several Authors (5,6,8,29) focused on the role of the so-called “red veins”. These AVM draining veins contain arterialized blood and sustain arterial pressure. Therefore, they may be easily mistaken for arteries and their wall may be easily disrupted. Third: both the arterial and venous AVM components express the S2 marker, which indicates a contractile phenotype of smooth muscle cells. Accordingly, the venous components of cerebral AVMs can be easily misinterpreted as arterial parts (16). There are three main hypotheses about the origin of the AVM-AAs: 1) both lesions are congenital malformations (2); 2) their association may be casual and accidental(13,23); 3) the aneurysm may occur due to hemodynamic stress related to the AVM increased flow (1,9,20,25,27). This flow-related hypothesis would be supported by the rare cases of aneurysm enlargement associated with ruptured AVM (11), by the higher incidence of aneurysms in case of high-flow AVMs, and by the well documented possibility of aneurysm shrinkage following the abolition of the AVM flow (22,27,28,33,36). In our mind, these hypotheses do not contradict each other, but may be all valid since different types of AVM-AAs do exist.

Relationships between AVMs and Aneurysms

The overall incidence of AVM-AAs would range from 5% to 50% in the main AVM series (22,26,30,33,38). Of course, the flow-related aneurysms are more likely in large and high-flow AVMs (1,21,27,28,33,35). In fact, in our series, in 21 of 34 pts (62%) with aneurysms, the associated AVM was Grade 3 or 4.

Basing on their relationships with the AVM nidus, the AVM-AAs may be grossly divided in prenidial (arterial aneurysms) or in intra- and post-nidal aneurysms (“venous aneurysms”). The prenidial aneurysms are more likely flow-related and tend to be concentrated on the own AVM vessels and may be on turn divided into remote (FR-type) and adjacent (FA-type) according to their

location regarding the AVM nidus. Indeed, some distal arterial aneurysms should be properly considered as “pseudo-aneurysms” because they develop from disruption of thin-walled vessels during the acute phase of the hemorrhage. These false aneurysms can be differentiated from the true FA-type aneurysms because they were not present before the hemorrhage, otherwise because the superselective DA shows typical features of dissecting lesions such as persistent filling defects, stenosis, and so on (12,33,37). Of course, such lesions cannot be actually considered as aneurysms and should be not included in the risk analysis (33).

Most of the AVM-AAs (up to 70%) that are reported in the Literature are described on the feeding arteries, whereas the intra- and post-nidal aneurysms are relatively a few (33). It is our opinion that the incidence of FA- and V-types aneurysms could be quite higher if superselective catheterization for diagnostic angiography would be used more extensively (10,15,24,26,30,39).

In case of hemorrhage, the method to attribute bleeding to the aneurysm or the AVM represents a not yet completely settled question. There are cases where the bleeding lesion is easily identifiable: for instance, SAH in presence of an aneurysm well embedded in the CSF space with a distal AVM, such as in our illustrative Case 1. Clearly, when the aneurysm is close to the AVM, the origin of hemorrhage may be less simple to be understood. According to some Authors (12,31,33), hemorrhages can be attributed to FA- or V-types aneurysms when these lesions appear on DA or MRI as **cavities into or** at the margins of hemorrhagic areas (such as in our Illustrative case 2). Pritz et al (32) carefully described hemorrhages due to venous dilatations in their AVM series. In the vast majority of their cases, the MRI showed blood around the venous lesions, **such as in the case we are reporting in Figure 2(E-F-G).**

Hemorrhagic Risks of the AVM-AAs

The yearly cumulative risk of hemorrhage for AVM-AAs has been estimated at 7% for year in case of unruptured AVM (3,33). This rate appears quite higher than the bleeding risks of both unruptured aneurysms < 10 mm (about 1% for year) (17,18,19,34) and unruptured AVMs (about 2-4% for year) (10).

Thompson et al (38) tried to predict the risk of hemorrhage for AVM-AAs: these Authors found that the pts age and the number of aneurysms had no statistically significant influence. Lv et al. (24) **reported greater risk of hemorrhage in patients with proximal aneurysms than in patients with intranidal aneurysms** and recommended immediate treatment in all cases of AVM-AAs. However, this advice appears not completely sharable: other Authors (26,33) identified the intranidal aneurysms as the more dangerous with a yearly risk rate of hemorrhage of 9.8 %. Moreover, the proximal (FR-type) aneurysms, such as the so-called pedicle aneurysms, may significantly decrease or even disappear when they are not treated at time of AVM obliteration (26,27,28,33). Miyasaka et al (27) reported an overall shrinkage rate of 14% for AVM-AAs during the course of treatment of the AVMs. Redekop et al (33) reported 50% of spontaneous regression of untreated AVM-AAs following Gamma-Knife surgery for AVMs. These Authors even reported complete resolution of FA- and V-types aneurysms in 80% of cases provided that the AVMs were completely obliterated. These higher regression rates in distal than in proximal aneurysms was reported only by these Authors, who tried to explain these figures by the radiosurgical effect of decreasing the blood flow into the nidus.

Analysis of our series

Our global series of 400 cerebral AVMs did not include any case of UR-type aneurysm that presented with hemorrhage. Moreover, none of these aneurysms bled during a **mean** follow-up of 5 years. Therefore, we think that these remote aneurysms have the same risks of any other cerebral aneurysm not associated with AVM, that means their bleeding propensity should be estimated basing on their size and location just as in case of any unruptured cerebral aneurysm (17,18). Conversely, the hemorrhagic risks resulted undoubtedly higher in flow-related aneurysms with bleeding propensity influenced by aneurysm size and above all by aneurysm location regarding the AVM nidus. At the same time, the risk of rupture for flow related aneurysms resulted unaffected by the AVM angio-architecture (type of drainage, grade, and recruitment of cortical veins). We do realize our sample size is small, but the relationships between aneurysm location and AVM nidus appeared as the only crucial factor for hemorrhage.

Under any aspect, the UR-type aneurysms must be considered as common unruptured aneurysms and may be treated or not independently from the AVM management; conversely the flow-related lesions are riskier and may entail more aggressive indications for treatment, especially if they are close to the nidus or even on the venous site. Accordingly, we do not believe that treatment is *tout-court* always indicated in all cases of AVM-AAs, regardless their type.

Among the flow related aneurysms, the FR-type lesions represent an intermediate type and share some aspects with the UR-type. Our series included 6 pts with FR-type AVM-AAs: one of these pts harbored an aneurysm larger than 10 mm (Figure 3); this was the only pt experiencing hemorrhage as presenting symptom; conversely, in the remaining 5 pts, the aneurysms were less than 10 mm and completely asymptomatic; no treatment was initially indicated but no bleeding occurred throughout the follow up. These data probably mean that, likewise in UR-type aneurysms, even in the FR-type the risk of hemorrhage does not significantly differ from that of general unruptured aneurysms (17,18).

On the other hand, the FA- and the V-types aneurysm appeared to behave quite differently. Their bleeding rates were respectively 91.7% and 86.4% (19/22). Accordingly, we can state that aneurysms which are adjacent, intranidal, or postnidal are high risk lesions. These lesions share the fact that they are close to the AV shunt, that means they originate where the flow, the pressure and the shearing stress on the vessel wall are greater. According to Elhammady et al (10), **both the small adjacent** arterial dilatations, which can be seen close to the nidus (for example aneurysms fed by perforators arteries) and the intra-postnidal aneurysms (venous dilatation) have a displastic etiology. Probably, at nidus level, there are aneurysms on the proximal feeders, which are properly to be considered arterial, and intra-nidal and post-nidal aneurysms, which are properly to be considered venous. Anyway, several Authors (5,6,8,14,16,29) outlined the similarities between the vessels forming the AVM nidus and those forming the drainage. Therefore, in cerebral AVMs, it is quite difficult (maybe impossible) to identify precisely the point where the arteries end and the veins start. Regardless if it is arterial or venous, vessel wall dilatations originate because of the continuous action by the blood with increased flow and pressure (20). Undoubtedly, hampered venous outflow with venous engorgement and venous hypertension increases the probabilities of dilated vessels and ruptures. Venous ectasiae, varices, pouches, and “venous aneurysms” (Figure 2) are known as risk factors for hemorrhage, whereas AVMs without any venous anomaly are unlikely to bleed. Therefore, it is probable that such vessel dilatations (either *venous-like* on the arterial site or *true-venous* on the venous site) can account for the higher propensity to bleed of FA- and V-types aneurysms. The type of hemorrhage represents another confirmation of the higher dangerousness of the FA- and V-types lesions: most hemorrhages due to the rupture of AVM-AAs are intracerebral and/or intraventricular, that is close to the nidus (such as in Illustrative case 2); conversely, there are few reported cases of AVM-AAs causing SAH (such as in Illustrative case 1), as it should be expected if the bleeding originated from true arterial (UR- and FR-types) aneurysms. The aneurysm size is generally known as a predictor of the hemorrhagic risk. The ISUIA studies (17,18) estimated that previously unruptured aneurysms less than 7 or 10 mm have an annual risk

of rupture ranging from 0.05% to 0.8 %. In our series of AVM-AAs, there was only 1 bleeding aneurysm larger than 10 mm. As already mentioned, this was a FR-type aneurysm, and the major role in aneurysm rupture was probably played by the size rather than by the location or the association with AVM. Indeed, the vast majority of bleeding aneurysms were FA- and V-types lesions smaller than 10 mm. In these cases, it was the location near the nidus to play the major role in determining the hemorrhage in comparison with the size.

The identification of the different AVM-AAs is not merely academic since the misinterpretation of the aneurysm origin may lead to the attribution of different risk of bleeding. Although we found different behaviours in different aneurysms, indeed, the risk of bleeding for each given unruptured AVM-AA remains not precisely quantifiable. Furthermore, presently there are no reliable information about the risk of rebleeding. We think that a perspective study with a higher number of enrolled pts is needed.

Conclusions

The retrospective analysis of our series showed that the association of aneurysms and AVMs is not exceptional. Most of these aneurysms presented with hemorrhage, and when hemorrhage occurred, the bleeding lesion was always the aneurysm. Different types of AVM-AAs carry different hemorrhagic risks. The UR-type and the FR-type have the same risk of any other cerebral aneurysms. That means they should be regarded taking into account their location, size and morphology as reported by the INSUIA Studies. The FA-type and the V-type are quite more dangerous. Accordingly, the correct identification of the type of aneurysm is mandatory. This may be accomplished through the careful interpretation of the angiographic visualization times which allows the differentiation between arterial lesions (UR- and FR-types) and FA-type or true venous lesions (V-types).

The need for correct recognition of the various AVM-AAs cannot be overemphasized. The prioritization and indications for treatment should be addressed taking into account the type of AVM-AA one is facing and its different hemorrhagic risks.

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Figures

Figure 1. Schematic drawing of the different AVM-AAs. Basing on their relationships with the AVM nidus, these may be divided in prenidial (arterial aneurysms) or in intra- and postnidial aneurysms (venous aneurysms). The prenidial aneurysms are: 1- Unrelated (UR-Type); 2-3 flow-Related Remote (FR-type) and Adjacent (FA-type) respectively. The intra- and post-nidal are “venous aneurysms” (V-Type): 4-*Venous Pouches*: wall blebs originating on the venules of the nidus or true berry aneurysms originating on the first tract of the main AVM drainage.; 5-*Variceal enlargements*: wall blebs located along the venous drainage; 6- varix

Figures 2. The main angiographic features of different intra- and post-nidal venous aneurysms. A- Cerebral MRI (T1-weighted) showing a cavity (arrow) at the margin of the area of hemorrhage, B- cerebral angiography showing a right mesial temporo-occipital AVM fed by posterior cerebral branches with intranidal “*Venous Pouches*”: these were blebs originating on the venules of the nidus and had no defined relationship with the draining veins (arrow). C- CT scan showing an intracerebral parieto-occipital hemorrhage D: Cerebral angiography showing a small ruptured parietal AVM: a true berry “Venous Aneurysm” originated on the first tract of the main AVM drainage (arrow); E-F-G: Cerebral MRI and DA showing of a small ruptured temporo-basal AVM with a haemorrhage around “*Variceal Enlargements*” (arrow): this consisted of wall blebs due to progressive wall wearing, located more distally on the draining vein (arrow); H-I: DA showing a wide venous drainage enlargement of the left parietal AVM properly termed “*Varix*”.

Figures 3. A: TC scan showing SAH at the basal cistern; B-C-D: cerebral angiography with 3D reconstruction showing a large ruptured left middle cerebral artery aneurysm on the main feeders of a grade 2 temporal AVM; E- Post-operative angiography showing surgical clipping of the aneurysm and removal of the malformation; F: 9 yrs follow-up cerebral MRI was negative for ischemic lesion.

Figures 4. A- Cerebral MRI showing a cavity (arrow) at the margin of the area of an intraventricular hemorrhage B: DA showing a small deep AVM fed by middle cerebral artery perforators with a small ectasic venous drainage; C: intra-operative image (transcallosal-transventricular approach) showing a venous aneurysm at the level of the venous drainage origin; D: post-operative cerebral angiography showing the surgical removal of the malformation and the venous aneurysm.

Table 1: Post-operatively patients evaluation by the modified Rankin-Scale. Wilson et al, 2005(40); Spetzler and Martin, 1986 (35)

	G I	G II	G III	G IV	G V	N.	%
Rankin 0-1	2	9	11	2	-	24	70,6
Rankin 2-3	-	1	5	1	-	7	20,6
Rankin 4-5	-	-	-	2	-	2	5,9
Rankin 6	-	1	-	-	-	1	2,9
No pat.	2	11	16	5	-	34	100

Pat=patients; G = grade

Table 2: Main angiographic features of 34 AVMs associated with aneurysms Spetzler and Martin, 1986 (35)

	Size		Drainage		Recruitment	
	≤3	>3	S	D	0	1
Grade I (2)	2	-	2	-	2	-
Grade II (11)	10	1	10	1	10	1
Grade III (16)	9	7	3	13	10	6
Grade IV (5)	-	5	-	5	-	5
Tot. (34)	21	13	15	19	22	12

Table 3: Hemorrhage as the presenting symptom correlated with the various aneurysm types

Bleeding	Type of aneurysm				Tot.
	FA-type	FR-type	V.type	UR-type	
N	1 6.67	5 33.33	4 26.67	5 33.33	15 100.00
Y	11 36.67	1 3.33	18 60.00	0 0.00	30 100.00
Tot.	12 26.67	6 3.33	22 48.89	5 11.11	45 100.00

* One of these aneurysms bled during the follow-up

FA = flow-related adjacent aneurysms ; FR = flow-related remote aneurysms ; V = intra-postnidal "venous aneurysms". ; UR = unrelated aneurysms.

Table 4 Treated and not treated aneurysms

Treated	Type of aneurysm				
	FA-type	FR-type	V-type	UR-type	Tot.
N	2	5	2	5	14
Y	10	1	20	0	31
Tot.	12	6	22	5	45

FA = flow-related adjacent aneurysms ; FR =: flow-related remote aneurysms ; V = intra-postnidal “venous aneurysms”. ; UR = unrelated aneurysms.

Table 5: odds ratio of bleeding of FA,FR and UR- types vs. V- type and p-values, by univariate logistic regression with exact algorithm

Bleeding	Odds Ratio	95% CI for OR		Significance
FA-type vs V- type	1.71086	0.11962	99.34712	p > 0.9999
FR-type vs V- type	0.05190	0.00089	0.62673	p = 0.0132
UR-type vs V -type	0.04364	0.00000	0.37817	p = 0.0031

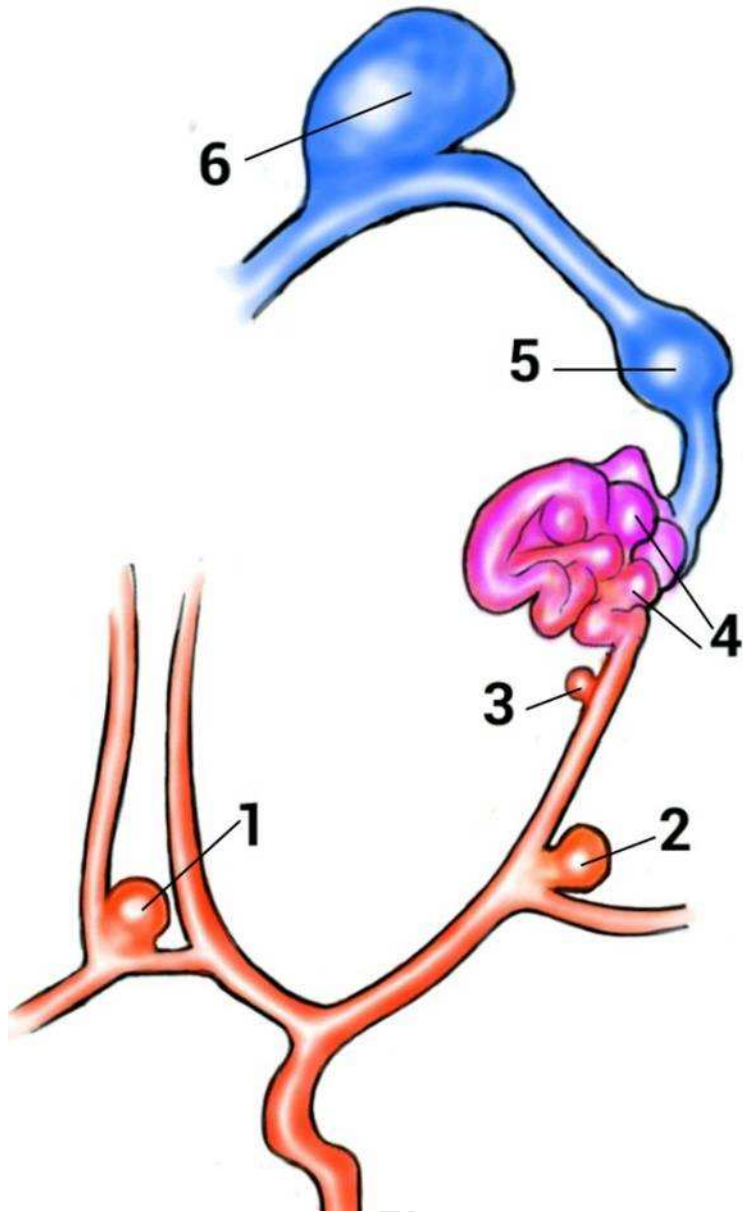
FA = flow-related adjacent aneurysms ; FR =: flow-related remote aneurysms ; V = intra-postnidal “venous aneurysms”. ; UR = unrelated aneurysms.

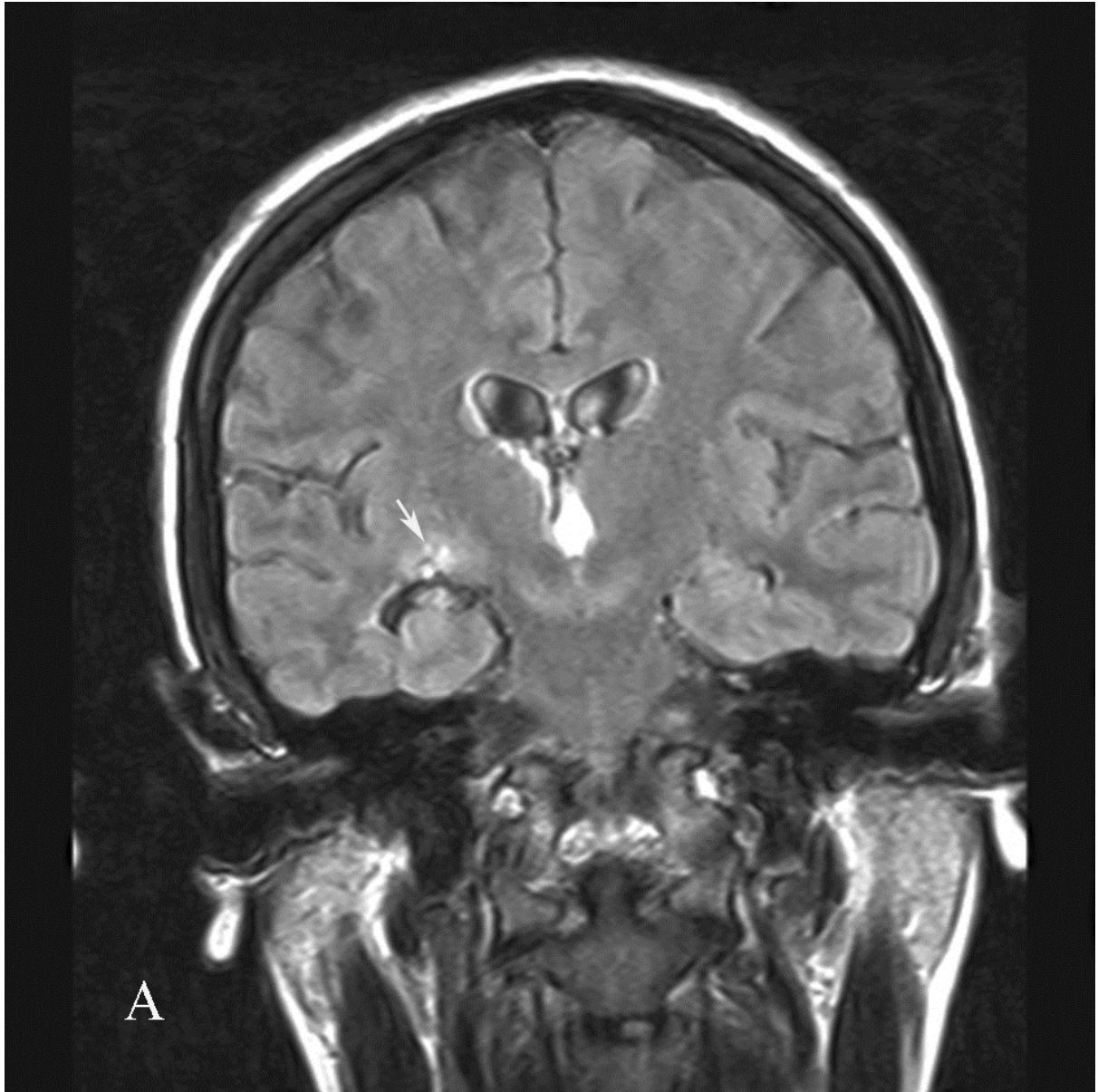
Table 6: odds ratio of bleeding of FR and UR types vs. V+D-types together and p-values, by multivariate logistic regression with standard algorithm

Bleeding	Odds Ratio	95% CI for OR		Significance
FR-type vs V+D types	0.01473	0.00070	0.31073	p=0.007
SM grade	0.18716	0.00861	4.06883	p=0.286
AVM-size	2.65783	0.16186	43.64297	p=0.494
Deep drainage	1.02859	0.03110	34.02294	p=0.987
Recruitment	2.82100	0.09421	84.47199	p=0.550
Rankin-Score	1.36824	0.39013	4.79862	p=0.624

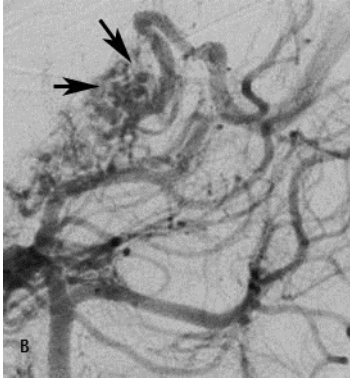
FR = flow-related remote aneurysms ; V = intra-postnidal “venous aneurysms” ; D = distal ; SM = Spetzler and Martin ; AVM = arteriovenous malformation

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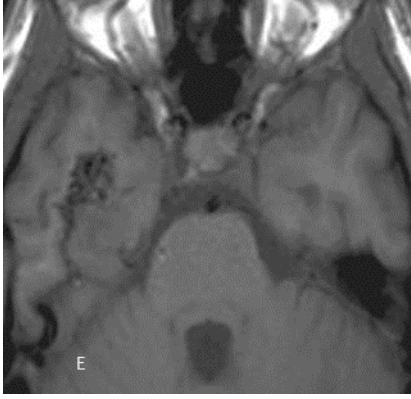
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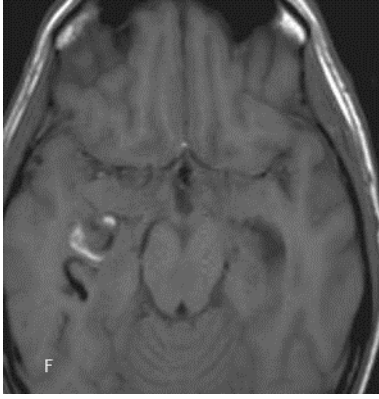
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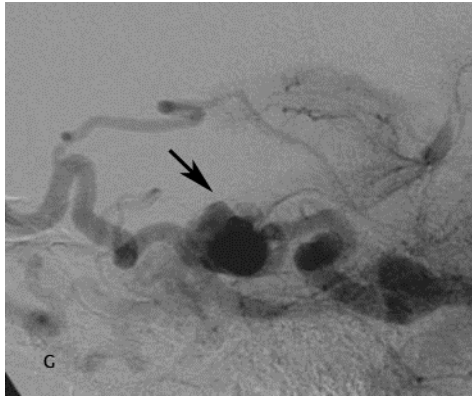
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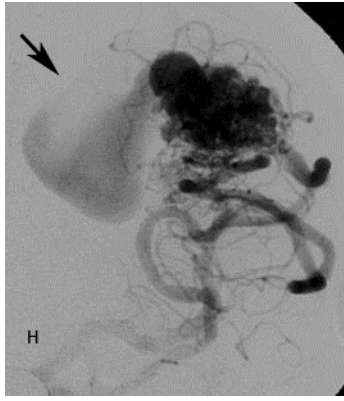
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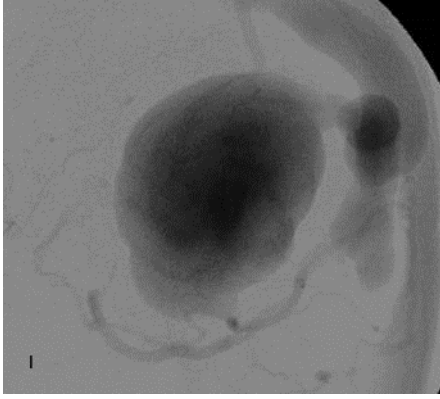
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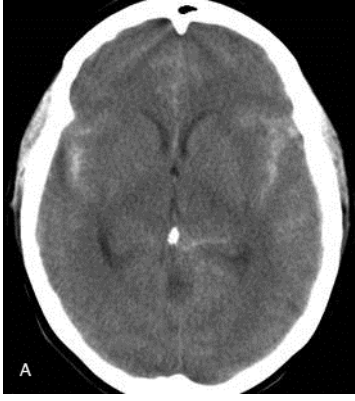
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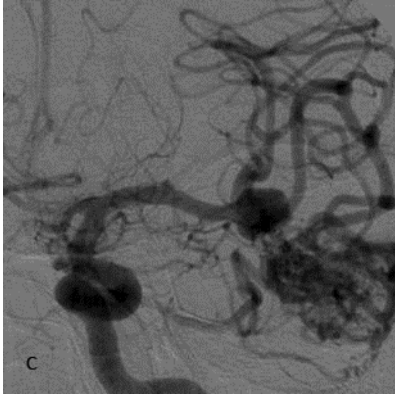
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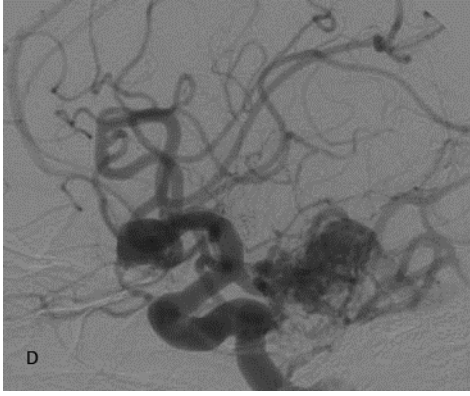
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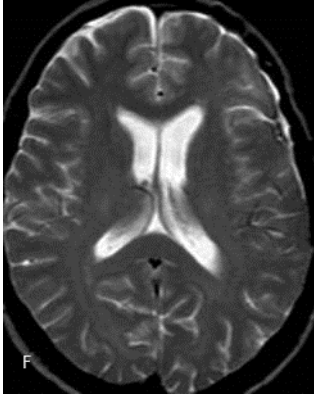
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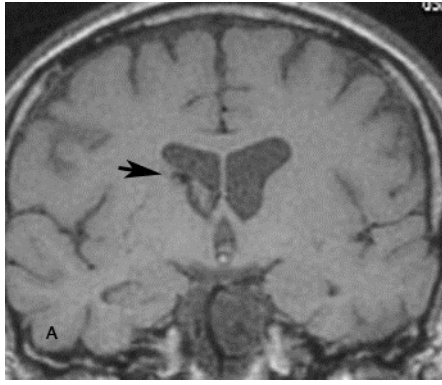
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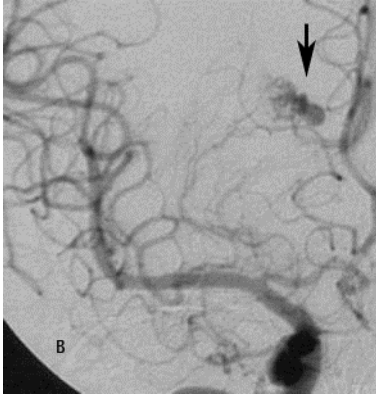
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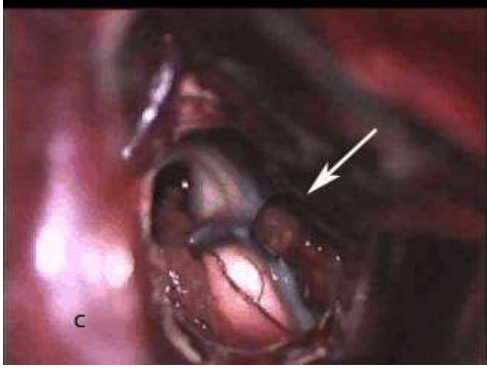
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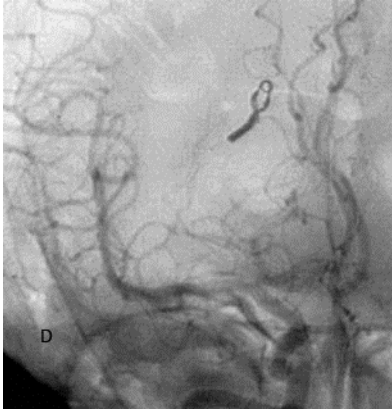
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Abbreviations

AVM-AAV: arterial and venous aneurysms associated with arteriovenous malformation.

UR: unrelated aneurysms.

FR: flow-related remote aneurysms.

FA: flow-related adjacent aneurysms.

V : intra-postnidial “venous aneurysms”.

AVMs: arteriovenous malformations.

AVM-AAs: aneurysms associated with AVM.

CT: computer tomography scan.

MRI: magnetic resonance imaging.

DA: digital angiography.

SAH: subarachnoid hemorrhage.

IVH: intraventricular hemorrhage.

ICH: intracerebral hemorrhage.

GLM: general linear model.

AGF: angiography.

ISUIA: international study unruptured intracranial aneurysms.

pt: patient.