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Angioarchitectural Characteristics Associated with Complications of Embolization in Supratentorial Brain Arteriovenous Malformation

J. Pan, H. He, L. Feng, F. Viñuela, Z. Wu, and R. Zhan

ABSTRACT

BACKGROUND AND PURPOSE: Embolization is an important therapeutic technique in brain arteriovenous malformations; however, little has been reported on the factors contributing to complications. We retrospectively reviewed a large series of supratentorial brain AVMs to identify the angioarchitectural characteristics that might be associated with the complications of embolization and poor clinical outcomes.

MATERIALS AND METHODS: The clinical and angiographic features of 130 consecutive patients with supratentorial brain AVMs embolized with ethylene-vinyl alcohol copolymer in our hospital from 2005–2008 were retrospectively reviewed. None of these patients had prior embolization. Complications were classified as transient neurologic deficits, persistent neurologic deficits, and death. Univariate and multivariate analyses were conducted to assess the angiographic features in patients with and without complications.

RESULTS: Twenty-three complications occurred in 130 embolization procedures, 13 (10%) were transient neurologic deficits (9 ischemic and 4 hemorrhagic), 9 (6.92%) were persistent neurologic deficits (7 ischemic and 2 hemorrhagic), and 1 death occurred. By univariate analyses, eloquent cortex (OR, 2.57; 95% CI, 1.08–3.42) and exclusive deep venous drainage (OR, 4.56; 95% CI, 1.28–9.67) were correlated with procedural complications. The impact of eloquent cortical location ($P = .001$) and exclusive deep venous drainage ($P = .035$) on complications were also demonstrated by multivariate analysis. Eloquent cortex mainly resulted in permanent ischemic neurologic deficit; occlusion of drainage vein was significantly correlated with periprocedural hemorrhage in supratentorial brain AVMs with subtotal and partial embolization.

CONCLUSIONS: In a retrospective study on supratentorial brain AVMs with first-time embolization, 6.92% of patients had permanent neurologic deficit or death. Eloquent cortical location and exclusive deep venous drainage were associated with complications.

ABBREVIATIONS: sbAVM = supratentorial brain arteriovenous malformation; EVOH = ethylene-vinyl alcohol copolymer; PVA = polyvinyl alcohol

Embolization is an important adjunctive therapy to microsurgery and radiosurgery in the multidisciplinary management of arteriovenous malformations.^{1–3} Recent advances in endovascular embolization techniques including flow-directed microcatheters and the liquid embolic agents *n*-butyl-cyanoacrylate and ethylene-vinyl

alcohol copolymer (EVOH; Onyx, ev3, Irvine, California)⁴ make it possible to cure AVMs with embolization alone.^{5,6}

Because endovascular treatment might result in hemorrhage and ischemic neurologic dysfunction, embolization of unruptured AVMs remains controversial, particularly in supratentorial brain AVMs (sbAVMs), which have a lower risk of hemorrhage than infratentorial AVMs. The reported complication rates of embolization varied from 3–11%^{2,7–10} and were associated with angiographic features.⁷

In the present study, we retrospectively reviewed 130 patients with sbAVMs to identify angioarchitectural characteristics that might be associated with the complications of embolization and poor clinical outcomes.

MATERIALS AND METHODS

All patients referred to our institution were assessed by a multidisciplinary team of neuroradiologists, neurosurgeons, and neu-

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rologists for the therapeutic option on the basis of CT, MR imaging, and DSA. A total of 130 consecutive patients with sbAVMs were diagnosed and embolized with Onyx for the first time during the period January 1, 2005 to December 31, 2008, and their demographic, clinical, and angioarchitectural data were reviewed retrospectively. Patients with prior treatment (surgical removal, embolization, radiosurgery) were excluded from the study.

Initial sbAVM presentation was defined as hemorrhage, ischemic neurologic deficit, headache, seizures, and incidental findings. Angioarchitectural characteristics such as location and size of AVM, arterial feeders and coexisting aneurysms, venous drainage, and venous morphology were retrospectively evaluated.

AVM locations were grouped into eloquent cortex, noneloquent cortex, midline region (ventricle, corpus callosum), and deep region (basal ganglia, internal capsule, and thalamus). Spetzler-Martin grade was assessed in each AVM, and sizes were classified into small (3 cm), medium (3 cm and 6 cm), and large (6 cm). Arterial feeders were categorized as terminal and perforating. Terminal feeding arteries were prominent arteries that connected directly to the nidus, whereas perforating feeders referred to the pattern of several small, short arteries arising from a large parent artery and penetrating brain parenchyma to reach the AVM nidus. The presence of coexisting arterial aneurysms was divided into perinidal and intranidal aneurysms. Remote flow-related or unrelated aneurysms were not taken into account in this study. Venous drainage was noted as deep, superficial, and combined groups. Venous morphology was described according to the presence or absence of ectasia and stenosis. Ectasia was defined as focal dilations that were at least twice the size of the venous diameter. A 50% focal reduction of the venous diameter was considered as a significant stenosis.

Embolization degree was classified into partial (<90%), subtotal (\geq 90%), and complete (100%) embolization. Neurologic deficits were assessed by a neurosurgeon/neurologist according to NIHSS. CT and MR imaging were performed after embolization to identify postprocedural hemorrhage and ischemia. Postprocedural mRS was assessed, and complications of embolization were categorized as transient (new onset of neurologic deficit that resolved completely within 7 days) and persistent neurologic deficit. Neurologic deficits were further divided into ischemic and hemorrhagic.

The data were managed and analyzed by use of SPSS software (version 13.0; IBM, Armonk, New York). We conducted analyses stratified by each variable (age, sex, nidus size, etc) to evaluate its impact on complications of embolization. Furthermore, multivariate analyses (backward conditional logistic regression) were conducted after the adjustment for some variables that demonstrated and correlated with a significantly increased risk of embolization complications in univariate analyses to assess the effect of modification and interaction among potential risk factors. A probability value of <.05 was considered statistically significant in each analysis.

RESULTS

Of the 130 patients with sbAVM who underwent embolization, there were 78 men and 52 women, ranging from 5–64 years of age (mean, 30.27 ± 12.45 years). Initial presentations included 79

Table 1: Demographic and clinical characteristics of 130 patients with sbAVM embolization

Characteristics	No. (%)
Sex	
Male	78 (60%)
Female	52 (40%)
Age, y	
<18	27 (20.77%)
18–49	100 (76.92%)
\geq 50	3 (2.31%)
Initial presentation	
Hemorrhage	79 (60.77%)
Ischemia	11 (8.46%)
Headache	13 (10%)
Seizures	20 (15.38%)
No symptoms	7 (5.38%)

Table 2: Preprocedural angioarchitectural characteristics of 130 patients with sbAVM embolization

Angiographic Features	No. (%)
Location	
Eloquent cortex	44 (33.85%)
Noneloquent cortex	62 (47.69%)
Midline	12 (9.23%)
Deep	12 (9.23%)
Size	
\leq 3 cm	32 (24.62%)
3–6 cm	80 (61.54%)
\geq 6 cm	18 (13.85%)
No. of feeders	
1	17 (13.08%)
2	28 (21.54%)
\geq 3	85 (65.38%)
Arterial feeders classification	
Terminal	95 (73.08%)
Perforating	35 (26.92%)
No. of draining veins	
1	55 (42.31%)
2	37 (28.46%)
\geq 3	38 (29.23%)
Venous drainage classification	
Exclusive superficial	79 (60.77%)
Exclusive deep	16 (12.31%)
Combined	35 (26.92%)
Venous morphology	
Venous reflux	35 (26.92%)
Venous ectasia	29 (22.31%)
Venous stenosis	46 (35.38%)
Coexisting aneurysm	
Intranidal	30 (23.08%)
Perinidal	7 (5.38%)
Spetzler-Martin classification	
I–II	50 (38.46%)
III	36 (27.69%)
IV	30 (23.08%)
V	14 (10.77%)

spontaneous hemorrhages, 11 ischemic manifestations, 13 headaches, 20 seizures, and 7 nonsymptomatic (Table 1).

The preprocedural angioarchitectural characteristics are summarized in Table 2. Most the sbAVMs were medium-sized (61.54%) and located in noneloquent cortices (47.69%). Perforating feeders were found in 35 cases (26.92%), whereas 16 patients (12.31%) had exclusive deep venous drainage. Coexisting aneurysm was noted in 37 cases, of which, 30 (23.08%) were in-

Table 3: Hemorrhagic complications in 38 sbAVMs with obliteration of draining vein

Complication	Embolization	Complete ^a	Subtotal (Near Complete ^a)	Partial
Hemorrhage		0	2 (0)	3
No hemorrhage		8	8 (4)	17

Note:— χ^2 test.

^a $P < .05$, significant difference.

Table 4: Complications of embolization in 130 patients with sbAVMs

Complications	No. (%)
TND	
Ischemic	9 (6.92%)
Hemorrhagic	4 (3.08%)
PND	
Ischemic	7 (5.38%)
Hemorrhagic	2 (1.54%)
Death	
Hemorrhagic	1 (0.77%)

Note:—TND indicates transient neurologic deficit; PND, persistent neurologic deficit.

trianid aneurysms. According to the Spetzler-Martin grading system, the distribution of sbAVMs were 16 in grade I (12.31%); 34 in grade II (26.15%); 36 in grade III (27.69%); 30 in grade IV (23.08%); and 14 in grade V (10.77%).

All patients were embolized with Onyx. The average number of catheterized feeders was 1.26, and the volume of embolic agent was 0.3–9.5 mL (average, 2.5 ± 1.77 mL). Endovascular treatment achieved complete embolization in 28 patients, subtotal in 26 patients, and partial in 76 patients. In the procedure, draining veins were unexpectedly occluded in 38 cases and associated with hemorrhage in 5 cases (Table 3). Among the patients who had subtotal embolization, 4 were nearly complete, with the residual AVMs approximately 1% of their preprocedural volumes.

After embolization, there were 13 transient neurologic deficits (9 were ischemia and 4 were hemorrhage), 9 persistent neurologic deficits (7 ischemia and 2 hemorrhage), and 1 death occurred (hemorrhage) (Table 4). Eloquent cortex location was the main risk factor of symptomatic cerebral ischemia and ischemic persistent neurologic deficit (5/7, 71.4%) after embolization ($P < .05$). The number of catheterized feeders and the volume of embolic agent were not significantly correlated with postprocedural complications ($P > .05$).

By univariate analyses (Table 5), eloquent cortex location (OR, 2.57; 95% CI, 1.08–3.42) and exclusive deep venous drainage (OR, 4.56; 95% CI, 1.28–9.67) were correlated with postprocedural complications ($P < .05$). Eloquent cortical location was associated with persistent ischemic neurologic deficit ($P < .05$); occlusion of the drainage vein was significantly correlated with postprocedural hemorrhage in AVMs with subtotal and partial embolization (Table 3). The impact of eloquent cortical location ($P = .001$) and exclusive deep venous drainage ($P = .035$) on embolization complications were demonstrated by backward conditional logistic regression.

Spetzler-Martin classification of 130 sbAVMs significantly changed after embolization (Table 6), with significantly more patients in grade I than before the procedure (33.33% versus 16.31%, $P < .05$), and patients in other grades decreased. There were significantly more patients with an mRS of 0 and fewer patients with an mRS of 1 after embolization (Table 6), partly attrib-

Table 5: Demographic, clinical, and angioarchitectural characteristics predictive for embolization complications by univariate analysis

Characteristics	OR (95% CI)	P Value
Sex		
Male	0.84 (0.33–2.10)	.75
Age, y		
<18	0.89 (0.31–2.41)	.78
18–49	1.09 (0.37–2.76)	.84
≥ 50	1.16 (0.17–11.36)	1.01
Initial presentation		
Hemorrhage	1.15 (0.59–2.94)	.49
Ischemia	0.65 (0.14–3.27)	1.00
Headache	1.86 (0.93–5.63)	.57
Seizures	0.64 (0.37–2.00)	.55
No symptoms	0.91 (0.17–4.39)	.70
Location		
Eloquent cortex	2.57 (1.08–3.42)	.02
Noneloquent cortex	0.38 (0.24–0.86)	.02
Midline	0.55 (0.19–2.42)	.79
Deep	1.41 (0.29–2.85)	.51
Size		
≤ 3 cm	1.06 (0.42–2.40)	.79
3–6 cm	0.80 (0.33–1.29)	.23
≥ 6 cm	2.45 (0.57–5.32)	.17
No. of feeders		
1	0.39 (0.06–1.54)	.38
2	1.75 (0.76–3.21)	.26
≥ 3	0.85 (0.47–3.84)	.72
Classification of feeders		
Terminal	0.61 (0.35–1.97)	.32
Perforating	1.64 (0.79–4.58)	.25
No. of draining veins		
1	0.73 (0.43–2.96)	.98
2	1.57 (0.58–3.63)	.34
≥ 3	0.62 (0.34–1.89)	.43
Drainage classification		
Exclusive superficial	1.04 (0.77–2.52)	.90
Exclusive deep	4.56 (1.28–9.67)	.00
Combined	0.24 (0.09–0.53)	.03
Venous morphology		
Venous reflux	1.91 (0.51–2.98)	.77
Venous ectasia	2.24 (1.32–9.88)	.26
Venous stenosis	1.50 (0.26–2.34)	.19
Coexisting aneurysm		
Intranidal	0.99 (0.23–3.81)	.22
Perinidal	1.52 (3.72–8.50)	.61
Spetzler-Martin classification		
I–II	2.32 (0.21–9.87)	.48
III	0.58 (0.70–4.05)	.54
IV	1.61 (1.22–4.53)	1.20
V	0.83 (0.06–10.29)	1.00
Embolization degree		
Complete	0.87 (0.27–3.02)	.27
Subtotal	0.71 (0.40–1.60)	.13
Partial	1.92 (1.21–4.07)	.17
Venous occlusion	1.26 (0.94–2.83)	.84

uted to the recovery from their initial hemorrhage or ischemic event.

DISCUSSION

Endovascular embolization is an important part of the multimodality treatment for brain AVMs.^{11–13} Improvements in microcatheter technology and embolic agents, especially *n*-BCA and EVOH, have led to an increased curative rate of brain AVMs.^{5,6,11} Furthermore, embolization can reduce the size and flow of AVMs,

Table 6: Spetzler-Martin classification and mRS score before and after embolization in 130 patients with sbAVMs

Grade	Preprocedural, No. (%)	Postprocedural, No. (%)
Spetzler-Martin classification		
I	16 (16.31%)	34 (33.33%) ^a
II	34 (26.15%)	20 (19.61%)
III	36 (27.69%)	28 (27.45%)
IV	30 (23.08%)	16 (15.69%)
V	14 (10.77%)	4 (3.92%)
mRS		
0	10 (7.69%)	29 (22.31%) ^a
1	79 (60.77%)	54 (41.54%) ^a
2	19 (14.62%)	20 (15.38%)
3	11 (8.46%)	11 (8.46%)
4	5 (3.85%)	12 (9.23%)
5	6 (4.62%)	3 (2.31%)
6	0 (0%)	1 (0.77%)

Note:— χ^2 test.

^a $P < .05$, significant difference.

improving the safety and efficacy of microsurgery and radiosurgical treatment for brain AVMs.^{14–18} In this series of 130 sbAVMs that underwent embolization for the first time, there was complete embolization in 28 patients (21.54%) and subtotal embolization in 26 patients (20%). In addition to the cases of complete obliteration of brain AVMs, patients in Spetzler-Martin grade I increased significantly after embolization (preprocedural, 16.31% versus postprocedural, 33.33%; $P < .05$) and the average Spetzler-Martin grade in the series declined (preprocedural, 2.94 versus postprocedural, 1.86; $P < .05$).

Either curative or adjuvant embolization can result in postprocedural hemorrhage and ischemia. Recent studies reported morbidity ranging from 3–11%, and mortality from 0–4%,^{2,4,5,7,8,11,19–26} with associations to angioarchitecture, embolic agents, microcatheters, and the manipulator's skills. Studies on different embolization materials, such as silk,²⁴ polyvinyl alcohol (PVA) and coil,²⁵ Onyx,¹¹ and *n*-BCA,²³ showed 1.4%, 13%, 19.5%, and 50% rates for morbidity and 0%, 0%, 2.9%, and 1.9% for rates of mortality, respectively. Frizzel and Fisher²⁷ reviewed 32 series of brain AVM embolization studies and revealed that permanent neurologic deficit and mortality were 9% and 2% before 1990, decreasing to 8% and 1% after 1990. Because some embolic agents such as PVA and isobutyl cyanoacrylate are no longer in use and new materials such as Onyx have been widely adopted, the complications of embolization should be reassessed. Moreover, the statistical bias caused by different embolic materials, different locations of AVMs, and technical-related complications need to be evaluated. We reviewed 11 series of embolization by use of *n*-BCA and Onyx (Table 7)^{2,4,5,7,8,11,19–22} and retrospectively studied sbAVMs treated by flow-directed microcatheters and liquid embolic agents in 5 recent years. We found a complication rate of 6.4–21%, permanent neurologic deficit of 1.6–12.2%, and mortality rate of 0–2.9%.

Complications of embolization can be categorized into technical-related and non-technical-related. Technical-related complications included vascular perforation, normal branch occlusion, and bleeding caused by catheter removal. Recent improvement in flow-directed microcatheter and nonadhesive embolic agents has reduced the risk of microcatheter delivery and removal. In our

Table 7: Embolization complications by *n*-BCA and/or Onyx according to the literature (11 series)

Series [Reference]	Patients	Materials	Complication, %	PND, %	Mortality, %
Taylor et al [2]	201	<i>n</i> -BCA/Onyx	21	11	2
Van Rooij et al [4]	44	Onyx	13.8	4.6	2.3
Katsaridis et al [5]	101	Onyx	14.9	7.9	2.9
Ledezma et al [7]	168	<i>n</i> -BCA	16.1	6.5	1.2
Haw et al [8]	306	<i>n</i> -BCA	6.4	3.9	0
Panagiotopoulos et al [11]	82	Onyx	19.5	3.8	2.4
Jayaraman et al [19]	192	<i>n</i> -BCA/Onyx	15.7	1.6	0
Starke et al [20]	275	<i>n</i> -BCA	14	2.5	0
Hauck et al [21]	107	Onyx	17	12.2	0
Velat et al [22]	88	<i>n</i> -BCA/Onyx	13.6	4.5	2.2
Present study	130	Onyx	17.7	6.9	0.8

Note:—PND indicates persistent neurologic deficit.

series with sbAVM embolization, contrast extravasation was noted in 3 cases during the procedure. None of these 3 patients ended with persistent neurologic deficit because of timely occlusion of microperforation sites. The technical-related complication rate in the present study was 2.31%, less than the results of Ledezma et al⁷ and less than our non-technical-related complications (21/130, 16.15%).

Non-technical-related complications are mainly associated with angioarchitectural characteristics of brain AVMs. Periprocedural hemorrhage rate was 3–15%,^{28–30} probably related to hemodynamic changes and alteration in nidus pressure.^{30,31} Picard et al²⁸ demonstrated that venous outflow obstruction was correlated with hemorrhagic presentation after embolization. Furthermore, by progressively blocking draining veins in an AVM model, Hademenos and Massoud³² revealed that venous stenosis or occlusion would result in redistribution of blood flow in the nidus and cause intranidal hypertension. Nonetheless, not all venous occlusion resulted in hemorrhage; the extent and severity of outflow obstruction matter as well. In the present study, venous occlusion occurred in 29.23% of all 130 cases and did not correlate with embolization complications in the univariate model. In the 38 patients with venous occlusion, no postprocedural hemorrhagic presentation occurred when the AVM was completely or nearly completely embolized, whereas a significantly higher hemorrhage rate was seen in the subtotal and partial embolization group (0% versus 23.81%, $P < .05$). This result suggested that imbalance between inflow and outflow could be a predictive factor of postprocedural hemorrhage and that to avoid rupture of the residual AVM, sbAVMs should be completely or nearly completely embolized as soon as possible when venous outflow obstruction is identified.

Normal perfusion pressure breakthrough related to disruption of cerebral vascular autoregulation³³ and delayed venous thrombosis have been postulated as the etiologies of periprocedural hemorrhage. There was no normal perfusion pressure breakthrough in our series because blood pressure was tightly controlled in all patients immediately after embolization. One patient with subtotal embolization (and reserved draining veins) had severe brain edema, which could be attributed to delayed venous thrombosis and stagnation. Purdy et al³⁰ suggested that delayed venous outflow obstruction might occur because of sluggish blood flow rather than direct venous occlusion by embolic agents.

Although hemorrhage results in poorer outcome, ischemic events were the most common complications of AVM embolization.^{2,4,5,7,8,11,19-22} Sixteen patients (12.31%) in our series had cerebral infarction after embolization, with persistent neurologic deficits in 7 patients. Because of rapid shunting and complex angioarchitecture, perinidal or intranidal normal arteries were very difficult to identify, and neurologic deficits could result from occlusion of these arteries. The present study revealed that sbAVMs located in eloquent cortices had a significantly higher rate of postprocedural persistent ischemic neurologic dysfunction.

In addition to AVM location, other angioarchitectural characteristics that contribute to nonmanipulated complications of embolization remain controversial.^{2,7,8,19,20,34-37} Haw et al⁸ reviewed 306 consecutive patients and 513 embolization sessions from 1984–2002 at the University of Toronto and suggested that the factors associated with complications included the presence of a high-flow fistula or fistulous component to the nidus, eloquent cortex involvement, or venous glue embolization. The long interval of data collection (1984–2002) could have undermined the validity of these conclusions because significant advancement in the embolization technique occurred during this time period. Among all angiographic parameters investigated in 168 consecutive patients and 295 embolization sessions, Ledezma et al⁷ found that Spetzler-Martin grades III–V were significantly associated with unfavorable outcomes and embolization complications. Gobin et al³⁸ revealed that embolization complications were 0% (grade II), 5% (grade III), 15% (grade IV), and 22% (grade V) in their 125 patients studied on Spetzler-Martin classification. On the other hand, studies of Hartmann et al³⁶ and Kim et al¹⁰ failed to demonstrate the correlation between Spetzler-Martin grade and embolization complication and found that embolization sessions were the primary factor for postprocedural complications.

To eliminate the statistical bias caused by embolization sessions, we studied the complications of first-time embolization of 130 sbAVMs and demonstrated that postprocedural complications were associated with eloquent cortical location (OR, 2.57; 95% CI, 1.08–3.42) and exclusive deep venous drainage (OR, 4.56; 95% CI, 1.28–9.67) but not with Spetzler-Martin classification in univariate and multivariate models. The result suggested that the required multiple sessions in large AVMs but not the AVM size itself might be associated with procedural complications.^{10,36} The higher complication rate in sbAVMs with exclusive deep venous drainage could be related to the relative lack of a collateral drainage pathway, making them prone to venous outflow obstruction by embolic agents. This observation may also be confounded by the deep location of these AVMs. Thus, sbAVMs with functional cortex and exclusive deep venous drainage would be more difficult to treat and would be at greater risk for embolization complications than the other types of sbAVMs.

CONCLUSIONS

Embolization is a safe treatment technique for supratentorial AVM, with the development of flow-directed microcatheters and liquid embolic agents. Eloquent cortical location and exclusive deep venous drainage were significantly associated with embolization complications, and venous outflow occlusion in cases with

subtotal and partial embolization might be a predictive factor for periprocedural hemorrhage.

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