Hemodynamic Characteristics of Cerebral Arteriovenous Malformation Feeder Vessels With and Without Aneurysms

Sophia F. Shakur, MD; Sepideh Amin-Hanjani, MD; Hassan Mostafa, MD; Fady T. Charbel, MD; Ali Alaraj, MD

Background and Purpose—The pathogenesis of aneurysms associated with cerebral arteriovenous malformation (AVM) feeder vessels is poorly understood. We sought to determine the hemodynamic characteristics of AVM feeder vessels with and without aneurysms.

Methods—Patients with AVMs associated with feeder aneurysms who had flow, vessel diameter, and wall shear stress measured before treatment using quantitative magnetic resonance angiography were retrospectively reviewed. Feeders within each AVM were classified into 2 groups based on presence or absence of aneurysms. Hemodynamic parameters were calculated for each arterial feeder and then compared between the 2 groups.

Results—Eleven patients had AVMs with feeder aneurysms. Of 35 total feeder arteries, 12 had an aneurysm and 23 feeders did not have any aneurysms. Absolute mean flow was higher (510.2 versus 438.4 mL/min; \(P=0.53\)) and vessel diameter was lower (4.0 versus 4.8 mm; \(P=0.24\)) in feeders with aneurysms but not significantly. However, wall shear stress (96.2 versus 28.0 dynes/cm²; \(P=0.04\)) was significantly higher in feeders with aneurysms.

Conclusions—Wall shear stress is significantly higher among cerebral AVM feeders harboring aneurysms. Despite similarly high flows, feeder artery diameter tended to be smaller if an aneurysm was present, suggesting that AVM feeders with aneurysms are a subgroup in which vessel remodeling cannot compensate for increased blood flow. (Stroke. 2015;46:1997-1999. DOI: 10.1161/STROKEAHA.115.009545.)

Key Words: aneurysm ■ arteriovenous malformations ■ cerebral ■ hemodynamics ■ magnetic resonance angiography ■ shear stress

The association of cerebral arteriovenous malformations (AVMs) with intracranial aneurysms is well-documented in the literature, with an estimated prevalence of 10% to 20%.1,2 However, the pathogenesis of feeder artery aneurysms, which arise from arteries supplying the AVM, is poorly understood.1,3 The prevailing pathophysiological mechanism responsible for feeder aneurysm formation is thought to be hemodynamic, but this hypothesis is largely based on anecdotal evidence of the high occurrence of aneurysms with AVMs and aneurysm regression after AVM obliteration.1,3-5 In this study, we aimed to determine the hemodynamic characteristics of AVM feeder arteries with and without aneurysms using quantitative magnetic resonance angiography.

Methods

Patient Selection

After institutional review board approval, clinical data for all patients with a cerebral AVM who underwent quantitative magnetic resonance angiography at our institution between 2007 and 2014 were reviewed. AVMs associated with feeder aneurysms, defined as aneurysms arising from arteries supplying the AVM, were identified based on digital subtraction angiography. Feeders were classified into 2 groups, those with and those without aneurysms. Intranidal aneurysms were not included.

Flow, Vessel Diameter, and Wall Shear Stress Measurements

All patients in this study underwent quantitative vessel flow rate and size measurements of the extracranial and intracranial arteries using quantitative magnetic resonance angiography before any treatment of the AVM. This technique has been described and validated previously6,7 and was implemented using the commercially available software, Noninvasive Optimal Vessel Analysis (NOVA, VasSol Inc, River Forest, IL); further details are provided in the online-only Data Supplement.

Flow and diameter were measured within the primary arterial feeders proximal to the AVM or proximal to the aneurysm when present in these same anatomic locations: internal carotid artery, cervical segment; anterior cerebral artery, A2 segment; middle cerebral artery, M1 segment; and posterior cerebral artery, P2 segment. An illustrative case is shown in Figure I in the online-only Data Supplement.
Once blood flow and vessel diameter were measured, wall shear stress (WSS) was calculated using the Hagen–Poiseuille equation:

\[ \text{WSS} = \frac{32 \mu Q}{\pi D^3} \]

WSS is in dynes/cm², \(Q\) is the volumetric flow rate in mL/s, and \(D\) is the vessel diameter in cm. \(\mu\) is the blood viscosity in poise and was assumed to be constant (0.035 poise). This method was previously described by Zhao et al.8

Statistical Analysis
Mean flow, diameter, and WSS were compared between the 2 groups using the independent 2-tailed Student \(t\) test. Exponential regression analysis was used to assess the relationship between blood flow, vessel diameter, and WSS in the 2 groups. All analyses were performed with SPSS (Version 22; IBM Inc).

Results

Patient Characteristics
Eleven patients had AVMs with feeder aneurysms. Among these AVMs, there were 35 total feeder arteries, 12 feeders with and 23 feeders without an aneurysm. Cohort characteristics are summarized in Table.

Mean Flow, Diameter, and WSS in Feeder Arteries With Versus Without Aneurysms
Absolute mean feeder artery flow (510.2 versus 438.4 mL/min; \(P=0.53\)) was similar between the 2 groups and vessel diameter (4.0 versus 4.8 mm; \(P=0.24\)) tended to be lower in feeders with aneurysms, but not significantly. However, WSS (96.2 versus 28.0 dynes/cm²; \(P=0.04\)) was significantly higher in feeders with aneurysms (Figure 1).

Flow Versus Diameter in Feeder Arteries With and Without Aneurysms
Exponential regression analysis demonstrated that higher flows were significantly associated with larger vessel diameter in AVM feeders (\(R^2=0.52; P=0.01\)) and without aneurysms (\(R^2=0.46; P=0.001\)). Importantly, at most flow rates, feeders with aneurysms had smaller diameters and subsequently higher WSS than feeders without aneurysms (Figure 2).

Discussion
Since Walsh and King9 described the first clinical case of a cerebral AVM with a feeder aneurysm, numerous studies have confirmed this association and speculated on its pathogenesis.2 High blood flow to the AVM is postulated to be the main impetus for aneurysm development, yet the majority of AVMs are not associated with feeder aneurysms, thereby implicating a different hemodynamic factor.1,3–5,10 Brown et al found that

<table>
<thead>
<tr>
<th>Table. Clinical, Anatomic, and Hemodynamic Characteristics of Arteriovenous Malformation Feeders With and Without Aneurysms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical characteristics</td>
</tr>
<tr>
<td>Mean age, y (range) 45 (25–72)</td>
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<tr>
<td>Hemorrhagic presentation (% of cohort) 9.1</td>
</tr>
<tr>
<td>Anatomic features</td>
</tr>
<tr>
<td>Spetzler–Martin grade (% of cohort) 1 (37)</td>
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<tr>
<td>2 (27)</td>
</tr>
<tr>
<td>3 (18)</td>
</tr>
<tr>
<td>4 (9)</td>
</tr>
<tr>
<td>5 (9)</td>
</tr>
<tr>
<td>Mean volume, mL (range) 16.7±17.7 (0.9–54.0)</td>
</tr>
<tr>
<td>Hemodynamics</td>
</tr>
<tr>
<td>Feeder artery type (% of feeder vessels)</td>
</tr>
<tr>
<td>ICA (36)</td>
</tr>
<tr>
<td>A2 (27)</td>
</tr>
<tr>
<td>M1 (23)</td>
</tr>
<tr>
<td>P2 (14)</td>
</tr>
<tr>
<td>ICA (25)</td>
</tr>
<tr>
<td>A2 (25)</td>
</tr>
<tr>
<td>M1 (33)</td>
</tr>
<tr>
<td>P2 (17)</td>
</tr>
<tr>
<td>Mean flow, mL/min (median, range) 438.4±326.1 (423.5, 20–1086)</td>
</tr>
<tr>
<td>Mean vessel diameter, mm (median, range) 4.8±1.9 (4.0, 2.2–8.0)</td>
</tr>
<tr>
<td>Mean WSS, dynes/cm² (median, range) 28.0±19.0 (24.1, 2.4–77.9)</td>
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</table>

ICA indicates internal carotid artery; and WSS, wall shear stress.
AVM flow and shunt characteristics, assessed on angiography by the number and size of feeders as well as time between arterial and venous phases, were similar in AVMs with and without feeder aneurysms and instead suggested that higher flow velocities in feeders with aneurysms could result in turbulence and hemodynamic stress. However, only 1 other study has directly measured and compared hemodynamic parameters in AVM feeder arteries with and without aneurysms. Using time-resolved 3-dimensional magnetic resonance angiography, Illies et al. found no significant correlation between altered transit time and presence of a feeder aneurysm. Further evaluation of other hemodynamic characteristics, though, was lacking in their study. Here, we report that feeders with aneurysms have similar flow rates but smaller diameters compared with those feeders without aneurysms, and consequently, significantly increased WSS. These results overall support the idea of WSS as the likely culprit in AVM feeder aneurysm pathogenesis. Our findings corroborate the fact that WSS has been implicated as an important biomechanical stimulus for vessel remodeling and demonstrate its potential impact on cerebral AVM feeder vessels.

Limitations of our study are its retrospective design and small sample size. Nonetheless, it is the first study of its kind. In addition, while the Hagen–Poiseuille equation assumes steady, laminar flow of a Newtonian fluid in straight rigid vessels, which is violated in AVMs, it provides a useful estimate of WSS. The possibility for flow and vessel caliber to be affected by vessel type is a concern when grouping together different AVM feeders. Consequently, feeders of the same AVM with and without aneurysms were assessed to control for vessel type.

Conclusions
WSS is significantly higher among cerebral AVM feeders with aneurysms, and so AVM feeder vessels with and without aneurysms are hemodynamically different. Despite similarly high flows, feeder artery diameter tended to be smaller in feeders with aneurysms, suggesting that AVM feeders with aneurysms are a subgroup in which vessel remodeling cannot compensate for increased blood flow.

Disclosures
Dr. Amin-Hanjani received research grant from the National Institutes of Health, and research support (no direct funds) from GE Healthcare, VasSol Inc. Dr. Charbel received ownership interest from VasSol Inc and is a consultant of Transonic. Dr. Alaraj is a consultant of Cordis-Codman and received research grant from the National Institutes of Health. The other authors report no conflicts.

References
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Supplemental Methods

QMRA technique

All subjects underwent phase contrast quantitative magnetic resonance angiography (QMRA) performed on a 1.5 Tesla or 3.0 Tesla magnetic resonance (MR) system (Sigma VHi, GE Medical system, Milwaukee, WI) using a 4-channel neurovascular coil. The volume flow rate measurements were acquired with the Noninvasive Optimal Vessel Analysis (NOVA) software (VasSol, Inc., River Forest, IL). To visualize major extracranial arteries in the neck, 2-dimensional (2D) MRA time-of-flight (TOF) technique (TR/TE, 23 ms/4.6 ms; flip angle, 60; FOV, 200mm; slice thickness, 2 mm; matrix, 256/192; NEX, 1 ) was performed first. Then, a 3D MRA TOF of the head was obtained with the following parameters: TR/TE, 23/3.3 ms; flip angle, 20; FOV, 220mm; section thickness, 1mm; matrix, 512 X256. MRA TOF images were received by the NOVA software on a separate workstation in order to reconstruct a 3D surface-rendering of the vasculature for determining the perpendicular scan plane to vessels of interest. Volume flow measurements based on these positions were performed (TR, 10-15ms; TE, 4-7ms; flip angle, 15; NEX, 4; slice thickness, 3 mm for intracranial arteries and 5 mm for neck arteries; FOV, 140 mm for intracranial arteries and 180mm for neck arteries; matrix, 256x192 for intracranial arteries and 256x128 for neck arteries). Velocity encoding was automatically adjusted by the NOVA software. All QMRA flow measurements were performed using an oblique 2D fast phase contrast sequence with retrospective gating. Volumetric flow rate (ml/min) in each artery was processed on the NOVA workstation after phase contrast images had been acquired.

The accuracy and precision of QMRA flow measurements using NOVA software have been published previously. Additionally, this technique has demonstrated utility in the hemodynamic evaluation of cerebrovascular pathologies and interventions, including extracranial carotid artery stenosis, intracranial angioplasty/stenting, carotid endarterectomy, and extracranial-intracranial bypass.
Supplemental Figures

Figure I

A. Identification of right PCA feeder aneurysm (white arrow) on digital subtraction angiography, left vertebral artery injection, anterior-posterior projection.

B. QMRA location of right PCA flow and diameter measurement just proximal to feeder aneurysm (yellow plane), anterior-posterior projection. Right PCA flow wave is shown above.

C. Flow map generated by NOVA software with right PCA flow rate of 582 mL/min circled in yellow.
Supplemental References


