# Fistula and Infratentorial Location, Characteristics That Contribute to Cerebral Arteriovenous Malformations, Lead to the Formation of Associated Aneurysms in Patients

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■ OBJECTIVE: **Because the formation of associated aneurysms (AAs) related to the characteristics of cerebral artriovenous malformations (cAVMs) is poorly recognized, the purpose of this study was to identify the responsible characteristics of cAVMs related to the formation of AAs and to identify patients with responsible characteristics related to the formation of AAs through the analysis of the outcomes of these patients after treatment.**

■ METHODS: **This study was performed to analyze the baseline characteristics of patients with cAVMs and AAs. The recurrent AA and residual size of cAVMs were used to evaluate the outcomes of patients after treatment. At the same time, the ROC curve was measured to gauge the relationship between the residual size of cAVMs and recurrent AAs in eligible patients.**

■ RESULTS: **Fifty (15.0%) patients with cAVMs and AA were confirmed; these patients had twice the hazard of hemorrhage as patients with only isolated cAVMs. An infratentorial location ($P < 0.001$) and fistula ($P = 0.002$) were independent predictors of the formation of AAs. After a mean 22.7 months follow-up, 2 patients developed recurrent AAs, and the annual recurrence rate for patients with responsible characteristics was 17.6%, but for all patients was 7.2%. The ROC curve showed that patients, specifically patients with responsible characteristics, the residual size of the cAVM was closely related to recurrent AA (area = 0.89, 95% confidence interval 0.81–0.97, $P = 0.023$, cut-off value = 82.5%).**

■ CONCLUSIONS: **Patients with cAVMs and AA who harbor a fistula or an infratentorial location tend to form AAs. To prevent recurrent AAs and decrease the subsequent risk of hemorrhage, complete obliteration of cAVMs or retrograding over 80% size of cAVMs is recommended.**

## INTRODUCTION

With a prevalence of 2.7%–58%, depending on various populations or methodologies.[1-4] cerebral arteriovenous malformation (cAVM)-associated aneurysm is a crucial component in the generation of intracranial hemorrhage. The correlation, however, between cAVMs and associated aneurysm (AA) is unclear, such as whether both lesions with independent features are diagnosed together incidentally[5] or whether there are hemodynamic changes related to the formation of AA,[6-10] with the majority of authors endorsing the latter.[4,11-13] Because controversy exists regarding the mechanism of AA, it is easily to misdirect therapeutic decision-making, especially in asymptomatic patients.

**Key words**
- Associated aneurysms
- Cerebral arteriovenous malformations
- Hemorrhage
- Nonresponsible characteristics
- Responsible characteristics

**Abbreviations and Acronyms**
**AAs**: Associated aneurysms
**cAVMs**: Cerebral arteriovenous malformations
**CI**: Confidence interval
**CTA**: Computed tomography angiography
**DSA**: Digital subtraction angiography
**MR**: Magnetic resonance
**OR**: Odds ratio
**ROC**: Receiver operating characteristic curve
**S-M**: Spetzler–Martin Grade

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The ultimate objective of treatment is the elimination of the risk of hemorrhage to prevent subsequent hemorrhage. cAVMs that are of a high grade or a large size often require multiple procedures before they are obliterated completely, and asymptomatic patients without risk factors for hemorrhage often have been inclined to be treated conservatively. Therefore, a residual or unchanged size of cAVM is observed more frequently, and during the time from diagnosis to the complete obliteration of the cAVM, the residual lesion usually is accompanied by a secondary hemorrhage, which already is a concern for many neurosurgeons.[4,10,14-17] This mechanism of hemorrhage in the residual lesion, however, is unclear; it may form a new or recurrent AA, which is deemed a risk factor for hemorrhage.[17] Therefore, it is necessary to explore further the characteristics of cAVMs that are correlated with AAs.

Concerning the correlation between cAVMs and AAs, hemodynamic alteration probably is responsible for the formation of an AA, and the characteristics of cAVMs, such as fistula, may affect hemodynamic alteration. As one could infer, there are certain characteristics of cAVMs that are related to the formation of AAs. In addition, factors associated with the production of AAs, such as high flow and large size, have been reported in case reports.[4,7,8,17]

Therefore, we used a univariate or multivariate logistic regression model to analyze the baseline characteristics of cAVMs encountered from 1999 to 2013 in our institution to identify responsible characteristics and to evaluate the outcomes of patients with these characteristics after treatment to identify future patients who might be at risk of developing AA and understand the association of the residual size of the lesion and recurrent AA.

## MATERIALS AND METHODS

### Patients

This study was approved by Institutional Review Board of Zhujiang Hospital, and informed consent was obtained from the participants. This cohort of 472 patients with cAVMs was diagnosed by digital subtraction angiography (DSA), computed tomography angiography (CTA), and magnetic resonance (MR) or MR angiography from 1999 to 2013. In 472 patients, 64 patients with cAVMs and coexisting AAs were confirmed, in whom 50 (10.6%) were eligible according to the following exclusion criteria: (1) patients with a history of previous treatment; (2) patients with insufficient or absent dates; (3) patients with multiple cAVMs; (4) patients with coexisting aneurysms unrelated to cAVMs (including concurrent aneurysm divided into 3 types: aneurysm was unrelated to cAVMs, flow-related aneurysm, or intranidal aneurysm); and (5) patients concomitant pseudoaneurysms. Figure 1 shows the process of data selection. In addition, patients entered into prospective databases at the time of diagnosis, and the dates were collected by reviewing inpatient and outpatient chart and by analyzing diagnostic and angiogram. Moreover, 2 senior neurosurgeons adjudicated these results that include demography, imaging results, clinical manifestations, complications, subsequent management and neurological outcomes in eligible patients.

### Radiologic Evaluation

Detailed angioarchitectural dates on every cAVM were recorded, and every eligible patient underwent superselecive microcatheterization angiography. cAVMs were assessed for size in 3 planes (the maximum nidus diameter as <3 cm, 3−6 cm, and 6 cm), location (infratentorial location vs. supratentorial location), and eloquent area (including deep ventricular nuclei, thalami, ventricles, brainstem, or motor, sensation, and linguistic area). The 5-tier Spetzler−Martin grading system (S-M) was used. Venous drainage was characterized by the presence of deep venous drainage and drainage venous outflow was presence of ectasia or stenosis. AAs were classified as intranidal and flow-related aneurysms. The feeding artery was documented as anterior, posterior circulation, or both. The fistula was characterized by the absence or presence of fistula.

### Treatment Regimen

Patient management was based on an interdisciplinary consensus that included neurosurgeons, neuroradiologists, and neurologists. Patients with cAVMs concurrently with AA were examined for clinical and neurologic symptoms, type of presentation with or without hemorrhage, or a special consideration on the potential source of bleeding (e.g., deep venous drainage, or AA) needed to make a treatment decision, except for against the patient's will. If clinical or neurologic symptoms (including hemorrhage) were the result of either cAVM or AA, the symptomatic lesion was prioritized; however, if the root of the clinical or neurologic symptoms, whether because of the cAVMs or AA, could not be determined, especially for cAVMs concurrent with intranidal AA, both lesions were removed simultaneously. Actually, based on confined surgical exposure when 2 lesions (cAVMs and concurrent AA) are exposed difficultly, it is impossible to treat both lesions by microsurgery simultaneously, thus staged treatment would be implemented.

If the AA was considered as the potential source of bleeding, the best treatment was microsurgical clipping or embolization, performed as soon as possible. For ruptured AAs, we first secured the aneurysm by using microsurgery or embolization within 72 hours and then strived to treat the cAVM. If a ruptured AA was confirmed within the nidus of the cAVM, both lesions were treated by microsurgery or endovascular embolization simultaneously. For unruptured AAs, we still sought to eliminate as much of AA as possible before obliterating the cAVM because the mechanism of AAs are entirely different from independent aneurysms, which aren't correlated with cAVMs. If some of the existing unruptured AA was difficult to treat through embolization or microsurgery, we sought to obliterate as much of the cAVM as possible.[17]

After a cAVM ruptured, therapy for cAVM was always deferred for 3−4 weeks on the condition that it was not life-threatening. If patients present the cerebral hernia secondary to hemorrhage, microsurgery was performed emergently. For patients with small superficial cAVMs (<3 cm), microsurgery was recommended; however, in some patients with small deep lesion of cAVMs (<3 cm), radiosurgery was a possible choice. The remaining patients underwent embolization, according to Sahlein et al.,[18] who proposed the following 3 treatment criteria: (1) endovascular occlusion alone; (2) devascularization of as much of the cAVMs as possible before microsurgery or radiosurgery; and (3) aiming at a focal angioarchitectural weakness, either alone or in conjunction with microsurgery or radiosurgery.

As a result, there were 35 (70%) patients who received endovascular treatment, 8 (16.0%) who underwent microsurgery, 5 (10.0%) radiosurgery, and 2 (4.0%) who were managed conservatively. In 35 patients who underwent embolization, 12 patients were treated further by microsurgery, and 21 patients were treated further by

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