Role of the Bloodstream Impacting Force and the Local Pressure Elevation in the Rupture of Cerebral Aneurysms

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Background and Purpose—Inertial force of the bloodstream results in the local elevation of intravascular pressure secondary to flow impact. Previous studies suggest that this “impacting force” and the local pressure elevation at the aneurysm may have a large contribution to the development of cerebral aneurysms. The goal of the present study is to evaluate how the bloodstream impacting force and the local pressure elevation at the aneurysm influences the rupture of cerebral aneurysms.

Methods—A total of 29 aneurysms were created in 26 patient-specific vessel models, and computer simulations were used to calculate pressure distributions around the vessel branching points and the aneurysms.

Results—Direct impact of the parent artery bloodstream resulted in local elevation in pressure at branch points, and bends in arteries (231.2 ± 198.1 Pa; 100 Pa = 0.75 mm Hg). The bloodstream entered into the aneurysm with a decreased velocity after it impacted on the branching points or bends. Thus, the flow impact at the aneurysm occurred usually weakly. At the top or the rupture point of the aneurysm, the flow velocity was always delayed. The local pressure elevation at the aneurysm was 119.3 ± 91.2 Pa.

Conclusions—The pressure elevation at the area of flow impact and at the aneurysm constituted only 1% to 2% of the peak intravascular pressure. The results suggest that the bloodstream impacting force and the local pressure elevation at the aneurysm may have less contribution to the rupture of cerebral aneurysms than was expected previously. (Stroke. 2005; 36:1933-1938.)

Key Words: blood pressure ■ computer simulation ■ hemodynamic phenomena ■ intracranial aneurysm ■ stress, mechanical

The development of cerebral aneurysm is promoted by various physical factors associated with blood flow.1–4 Because cerebral aneurysms usually arise at the vascular branching point or the strong curvature, it is suggested that the physical force generated by blood flow impact may be particularly important.1–4

Flow impact results in 2 physical forces different in direction. One is the “impacting force,” which results from the inertial force of the bloodstream and acts perpendicular to the vessel wall.5 The other is the wall shear stress (WSS), the viscous friction of the bloodstream that acts parallel to the vessel wall.6 The role of the former force is intuitively assumed significant in the pathophysiology of cerebral aneurysms; however, this assumption needs to be proven with scientific evidence because the site of flow impact around the aneurysm and the magnitude of the impacting force has not been obtained yet.

The impacting force of the bloodstream can be considered as the local elevation of pressure at the area of flow impact, as described below.5,7 The kinetic energy of fluid is converted to pressure when the velocity decreases and vice versa. Thus, it is called “dynamic pressure” in the field of fluid mechanics. At the time of flow impact when the bloodstream changes its direction, the velocity decreases momentarily, and most of the dynamic pressure is converted to the static pressure. This results in the local pressure elevation at the area of flow impact. Previous study5,8 also states that the complex velocity distribution around the aneurysm results in the pressure elevation at the aneurysm.

Fluid dynamic simulation calculates the spatial distribution of the velocity and the pressure in a mathematical model of vessel, and this method can be applied to study the bloodstream impacting force and the local pressure elevation at the aneurysm. Cerebral arteries of the skull base, where the aneurysm usually occurs, are tortuous and branching, and the spatial pressure distribution in the vessel may come under the profound influence of this geometrical complexity. Thus, the mathematical models of vessel are

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created from the clinical diagnostic images for each case, and the flow phenomena around the aneurysm are simulated in the patient-specific vessel models in this study.

The goal of the present study was to evaluate how the bloodstream impacting force and the local pressure elevation at the aneurysm influences the rupture of cerebral aneurysms in the complex geometry of cerebral vasculature.

**Subjects and Methods**

**Patient Population**

From June 2001 to March 2003, 109 patients at our institutions were diagnosed with cerebral aneurysms by 3D digital subtraction angiography (DSA). Of these patients, a total of 29 aneurysms (14 aneurysms were diagnosed after the rupture, and 3 of them accompanied an unruptured one, respectively) in 26 patients (10 males, 16 females; mean age 61.9 years) were deemed of adequate quality for the creation of computational mesh and were used to construct computer models. Aneurysm location included the internal carotid artery (ICA; n = 14), the middle cerebral artery (MCA; n = 14), and the communicating artery of the anterior cerebral artery (ACA; n = 1). Nine ICA aneurysms and 1 MCA aneurysm arose from the sidewall of the parent artery (sidewall aneurysm), where no branch, or only a tiny branch, was recognized near the aneurysms. The other 19 aneurysms were recognized at the typical bifurcation (bifurcation aneurysm).

The number, location, and size of the aneurysms are summarized in Table 1. Written informed consent was obtained from each patient or his/her next of kin.

**Image Acquisition**

A 3D DSA was performed using a clinical C-arm angiography unit (ANGIOSTAR Plus; Siemens A.G.). Angiographic images with matrix size of 512×512 pixels were obtained with a 33-cm field of view, acquiring 50 exposures (70 kilovolt peaks; 400 mA; 10 ms) before and during the injection of contrast medium. Subtracted angiographic images were transferred to a Unix workstation equipped with 3D Virtuoso (Siemens A.G.). Regions for analysis were selected, and the images were reformatted into tomographic images with a pixel size of 0.13 mm and a slice thickness of 0.13 mm.

**Modeling of Vessels and Aneurysms**

Lumen boundaries were segmented with the threshold scheme, and the surfaces of the vessels and the aneurysms were constructed with a marching cubes algorithm using ImageDesign (Quint Corporation). Surface irregularities resulting from partial volume effects, truncated small arteries, and other noises were automatically corrected with using original software, and additional smoothing of the polygonal surfaces was performed manually. The analysis region included the vessels from the cavernous portion of the ICA to the vessels that were 10 to 15 mm distal to the aneurysm.

**Numerical Simulation**

Computer simulation of the bloodstream was performed using a commercially available finite-volume solver (SCRYU/Tetra for Windows Version 5; Software Cradle Co). The velocity fields were determined under the governing equations of continuity and Navier-Stokes. Spatial distributions of pressure was determined by solving the Poisson equation of pressure to complement the velocity fields.

Boundary conditions were defined using specific parameters. Blood was assumed to be an incompressible Newtonian fluid with a specific gravity of 1053 kg/m³ and a viscosity of 4.0×10⁻³ Nm⁻² per second. The viscoelastic properties of the vessel wall were neglected, and a rigid wall with no-slip condition was assumed. One typical blood velocity waveform of ICA was obtained with transcranial Doppler measurement (0.61 m/s at peak systole, 0.24 m/s at end diastole, and 57 bpm) and used to create the inlet boundary condition for all cases because this study focused mainly on the effect of the patient-specific vascular geometry around the aneurysm. From the blood velocity waveform of ICA, Womersley’s velocity profile (i.e., a cross-sectional velocity distribution of a developed pulsatile flow) was created for the inlets of each mathematical model as described in the previous literature. Traction-free boundary conditions were applied to all the outlets of the vessels. The width of the time step for the calculation was adjusted by the solver to control the Courant number <1.0. To confirm the numerical stability, calculations were performed for ≥3 cardiac cycles, and the result from the last cycle was used for analysis. This protocol required ~36 hours to complete the calculation of 1 case using a standard personal computer with a single Pentium 4 processor (3.0 GHz). The average Reynolds and Womersley numbers were 402 and 4.17, respectively, which implies a laminar flow condition.

**Data Analysis**

The spatial distribution of pressure in the vessel was visualized with colored contours from the computed pressure and analyzed qualitatively. Sites where the pressure elevates locally were recorded, and the flow structures were investigated with streamline visualizations and cross-sectional velocity field visualizations.

The computed pressure by the solver represents the spatial difference of pressure compared with the pressure of the outlet boundary, and thus, it comes under a considerable influence of the positional relationship between the measurement point and the outlet boundary. For quantitative comparison among cases, the “reference plane” that has an identical positional relationship with the measurement point was introduced, and it was defined as a cross-sectional plane perpendicular to the vessel axis located just proximal to the area of the local pressure elevation (Figure 1A). The spatially averaged pressure of this plane was used as a reference pressure, and the pressure difference between the computed pressure by the solver and the reference pressure was recalculated. The magnitude of this recalculated pressure was not affected by variation in the outlet boundary in each case and used for the statistical analysis with nonpaired t test or 1-way ANOVA. WSS distributions were also visualized with colored contours and were compared with the pressure distributions. The calculation of WSS from the velocity field was performed as described previously.

**Results**

Temporal changes of the computed pressure were in synchronization with the pulsatile flow velocity at the inlet section. Spatial differences in the pressure were greater during systole than during diastole. Thus, the pressure was analyzed at peak systole for all subsequent experiments.

**Luminal Pressure Elevation**

Qualitative analyses of 26 cases revealed 39 sites of the local pressure elevation in the luminal part of the vessel wall (Figure 1), all secondary to the direct impact of the parent artery bloodstream. The magnitude of the pressure elevation averaged among these sites was 231.2±198.1 Pa (mean±SD; 100 Pa [N/m²]=0.75 mm Hg). Although the local pressure elevation was greater at the branches (242.1±216.9 Pa) than at the bends (194.8±118.6 Pa; P=0.54; t test), it did not

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**Table 1. Site, Size, and Aspect Ratio (AR) of the Aneurysms**

<table>
<thead>
<tr>
<th>Site of Aneurysm</th>
<th>No.</th>
<th>Age (years)</th>
<th>Size (mm)</th>
<th>AR</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICA</td>
<td>14</td>
<td>61.9</td>
<td>6.29</td>
<td>1.27</td>
</tr>
<tr>
<td>MCA</td>
<td>14</td>
<td>62.7</td>
<td>4.65</td>
<td>1.05</td>
</tr>
<tr>
<td>ACA</td>
<td>1</td>
<td>50</td>
<td>8.28</td>
<td>2.38</td>
</tr>
<tr>
<td>Total</td>
<td>29</td>
<td>61.9</td>
<td>5.59</td>
<td>1.21</td>
</tr>
</tbody>
</table>

Numbers in parentheses indicate the number of ruptured aneurysms. Mean values are shown in age, size, and AR.
differ when comparing different types of vessels (ICA, MCA, or ACA; \( P = 0.98 \); ANOVA).

Aneurysmal Pressure Elevation

The local pressure was greater in the aneurysm (119.3 ± 91.2 Pa) than in the adjacent luminal area in all cases (Figure 2; Table 2). The bloodstream entered into the aneurysm with a decreased velocity after it impacted at the branch points or the bends. Thus, the flow impacts at the aneurysm occurred usually weakly. At the top or the rupture point of the aneurysm, the flow velocity was always delayed. The stasis of flow with a weak impact resulted in the local pressure elevation at the aneurysm. There was no significant difference in the degree of the pressure elevation when comparing...
TABLE 2. Magnitude of the Local Pressure Elevation at the Aneurysm

<table>
<thead>
<tr>
<th>Site of Aneurysm</th>
<th>Ruptured</th>
<th>Unruptured</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICA</td>
<td>114.9 (n=7)</td>
<td>117.2 (n=7)</td>
<td>115.9 (n=14)</td>
</tr>
<tr>
<td>MCA</td>
<td>117.3 (n=7)</td>
<td>127.1 (n=7)</td>
<td>122.2 (n=14)</td>
</tr>
<tr>
<td>ACA</td>
<td>...</td>
<td>123.0 (n=1)</td>
<td>123.0 (n=1)</td>
</tr>
<tr>
<td>Total</td>
<td>116.1 (n=14)</td>
<td>122.6 (n=15)</td>
<td>119.3 (n=29)</td>
</tr>
</tbody>
</table>

Mean values are shown in Pascal (N/m²).

The aspect ratio of the ruptured aneurysms (1.31±0.33) was higher than that of the unruptured aneurysms (0.97±0.37) in our cases (t test; P=0.03). However, the correlation coefficient between the aspect ratio and the local pressure elevation of the aneurysm was only 0.26 (P=0.24).

Flow Impact Around the Aneurysm

In 27 of 29 aneurysms, the bloodstream of the parent artery did not impact directly on the aneurysm. It impacted on the luminal wall proximal to the aneurysm orifice. After that, a substantial portion of the bloodstream remained and flowed away in the vessel lumen. This phenomenon was observed similarly in the bifurcation aneurysms (Figure 1A) as well as in the sidewall aneurysms (Figure 1E). In the remaining 2 aneurysms (both were the ruptured aneurysms), the aneurysm orifices were so large that the entire bloodstream entered into the aneurysm, and the bloodstream of the parent artery directly impacted the aneurysm wall (Figure 3). The magnitude of the local pressure elevation at the area of flow impact in these 2 aneurysms was 104.1 Pa (0.78 mm Hg) and 298.8 Pa (2.24 mm Hg), respectively. The flow velocity at the top or the rupture point of the aneurysm was always delayed in 29 aneurysms.

Discussion

Based on the flow simulation of clinically imaged vasculature, the present study demonstrated that flow impact resulted in the local elevation in pressure of 250 Pa (1.88 mm Hg) at branch points and bends of cerebral arteries. However, its magnitude was small compared with the total intravascular pressure, which is nearly equal to the pressure measured at radial artery that averages 128/82 mm Hg in healthy subjects, even when the bloodstream of the parent artery directly impacted on the aneurysm wall. These results suggest that the impacting force of the bloodstream may have a less significant role in the rupture of cerebral aneurysms than is expected intuitively.

Previous studies have demonstrated that the pressure of the aneurysm is locally elevated up to 3× higher than that of the luminal part. However, those studies only characterized the pressure fraction that was converted from the dynamic pressure (ie, the kinetic energy of fluid) rather than determining the contribution of the local pressure elevation to the total intravascular pressure. The present study demonstrated that the decreased velocity in the aneurysm leads to the local pressure elevation of 150 Pa (1.13 mm Hg), which only accounts for 1% of the peak intravascular pressure. Further, the magnitude of the pressure elevation in the aneurysm did not differ when comparing ruptured and unruptured aneurysms. Thus, the local pressure elevation at the aneurysm may also have less contribution to the rupture of cerebral aneurysms than is expected previously.

The magnitude of the impacting force and the local pressure elevation at the aneurysm are small compared with the total intravascular pressure; however, they are momen-
tarily values. A long-standing effect of these small forces cannot be expected from this study.

The flow dynamics around the aneurysm come under a considerable influence of the positional relationship between the aneurysm and the parent artery. The pressure elevation at the bifurcation aneurysm was slightly higher than that of the sidewall aneurysm; however, the contribution of pressure elevation of both aneurysm types was similarly small. Aspect ratio of the aneurysm, which also has been indicated to have a significant influence on the hemodynamics in aneurysms, also influenced little on the pressure elevation at the aneurysm. The reason why the different flow dynamics do not result in a considerable difference in the local pressure elevation may be that the dynamic pressure is considerably small compared with the energy of the static pressure.

As was shown in Figure 4, the flow impact results in high WSS on the distal side of the local pressure elevation. Although the magnitude of the WSS is as low as 2 Pa in the physiological condition, which is only 1% of the magnitude of the local pressure elevation, the WSS is the only force that acts parallel to the vessel and is related to the formation of cerebral aneurysms. The initial pathological changes of aneurysm formation are observed at distal side of the bifurcation apex. This corresponds to the area of high WSS but not at the area of flow impact and local pressure elevation. As to the rupture of aneurysms, the possible role of the high WSS mixed with low WSS in the aneurysm wall is also reported. Thus, the significance of the impact of the bloodstream in the development of cerebral aneurysms may be mediated by high WSS rather than elevation of the local pressure.

The number of cases analyzed in this study is limited; however, it might be stated from our results that the impacting force, which intuitively seems a potent physical force generated by flow, may have less significance than is expected.

Our simulations are based on the patient-specific vessel models. However, only 1 typical velocity waveform is applied on the inlet boundary, and the viscoelasticity of the vessel, which might differ among the cases, is neglected. More patient-specific simulation will be of benefit to predict the individual rupture risk of the aneurysms diagnosed before bleeding.

**Conclusions**

Impacting force of the bloodstream and the local pressure elevation at the aneurysm may have less effect on the rupture of cerebral aneurysms than is expected. Computer simulation of the bloodstream may be of utility in advancing our understanding of hemodynamic stress and the pathophysiology of vascular disease.
Acknowledgments

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References

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