

Venous Flow Rearrangement After Treatment of Cerebral Arteriovenous Malformations (AVMs): A Novel Approach to Evaluate the Risks of Treatment

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Key words

- Cerebral arteriovenous malformations
- Embolization
- Hematoma
- Hyperemia
- Seizures
- Surgery
- Surgery complications

Abbreviations and Acronyms

AV: Arteriovenous
AVM: Arteriovenous malformation
CT: Computed tomography
HC: Hyperemic complication

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INTRODUCTION

Despite progressively improving results globally, the treatment of cerebral arteriovenous malformations (AVMs) remains problematic. In particular, a series of hemodynamic events may be triggered into the surrounding brain, leading to edema or hemorrhage (2, 3, 5, 22, 29, 30, 32, 40). These complications have been named "hyperemic complications" (HCs) (3) and have been explained through two main mechanisms: active (arterial) hyperemia due to reperfusion of tissue previously hypoperfused because of an arteriovenous (AV) shunt (32) and passive (venous) hyperemia due to occlusion of the venous outflow (2). The correlation between such complication and AVM size and complexity is well known, but besides pathophysiology, several questions remain unsettled about their real incidence, clinical relevance, and possibility to be predicted and avoided.

■ **OBJECTIVE:** This study aims to identify the angiographic parameters that could help predict the risks of hyperemic complications (HCs) in the treatment of cerebral arteriovenous malformations (AVMs).

■ **METHODS:** The charts and the pre- and post-treatment angiographies of 400 consecutively treated patients with cerebral AVMs were retrospectively reviewed. Several parameters were analyzed: grade, size, drainage depth, number of the "recruited veins" (veins coming from the brain and joining the main AVM drainage), and "venous times" (the times of visualization of the nidus and the main drainage, of the "recruited veins," and finally of the normal cerebral veins). On this basis, two groups were identified: group 1, consisting of 309 patients (77.3%) with normal/subnormal venous times, and group 2, consisting of 91 patients (22.7%) with altered venous times and venous engorgement. Finally, the weight of the various parameters was measured by univariate and multivariate analyses.

■ **RESULTS:** An overall number of 245 patients (61.2%) achieved favorable outcomes. HCs occurred in a total of 28 patients (7%): No patient belonged to group 1, so that these adverse effects were reported in 30.7% of group 2 patients. The presence of deep drainage and the number of recruited veins resulted in statistically significantly different impacts on the risk of the different grades.

■ **CONCLUSIONS:** The statistical analysis allowed the identification of three different risk scores, which were named Nig-scores (Niguarda scores). Nig-score 0 means no risk of HCs and concerns patients without altered venous times; Nig-score 1 represents patients with intermediate risk, that is, with moderately altered venous times and few recruited veins; Nig-score 2 indicates high risk of HCs and refers to patients with markedly altered venous times.

In this paper, we review our own series of 400 consecutive patients undergoing treatment for cerebral AVMs, focusing on patients with HCs, their angiographic patterns, and the treatment-induced angiographic changes.

MATERIAL AND METHODS

Patient Population

A total of 400 consecutive patients with cerebral AVMs were managed during the period 1990–2010 at our department. Their charts and radiologic assessments were retrospectively reviewed. Age ranged from 8 to 68 years (mean = 36.2 years), whereas the male–female ratio was 6/5.

Clinical presentation consisted of hemorrhage in 199 patients (49.7%), seizures in 149 patients (37.3%), neurologic deficits in 109 patients (27.2%), and headache in 92 patients (23%). Fifty patients were asymptomatic (12.5%). On admission, all patients were classified according to the modified Rankin scale (33), and their lesions were categorized using the Spetzler and Martin grading system (31) (Table 1).

Treatment

The vast majority of grade I and II patients underwent direct microsurgical excision. Grade III patients were managed by a multimodality treatment, including preparative

Table 1. Correlation Between the Spetzler and Martin Grade (31) and the Rankin Scale Score (33) of the Patients on Admission and Discharge

Rankin Scale Scores		Grade I	Grade II	Grade III	Grade IV	Grade V	Total %
0–1	Initial	85	25	26	—	—	136
	Final	84	98	54	9	—	245 (61.25)
2–3	Initial	6	97	98	43	2	246
	Final	6	25	70	28	—	129 (32.25)
4–5	Initial	—	2	3	8	5	18
	Final	1	1	4	6	2	18 (4.25)
6	Initial	—	—	—	—	—	—
	Final	—	—	2	3	4	9 (2.25)
	Total	91	124	127	51	7	400 (100)

embolization followed by microsurgery and/or radiosurgery. Although some selected grade IV patients underwent elective treatment, in general, grade IV and V were treated only in case of life-threatening brain clots, progressively worsening neurologic symptoms, or recurring hemorrhages.

Accordingly, a total of 264 patients (66%) underwent direct surgery, 89 (22.2%) combined endovascular and surgical treatment, 23 (5.8%) combined endovascular and radiosurgical treatment, 11 (2.8%) only radiosurgery, 9 (2.2%) only endovascular treatment, and the remaining 4 (1%) endovascular plus surgical plus radiosurgical treatment. Therefore, a total of 389 patients (97.2%) were "invasively managed" by surgery, embolization, or both and 23 (5.8%) underwent only radiosurgery.

Posttreatment Assessments

All patients were angiographically restudied. Complete abolition of AV shunt was documented in 376 out of (96.6%) 389 "invasively managed" patients, whereas AVM residuals were seen in 13 cases (3.4%). One of these 13 patients experienced postoperative hemorrhage due to the AVM rest and required immediate reoperation. The remaining 12 patients harbored silent small AVM residuals and could be managed by subsequent radiosurgery. As to the remaining 11 patients (undergoing only radiosurgery), complete AVM occlusion was achieved in 5 cases, whereas 6 are still under observation owing to the relative shortness of the follow-up periods.

Analysis of the Venous Pattern

The initial and final (posttreatment) angiographies were carefully analyzed and compared. The main radiologic features and variations were noticed and recorded in a database. Particular attention was paid to the depth of the drainage and to the different times of visualization of the following:

1. The veins directly draining the AVM (main AVM drainage)
2. The veins coming from the brain but which appeared engorged by the AVM flow ("recruited veins") (These were defined as veins coming from the brain that joined the veins coming from the AVM, so that both the AVM and cerebral veins were drained by a final common system. Depending on local venous hypertension, the "venous recruitment" could be more or less extended.)
3. The normal cerebral veins (uninvolved veins).

The study of these veins allowed the identification of three main visualization times (Figure 1): 1) The "early venous time" was defined as the time of the first appearance of nidus and its main direct drainage. 2) The "intermediate venous time" was the phase of appearance of the "recruited veins"; during this time, the nidus and its direct AVM drainage were less clearly delineated whereas the veins draining both the AVM and the brain were more evident. 3) The "late venous time"

corresponded to the normal cerebral circulation time, namely, the time of visualization of the uninvolved cerebral veins. Of course, these times greatly depended on the amount and speed of the AV shunt and were assumed as an index of the degree of venous engorgement. The venous times were considered altered when the "early and intermediate times" quickly appeared and there was a prolonged interval between the "early and the late times." On the other hand, the venous times were considered normal/subnormal when the "intermediate time" was scarcely represented or even absent and there was no significant delay in the appearance of normal cerebral veins.

This analysis allowed the identification of two groups of patients with quite different features: Group 1 consisted of 309 patients (77.3%) with normal/subnormal venous times; all AVMs in this group resulted in sizes smaller than 3 cm and presented absent or scarce "venous recruitment"; all grade I and II patients belonged to this group together with 87 grade III patients. On the other hand, group 2 consisted of 91 patients (22.7%) with altered venous times and significant venous engorgement. All grade IV and V patients belonged to this group together with the remaining 40 grade III patients. To sum up, grade I or II patients and grade IV or V patients fell into two different categories whereas grade III patients split into the two groups (Table 2).

Statistical Analysis

The occurrence of HCs and their influence on final outcomes were correlated with the angiographic patterns. There was a significant difference (Fisher's exact test: $P < 0.0001$) in the incidence of HCs between group 1 (no case in 309 subjects) and group 2 (28 cases out of 91 subjects = 30.7%). Owing to the absence of HCs, the subjects in group 1 were excluded from the analysis, whereas all the variables of the patients in group 2 were submitted to descriptive analysis by tabulation. All the collected data were submitted to usual descriptive statistical analyses. Two-way tables were checked by using Fisher's exact test, and regular logistic regression was used to evaluate the association between HCs and all the other variables; in the case of perfect prediction exerted by a variable, logistic regression was

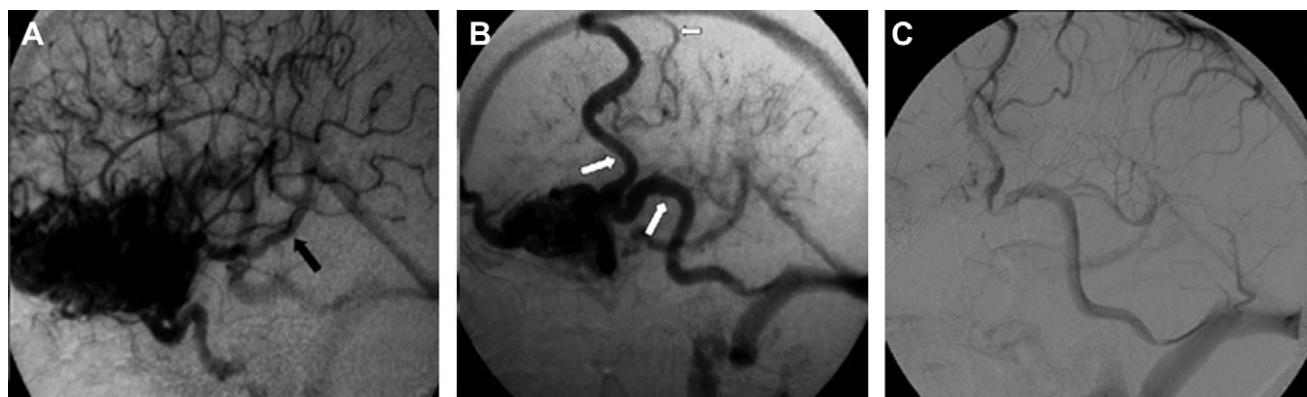


Figure 1. Initial angiographies obtained in a 42-year-old man with grade IV left temporal lobe arteriovenous malformation (AVM). The venous times are illustrated. (A) Preoperative angiogram showing the early visualization of the nidus and the main AVM drainage (black arrow) during a cerebral arterial phase. This time has been nicknamed "early venous time." (B) Preoperative angiogram obtained just in a little bit later when the recruited veins appear (large white arrows) together with recruited veins from the

brain. These veins were draining both the AVM and the brain. The nidus and its main drainage were going to be washed away while some unrecruited veins were coming to be visualized (small white arrow). This time has been nicknamed "intermediate venous time" (assigned Nig-score 1). (C) Postoperative angiogram showing normalization of venous times with preservation of the formerly recruited veins.

performed using an exact calculus algorithm. The Mann-Whitney U test was carried out to analyze the distribution of the Rankin score among patients with and without HCs. Statistical analysis was done with the Stata/SE 12.1 statistical package; the significance was assumed for $P < 0.05$.

RESULTS

Clinical Outcome

Outcomes correlated well with the initial Spetzler and Martin grading system (Table 1). A total of 245 patients (61.2%) were classifiable as Rankin 0–1, 129 patients (32.25%) as Rankin 2–3, 18

patients as Rankin 4–5 (4.25%), and 9 patients as Rankin 6 (2.25%). Treatment-related complications (e.g., ischemia, brain contusion, and intracranial clot) were reported in an overall number of 62 patients (15.5%). Overall complications and their consequences are listed in Table 3. They were ascribable to surgical maneuvers in 49 of 357 surgically treated patients (13.7%), whereas they were related to embolization in 13 of 125 endovascularly treated patients (10.4%). Emergency clot removal was required by 21 operated patients (5.8%) and by 11 embolized patients (8.8%).

Hyperemic Complications

The hyperemic mechanism was considered when edema, hemorrhagic infarction, and/or hematoma occurred in absence of AVM remnants, improper vessel occlusion, and/or technical errors. These conditions were seen in a total of 28 out of 400 patients (7%) and accounted for 45% of all the adverse events: they were related to microsurgery in 17 cases (4.7%) and to embolization in 11 cases (8.8%) (Table 3). All patients with HCs belonged to group 2, which means HCs were invariably associated with altered venous times.

Within group 2, in the univariate logistic analyses, using the HCs as endpoints and the other variables (size, grade, drainage, and so on) as independent regressors, we found the associations reported in

Tables 4–6. All the considered variables appeared as risk factors, with the exception of deep drainage, which did not seem to increase the risk of HCs. Paradoxically, in group 2, for what concerns grade III patients, deep drainage rather appeared as a protective factor against HCs, with the odds of HCs decreasing by 98.8% in presence of drainage ($P < 0.0001$).

Multivariate analysis was carried out simultaneously using all regressors, with the exception of grade, because grade and deep drainage was statistically significantly associated (Fisher's exact test, $P = 0.08$).

Tables 5 and 6 list the results of the multivariate model with HCs as the binary endpoint; the odds ratio of each single variable, in this table, is adjusted for the pooled effects of all other variables. The presence of deep drainage again was not associated with increased risk of HCs, even if adjusted by recruitment and Rankin score. Conversely, the Rankin score itself maintained its association with HC risk in the multivariate model (e.g., when adjusted by deep drainage and recruitment).

Furthermore, on including grade as well in the multivariate model (i.e., ignoring the association between grade and deep drainage), the absence of risk from deep drainage was confirmed ($OR = 0.025$, $P = 0.0012$); however, grade was not significantly associated with HCs ($P = 0.1016$) within group 2 patients. The only significant link between the grade and odds of HC

Table 2. Correlation Between the Spetzler and Martin Grade (31) and Altered Angiographic Times

Grade	Number	Group 1*	Group 2†
II	215	215	—
III	127	87 (68.4%)	40 (31.5%)
IV	51	7 (13.8%)	44 (86.2%)
V	7	—	7
Total	400	309 (77.2%)	91 (22.8%)

AVM, arteriovenous malformation.

*AVMs with relatively normal venous filling times.

†AVMs with rapid filling time and recruitment of normal cortical veins.

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406**Table 3.** Treatment Complications

	Embolization 13/125 (10.4%) Treated Patients				Surgery 49/357 (13.7%) Treated Patients			
	Total	Favorable	Morbidity	Mortality	Total	Favorable	Morbidity	Mortality
Hyperemic complications								
Group 1 (<i>n</i> = 309 patients)	—	—	—	—	—	—	—	—
Group 2 (<i>n</i> = 91 patients)	11	1	8	2	17	7	5	5
No hyperemic complications								
Ischemia	2	1	1	—	12	9	2	1
AVM rest	—	—	—	—	13	12	—	1
Extra/subdural hematoma	—	—	—	—	5	3	2	—
Brain contusion	—	—	—	—	2	2	—	—
Total	13	2	9	2	49	33	9	7

was seen comparing grade V versus grade III, whereas no differences were found comparing grade IV and grade III.

Indeed, within group 2, some differences in odds of HCs between grade IV and III were found: Grade III had significantly better results than grade IV if only patients with deep drainage were taken into account (OR = 6.568, *P* = 0.0152).

Finally, we found out that a randomly chosen patient among those with HCs had an 82.8% probability to have higher Rankin scores in comparison with a patient among those without HCs. Therefore, in general, HCs were significantly predictive of higher Rankin scores (Mann-Whitney *U* test, *P* < 0.0001).

Illustrative Cases

Case 1. A neurologically intact 45-year-old woman had history of cerebellar

hemorrhage that had occurred 6 months earlier. The initial angiography showed a large left cerebellar AVM supplied by cerebellar arteries. During the early angiographic phases, there was immediate evidence of a long and tortuous AVM venous drainage joined by numerous recruited cerebral and cerebellar veins (Figure 2A, B). Both the “early and intermediate venous times” were as anticipated and there was a prolonged interval before the “late venous time.” This AVM was classified as grade III and assigned to venous group 2 (a Nig-score of 2 was assigned). Direct surgical treatment was decided. Immediate postoperative computed tomographic (CT) scan (Figure 2C) was unremarkable, but a few hours later, this patient quickly worsened and repeated CT scans showed a large cerebellar clot (Figure 2D). Repeat angiography showed complete AVM excision, but

the distal part of the AVM venous drainage appeared partially thrombosed, and the previously visible “recruited veins” were now absent (Figure 2E, F). A sort of “venous stump” was visible at the level of the thrombosed drainage. The patient underwent clot excision, but there was no clinical improvement and death occurred 7 days postsurgery.

Case 2. A neurologically intact 54-year-old man with drug-resistant progressively worsening seizures harbored a large left temporal AVM with multiple feeders and a huge variceal drainage joined by numerous “collateral veins” (Figure 3A–C). The venous times were markedly altered. This AVM was classified as grade IV and assigned to the venous group 2 (a Nig-score of 2 was assigned). Combined endovascular/surgical treatment was decided and the AVM was embolized by particles. A few hours after the procedure, the patient became drowsy and hemiparetic. Urgent CT scan showed brain edema with midline shift, and the variceal drainage appeared hyperdense because of initial thrombosis (Figure 3D). A repeat angiography showed scarce visualization of the portion of the drainage shared by the AVM and brain (Figure 3E, F). Neither surgical nor endovascular treatment was indicated, but progressive worsening continued and heparinization was attempted. Within a few days, marked clinical and radiologic improvement was evident (Figure 3G). A repeat angiography showed reappearance of the drainage (Figure 3H, I). Two weeks later, the patient underwent surgery. Postoperative angiography documented that the AVM had been completely excised and the main collateral veins preserved (Figure 3J, K). One year later, the patient was hemiparetic with severe disability.

DISCUSSION

The Risk of Hyperemic Complications

HCs have been often cited to explain the posttreatment adverse effects that can occur in the brain around the AVMs, and undoubtedly they represent a real risk factor in the treatment of some complex AVMs (2, 3, 11, 13, 21, 30, 32, 42). Our and others’ series did not significantly differ for what concerns patient population, treatment modalities, and overall results. Posttreatment adverse effects in our series

Table 4. Main Angiographic Features in 91 Patients of Group 2

Grade	Number	Size >3 cm	Altered Venous Times	Recruitment of Cerebral Veins		Drainage	
				Moderate	Severe	Deep	Cortical
III	40	All	All	15	25	34	6
IV	44	All	All	16	28	44	—
V	7	All	All	—	7	7	—
Total	91	91	91	31	60	85	6

Table 5. Univariate Logistic Models with Hyperemic Complications as Binary Endpoint

Variable	OR	95% CI	P Value
Grade (IV vs. III)	1.677	0.611 to 4.604	0.315
Grade (V vs. III)	5.741*	2.098 to $+\infty$ †	0.0002
Recruitment (moderate vs. severe)	3.232	1.087 to 9.609	0.035
Rankin Scale score (4-5 vs. 2-3)	97.500	11.204 to 848.485	<0.0001
Rankin Scale score (6 vs. 2-3)	26.249	4.626 to 148.959	<0.0001
Deep drainage (Y vs. N)	0.045*	0 to 0.331†	0.0011

OR, odds ratio; CI, confidence interval; Y, yes; N, no.

*Calculated as median unbiased estimate using the exact algorithm

†Actually 97.5% CI

were in line with those reported in the general literature (9, 12, 18, 25, 29, 41).

It is well known that great AVM size means higher treatment risks. Some authors (22, 34) identified the diameter of 3 cm as a sort of watershed between simple and complex AVMs, with about 20% of HCs in the larger lesions. Pasqualin et al. (26) proposed to use the volume rather than the diameter and reported significantly higher rates of HCs in AVMs greater than 20 cm³.

Several authors investigated the venous pattern for what concerns the associated venous anomalies (10, 23, 41), the risks of spontaneous hemorrhage (1, 10, 14, 17, 19, 29, 35), and the risks of treatment (2, 8, 26, 29, 31, 32, 36), but there are few papers (5, 15, 30) that analyze treatment complications by the comparison of pre- and posttreatment angiographies. There are some angiographic features that point to drainage inadequacy and herald the risks of both spontaneous and posttreatment complications: size, length, amplitude, and tortuosity of the AVM drainage are all expressions of either venous overload (40) or hampered outflow, such as in case of

venous stenosis (35). In Da Pian's series (6, 26), surgical risks were higher in patients with evidence of "recruited veins" regardless if the drainage was superficial or deep. In addition to these aspects, the presence of numerous "recruited veins" has been regarded as indicative of the saturation of AVM venous drainage (8). Furthermore, Willinski et al. (39) proposed to classify the venous pattern basing on the number and tortuosity of the collateral veins as well as the delays of angiographic venous times and outlined how such features depended on different degrees of venous congestion.

The Venous Pattern and the "Wash-Out Effect"

Indeed, the existence of a common venous drainage shared by the brain and the AVM has been repeatedly described (2, 8, 30, 36, 40). Depending on the local blood pressure and the distance of these "recruited veins" from the AV shunt, their blood flow may be either inverted (toward the brain) or impaired but orthodromic (toward their natural outflow). In proximity of the AV shunt, the "recruited

veins" receive blood with higher pressure so that their flow is more likely inverted (4, 5, 37). These veins contain almost exclusively arterialized blood ("red veins") and represent the more probable site of AVM bleeding. They are actively flooding rather than draining the brain, so that their therapeutic obliteration should be harmless. On the contrary, less close to the AV shunt, the "recruited veins" receive blood with minor pressure, so that they become more or less engorged but can maintain their orthodromic flow. These veins contain mixed arterial and venous blood ("reddish/bluish veins"). This means they may be still draining functional brain (4, 5, 37), and their occlusion may have ominous consequences.

Both endovascular and surgical treatments consist of several steps of progressive AVM deafferentation with the final obliteration of the venous drainage as close as possible to nidus. The abolition of the AV shunt forces the redistribution of the local cerebral flow, a sort of "venous rerouting": the previously engorged "recruited" cerebral veins can get back to normal and resume their normal cerebral drainage. Natural thrombosis is obviously triggered at the point of drainage occlusion, but the restoration of distal normal venous flow should limit the extent of such thrombosis and maintain the patency of the drainage system, thus preventing undesired venous occlusion. This mechanism has been called the "venous wash-out effect" (4, 5, 37) (Figure 4). It may be seen in patients with favorable evolution: cerebral veins, which were initially precociously visible, become evident with normal venous times in the postoperative angiography (Figure 1). This means the normal venous hemodynamics had been restored.

Pathophysiology of the Hyperemic Complications

Unfortunately, there are cases where the "wash-out effect" may fail to prevent the distal extension of the venous thrombosis. This may occur irrespective of technical errors. In cases of great venous overload, the whole AVM/brain drainage system has adapted to receive high and fast flow, and which abruptly slows down and decreases following AVM excision or embolization. In this case too, the previously engorged "recruited veins" go back to resume normal drainage but now they must fill

Table 6. Multivariate Logistic Model with Hyperemic Complications as the Binary Endpoint

Variable	OR	95% CI	P Value
Recruitment (moderate vs. severe)	2.539	0.407 to 27.836	0.4602
Rankin (unitary increase)	11.942	3.501 to 54.703	<0.0001
Deep drainage (Y vs. N)	0.047*	0 to 0.416†	0.0048

OR, odds ratio; CI, confidence interval; Y, yes; N, no.

*Calculated as median unbiased estimate using the exact algorithm

†Actually 97.5% CI

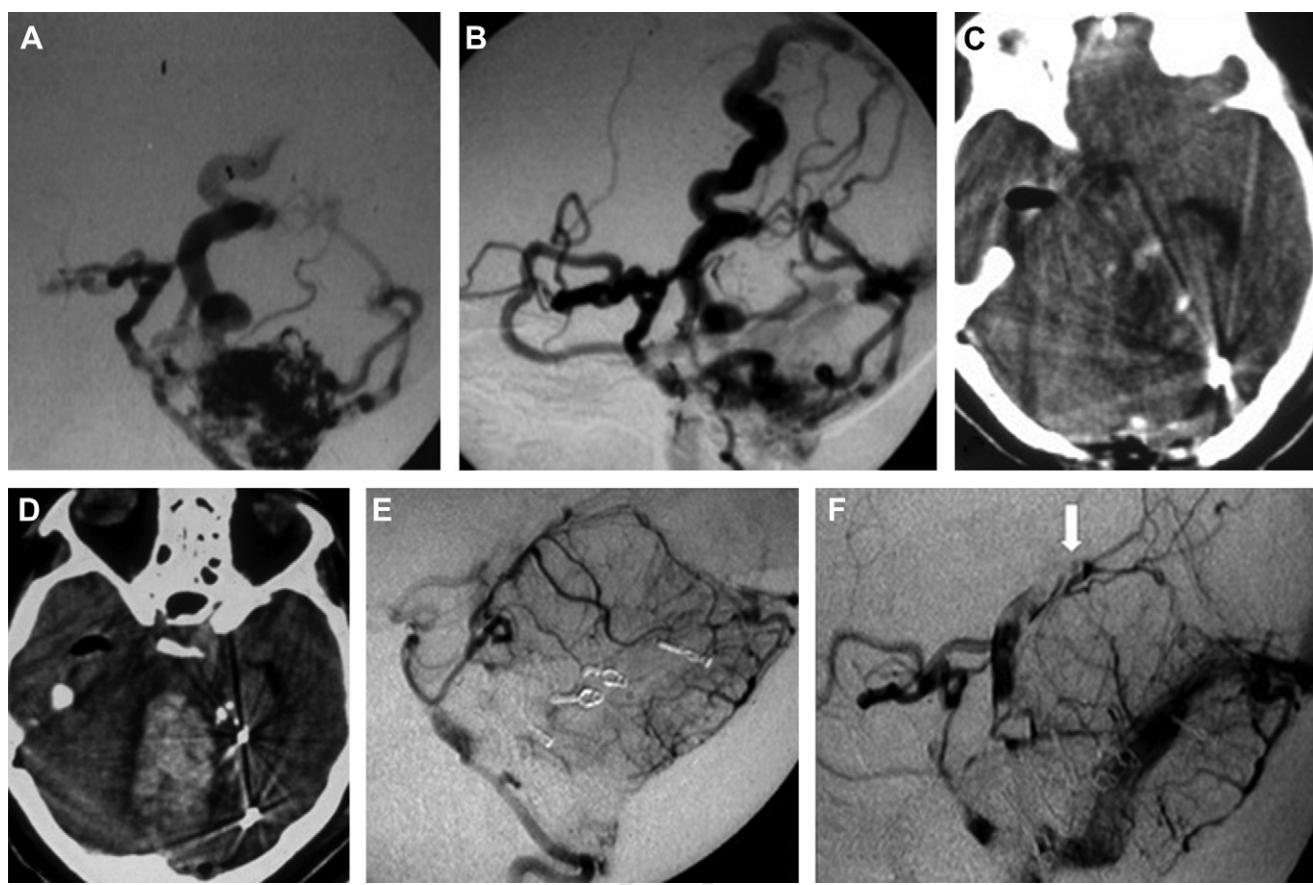


Figure 2. Images obtained in a 45-year-old woman (patient described in illustrative case 1) harboring a grade III left cerebellar hemisphere arteriovenous malformation (AVM) (Nig-score 2). **(A)** Earlier and **(B)** later preoperative angiograms obtained during the “intermediate venous times” showing a long and tortuous AVM venous drainage that was joined by numerous recruited cerebral and cerebellar veins. Venous engorgement was marked. The duration of this venous time was considerable and the normal unrecruited cerebral veins were quite delayed (“late venous time”).

(C) Postoperative computed tomographic (CT) scan showing an uncomplicated surgical field. **(D)** Repeated CT scan obtained when the patient neurologically worsened, showing a large cerebellar clot. **(E and F)** Repeated angiograms show complete AVM excision but ongoing partial thrombosis of the main draining veins can be seen. The occlusion of the distal part of the AVM drainage appeared evident and a sort of “venous stump” was visible (white arrow). The infra- and supra-tentorial recruited veins had vanished.

a vascular bed that may be too wide to maintain the wash-out. The thrombosis of veins with inverted flow (“red veins”) should remain unharmed because these veins do not drain the brain anymore, but if the occlusion arrives to the veins that, though engorged, are still draining the brain (“reddish/bluish veins”), then edema, hemorrhage, and venous infarction may occur (Figure 4). In these cases, the posttreatment angiogram may reveal the disappearance of one or more previously visible “recruited veins” coming from the brain. Stagnating segments of venous drainage may be evident too (Figure 2). These might be an expression of the inadequate “refilling venous flow” (4, 5, 37). Perhaps, these features could be

improperly defined as “venous stumps of the main drainage.” One patient in this series (Figure 3) was dramatically worsening after embolization because of the progressive extension of the thrombosis along the drainage system. Massive heparinization was effective in countering this phenomenon and allowing favorable evolution.

This failure to limit the extension of the thrombosis may follow both surgical and endovascular treatment. In these cases, it usually occurs soon after treatment. However, it could be hypothesized even to explain the delayed complications that may follow radiosurgery.

Indeed, the risks of HCs may be correlated to the “failure of the wash-out

effect,” which is in turn related to the magnitude of the venous recruitment and the severity of the alteration of the venous times. In the 1990s, several authors (2, 12, 27, 28) proposed that HCs could depend on venous rather than arterial changes. Al-Rodhan et al. (2) hypothesized that the HCs could be induced by occlusion of the venous outflow and proposed the term *occlusive hyperemia*. If we take into account the failure of the wash-out effect, it might appear that the venous occlusion is not directly related to the treatment and could occur in the absence of any technical error. Theoretically, multistage embolization may be able to progressively decrease the AV shunt and the venous engorgement, thus decreasing the risks of a failed

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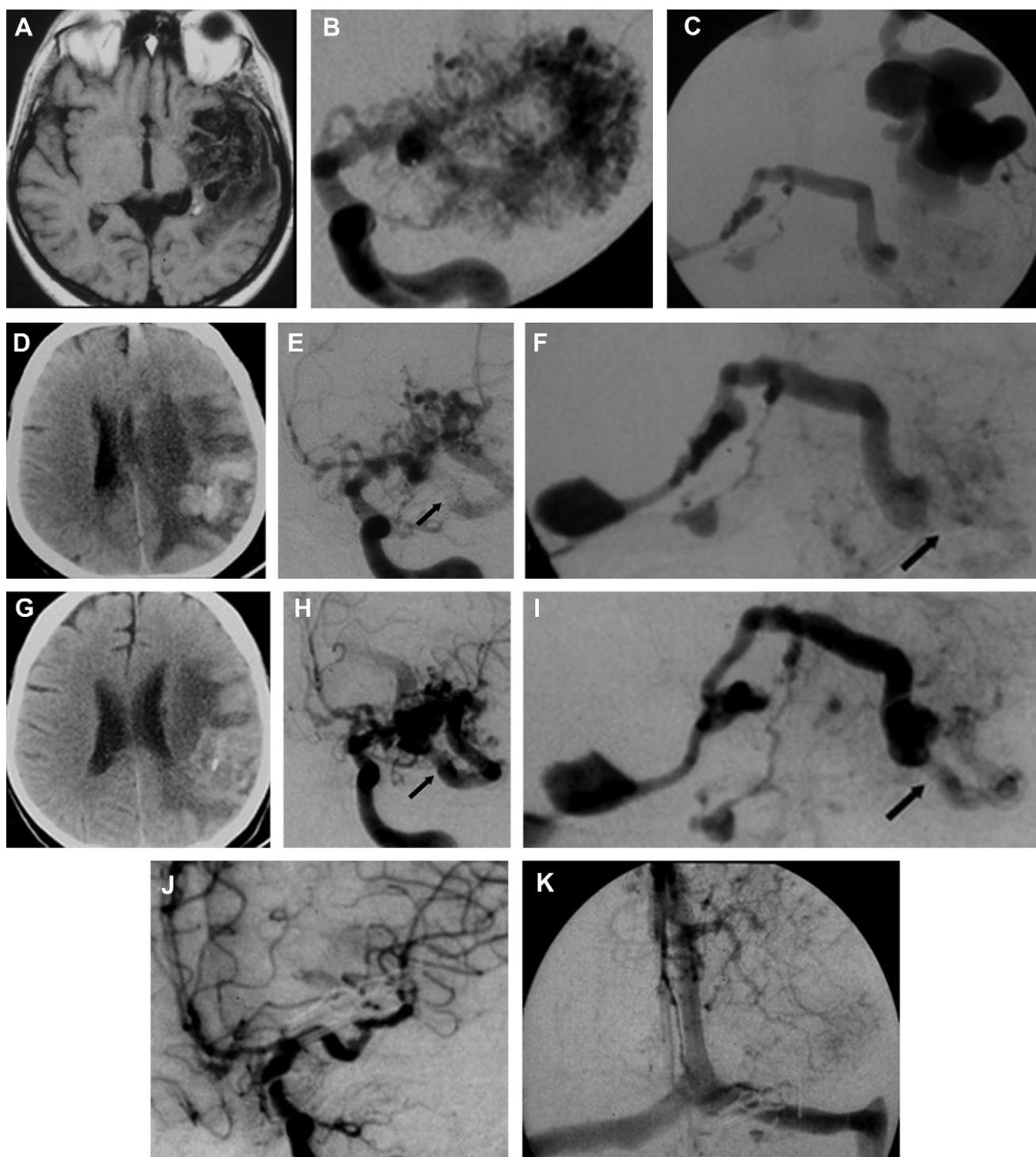


Figure 3. Images obtained in a 54-year-old man (patient described in illustrative case 2 harboring a grade IV left temporal lobe arteriovenous malformation [AVM]) (Nig-score 2). **(A)** Preoperative magnetic resonance imaging showing the size and location of the AVM. **(B and C)** Preoperative angiograms depicting a huge varicose AVM drainage, which was used also by numerous collateral veins from the brain. The engorgement was significant; the "intermediate venous time" was very precocious and the "late venous time" was extremely delayed. **(D)** Postembolization computed tomographic (CT) scan obtained as soon as the patient neurologically worsened. Important cerebral edema and midline shift were evident. The varicose drainage was

clearly visible because of its relative hyperdensity because of ongoing thrombosis. **(E and F)** Repeated angiograms confirming the partial thrombosis of the common drainage, which was now invisible in its initial portion, where a sort of "venous stump" had become evident (black arrows). **(G)** Repeat CT scan obtained a few days after heparinization when the patient neurologically improved. Edema and midline shift had decreased. **(H and I)** Further angiograms demonstrating the reappearance of the previously invisible common final drainage (black arrows). **(J and K)** Postoperative angiograms showing complete AVM excision with restoration of the normal hemispheric drainage.

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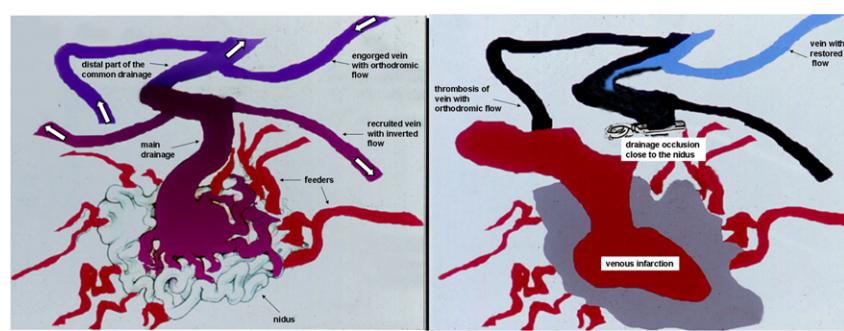


Figure 4. Schematic drawings of the initial AVM drainage and the postoperative failure of the "wash-out effect." In the initial sketch (left), there are two types of veins joining the main AVM drainage: the proximal ones with inverted flow toward the brain (red veins) and others which, still engorged, are still draining the brain (reddish/bluish veins). The distal part of the drainage is shared by both the AVM and the brain. In the final sketch (right), natural thrombosis occurs at the point of correct drainage occlusion close to the nidus. The thrombosis extension to the proximal red veins is harmless. However, the abrupt flow decrease in so wide a venous bed triggers more extended thrombosis that cannot be limited by the more distal veins with restored flow. Accordingly, these veins fail to maintain the patency of the common drainage, and the thrombosis may involve veins coming from the brain with subsequent hyperemic complications.

"wash-out effect" and HCs (4, 5, 15, 38). If this is the case, the embolization should aim to improve the venous times rather than to obtain extended nidus obliterations.

Analysis of the Present Series

An analysis of our results and interpretation of the statistical studies lead us to the following drawings: all AVMs patients can be roughly divided into three cohorts: those without risks of HCs, those with intermediate risks, and those with high risks. Grades I/II and grade V patients are immediately and easily ascribable respectively to low- and high-risk cohorts. Conversely, grades III and IV may be more difficult to assign to a given risk cohort: the former can be distributed over all the three risk groups and the latter may carry either intermediate or high risks. In fact, patients lying in the intermediate risk zone can be roughly identified as grades III and IV. However, statistical significance was found only in grade III patients when deep drainage was present, whereas a trend was evident in grade IV patients, when the venous recruitment was moderate (OR = 4.529, P = 0.089). In fact, in our sample, the absence of the deep drainage for grade III patients corresponded to 100% probability of HC (i.e., a 97.5% CI ranging from 54% to 100%). Accordingly, grade III patients without deep drainage are to be considered high risk for HCs in the same order of grade

V patients. This significant protective action by the deep drainage for grade III patients perhaps may be explained by the fact that the deep venous route could represent an alternative pathway to a possibly inadequate cortical system. In the same way, also the grade IV with deep drainage and important venous recruitment carried the same risks as grade V. Therefore, the magnitude of the venous recruitment appeared as an important factor to assign the grade IV patients to the intermediate or to the high-risk groups. Indeed, it is reasonable that lower the recruitment, the less is the venous engorgement and thus minor is the risk of HCs. However, the number of patients with these features was relatively small. Therefore, these data did not yield statistically significant results in our sample although a clear trend was evident. To sum, as to the risk of HCs, both the grades III and IV were quite heterogeneous. This was already known above all for what concerns grade III, which have been reported with different risk stratifications (7, 16, 20, 24). In particular, our analysis confirmed the results by Pandey et al. (24), who reported different risks for different AVM sizes among grades III patients.

CONCLUSION

The HCs still represent a main problem in the treatment of complex AVMs. The risk of HCs is undoubtedly related to the lesion

size and complexity of the venous pattern. We consider the "failure of the wash-out effect" as the pathophysiologic basis for HCs. Such a failure depends on the magnitude of the venous recruitment and the severity of alteration of the venous times.

On this basis, we classified our patients into three groups with different risks of post-treatment HCs. A score of severity was developed, which we have named the Nig-score (Niguarda score): Nig-score 0 includes patients without risks of HCs; Nig-score 1 consists of patients with intermediate HC risks; Nig-score 2 is composed of patients with high HC risks.

Patients with Nig-score 0 are identified by patients in our group 1 (i.e., those with normal or subnormal venous times); they include virtually all grade I and II patients and some grade III patients. Their main features consist of lesions smaller than 3 cm, with few or no recruited veins and no altered angiographic times. In all cases, the outcome of these patients was highly satisfactory (Rankin scores 0–1).

Patients with Nig-score 1 belong to our group 2 (i.e., those with altered venous times); they include some grade III and some grade IV patients. Their main features consist of lesions larger than 3 cm, with few recruited veins. To be considered here, grade III patients need the presence of deep drainage, and grade IV patients show a moderate recruitment. The final outcome of these patients mainly was a moderate disability (Rankin scores 2–3).

Patients with Nig-score 2 belong to our group 2 and present quite altered venous times in all cases; they include all the remaining grade III and IV patients and all from grade V. Their main features consist of lesions larger than 3 cm, with massive recruitment of cortical veins. The expected outcome of these patients would be severe disability or death (Rankin scores 4–5 and Rankin 6).

We do realize that our analysis cannot estimate the cumulative risk of AVM treatment. For instance, it does not take into account other determinant factors such as the presence of deep feeders. We are just proposing a method to evaluate the expected risk of HCs in a given patient. Of course, this will need a validation based on a higher number of patients. In particular, a prospective trial could help to select those grade IV patients who could benefit from active treatment.

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A couple of decades ago, Wilson et al. (40) invited neurosurgeons to "become vein watchers." In light of that, our method can be considered a novel approach to evaluate the HC risks from the point of view of veins.

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This paper is dedicated to the memory of Vincenzo Branca, M.D., and Massimo Collice, M.D. The former was a very skilled interventional neuroradiologist who spent much of his precious time together with us in retrospectively reviewing the angiograms of these patients. What he taught us about the interpretation of angiograms is invaluable. The latter was our chairman and master for more than 20 years. He pioneered neurovascular surgery in Italy and was held in high esteem all around the world. We are the last pupils of his School and we are trying to capitalize on his great inheritance.

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