Rationale and Objectives. The objective of this study was to investigate the relationship between hemodynamics patterns and aneurysmal rupture in cerebral aneurysms of the same morphology regardless their location. Particularly, terminal aneurysms in both the anterior and posterior circulation were studied.

Materials and Methods. A total of 42 patient-specific vascular models were constructed from three-dimensional rotational angiography images. All patients had terminal aneurysms at different arteries: a) middle cerebral; b) anterior communicating; c) internal carotid (terminus); d) internal carotid–posterior communicating; e) basilar; or f) anterior cerebral. Hemodynamics information (intra-aneurysmal velocity and wall shear stress distributions) was derived from image-based computational fluid dynamics models with realistic patient-specific anatomies.

Results. The group of aneurysms with an inflow jet that splits in two secondary jets, one of which enters the aneurysm before reaching one of the daughter vessels (type B), had the highest peak wall shear stress (WSS) and the highest rupture rate. The peak WSS averaged over each flow type showed a higher value in the ruptured group. The average peak WSS in the ruptured group (all types) was 188 dyn/cm² (compared to 118 dyn/cm² for the unruptured).

Conclusions. This finding is in agreement with a previous work in which only anterior communicating artery aneurysms were investigated. The significance of these findings is that, if they are statistically confirmed with larger number of cases, flow types could be directly observed during angiographic examinations and linked to WSS categories that may help evaluate which aneurysms are more likely to rupture.

Key Words. Cerebral aneurysm; computational fluid dynamics; hemodynamics; rupture; terminal aneurysm.
we found a possible association between both the flow pattern and the high wall shear stress with rupture (13). Given that most aneurysms had a flow pattern compatible with a terminal location, that single morphological type (terminal aneurysms) is investigated in this work.

**MATERIAL AND METHODS**

**Patients and Images**

A total of 42 consecutive terminal cerebral aneurysms were selected from our database for this study. Patients referred to the interventional neuroradiological service of the Inova Fairfax Hospital (Virginia) between 2003 and 2005, and diagnosed with cerebral aneurysms by conventional catheter angiograms and three-dimensional rotational angiography were considered. Rotational angiography images were obtained during a 180° rotation and imaging at 15 frames per second for a total of 8 seconds, by using an Integris system (Philips Medical Systems, Best, The Netherlands). The corresponding 120 projection images were reconstructed into a three-dimensional data set of 128 × 128 × 128 voxels covering a field of view of 54.02 mm on a dedicated Philips workstation. The selected aneurysms occurred at the bifurcation apex of a single inflow vessel subdivided into two branches of roughly the same diameter. This study included terminal cerebral aneurysms at different locations: 22 in the AcoA, 9 in the middle cerebral artery, 5 in the basilar artery, 3 in the internal carotid artery terminus, 2 at the internal carotid artery–posterior communicating artery bifurcation, and 1 in the anterior cerebral artery (anterior cerebral artery-pericallosa). In this sample, there were 25 ruptured aneurysms (59%) and 17 unruptured aneurysms (41%). Patient characteristics are included in Table 1. Examples of terminal cerebral aneurysms at different locations are shown in Figure 1. The rotational angiography images were obtained during a 180° rotation and imaging at 15 frames per second for a total of 8 seconds, using a Phillips Integris System. The corresponding 120 projection images were reconstructed into three-dimensional datasets of 256 × 256 × 256 voxels covering a field of view of 54.02 mm on a dedicated Philips workstation. The voxel data were exported to a PC for patient-specific computational modeling.

**Patient-Specific Models**

Patient-specific anatomical models of the aneurysm and connected arteries were constructed from the three-dimensional rotational angiography images using deformable models (14). The entire portion of the parent vessel upstream of the aneurysm visible in the three-dimensional rotational angiography images was reconstructed to generate appropriate velocity patterns at the aneurysm location (15). Simplification of the parent artery geometry may result in inaccurate flow patterns, loss of secondary flows, and change in the impaction zone over the aneurysm wall with the consequent change in the wall shear stress values. The anatomical models were smoothed (16), and vessel branches were truncated and extruded along the vessel axis (17). These geometrical models were used to generate high-quality volumetric finite element grids composed of tetrahedral elements with an advancing front technique (18–20). A minimum mesh resolution of 0.16 mm was prescribed, which resulted in meshes containing between 0.7 and 4.5 million elements.

A computational fluid dynamics simulation was carried out for each patient. Blood was modeled as an incompressible and Newtonian fluid with density $\rho = 1.0 \text{ g/cm}^3$ and viscosity $\mu = 0.04 \text{ Poise}$. The governing equations were the unsteady Navier-Stokes equations in three dimensions (21). Vessel walls were assumed rigid and no slip boundary conditions were applied at the walls. Patient-specific flow conditions are not always available because they are not part of the routine clinical examinations. Therefore, pulsatile flow conditions derived from phase-contrast magnetic resonance measurement in normal subjects were imposed at the inlet of the models. Physiologic flow rate waveforms imposed at the inlets of the computational domains were scaled according to the lumen cross sectional area for every model to have the same mean wall shear stress at the inlet (15 dyn/cm² in the internal carotid arteries and 10 dyn/cm² in the basilar arteries). It is important to note that the optimal arterial network that achieves flow with the minimal biological work should have a constant wall shear stress throughout the whole vascular system, which depends on the cross-sectional area, the mean flow rate, and the blood viscosity (22). Fully developed pulsatile velocity profiles were prescribed using the Womersley solution (23, 24). Assuming that the distal vascular beds of the two branches after the bifurcation of the parent artery have similar flow resistances, traction-free

### Table 1 Patient Characteristics

<table>
<thead>
<tr>
<th>Gender</th>
<th>No.</th>
<th>%</th>
<th>Location</th>
<th>No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>18</td>
<td>42%</td>
<td>Acom bilateral</td>
<td>11</td>
</tr>
<tr>
<td>Female</td>
<td>24</td>
<td>58%</td>
<td>Acom unilateral</td>
<td>11</td>
</tr>
<tr>
<td>Ruptured</td>
<td></td>
<td></td>
<td>MCA bifurcation</td>
<td>9</td>
</tr>
<tr>
<td>Yes</td>
<td>25</td>
<td>59%</td>
<td>BA tip</td>
<td>5</td>
</tr>
<tr>
<td>No</td>
<td>17</td>
<td>41%</td>
<td>Pcom</td>
<td>2</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td>ICA terminus</td>
<td>3</td>
</tr>
<tr>
<td>Min</td>
<td>35</td>
<td></td>
<td>ACA-pericallosa</td>
<td>1</td>
</tr>
<tr>
<td>Max</td>
<td>88</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>56</td>
<td></td>
<td></td>
<td>42</td>
</tr>
</tbody>
</table>

boundary conditions with the same pressure level were applied at outlet boundaries. If the model included small vessels branching off the parent vessel upstream of the aneurysm, the flow rate through these small branches were adjusted so that their pressure drop and wall shear stress distribution had no sudden change from the parent artery, which can result in unrealistically large velocity values. The Navier-Stokes equations were numerically integrated using a fully implicit finite element formulation that allows arbitrary timestep sizes (11). Two cardiac cycles were computed using a timestep size of 0.01 seconds (100 time-steps per cycle), and all the results reported correspond to the second cardiac cycle. In-house software was used for image processing and model reconstruction, grid generation, blood flow numerical simulations, and hemodynamic visualization and analysis.

**Hemodynamics Characterization**

Following a previous study of ACoA aneurysms (13), the aneurysmal flow patterns were classified into three different categories according to the way the flow jet splits from the parent artery into the aneurysm and daughter branches. The following flow types were considered: the main jet splits in three secondary jets, one of which enters the aneurysm; the inflow jet splits in two secondary jets, one of which is redirected towards one of the outflow branches while the other one first enters the aneurysm and then flows to the other branch; and the main jets first enters the aneurysm where it splits and flows to the two outflow branches. A sketch of the three flow types is presented in Figure 2.

To classify the flow patterns into these categories, visualizations of the intra-aneurysmal flow patterns at peak systole were created using instantaneous streamlines. Different colors were used for streamlines that originate in the parent artery and flow to each daughter branch without entering the aneurysm and for those that enter the aneurysm before flowing to the daughter branches. The streamlines were subdivided into four groups, depending on whether they enter the aneurysm or not and through which daughter branch...
they exit. The streamlines in each group were automatically counted, and the aneurysms were then assigned to different flow categories depending on the relative number of streamlines in each group. Examples of flow pattern visualizations used for flow characterization are presented in Figure 3.

Maps of wall shear stress (WSS) magnitude were created to visualize the distribution of shear forces on the aneurysm wall. The maximum wall shear stress (MWSS) in the aneurysms was computed from the wall shear stress distribution at the peak systole and recorded. A t-test was performed to study the significance of the difference of MWSS values in both groups.

RESULTS

It was found that in average ruptured aneurysms had larger MWSS than unruptured aneurysms. In particular, the MWSS averaged over the ruptured aneurysm group (271 dyn/cm²) exceeded by a factor larger than two that of the unruptured group (118 dyn/cm²). A t-test showed that the difference is significant at 95% of confidence level (P = .04). It was also observed that 90% of the aneurysms with MWSS higher than 250 dyn/cm² were ruptured. Two aneurysms, one in the middle cerebral artery and one in the ACoA, exhibited a pathological reduction of the lumen proximal to the aneurysms, resulting in extremely high wall shear stress values. These aneurysms (both ruptured) were excluded from further analysis. In that case, the MWSS averaged over the ruptured aneurysm still remains higher than in the unruptured group (188 dyn/cm²).

The number of ruptured and unruptured aneurysms in each flow type was counted. The results are presented in

Table 2
Number and Percentage of Ruptured (R) and Unruptured (UR) Aneurysms in each Flow Type

<table>
<thead>
<tr>
<th>Type</th>
<th>R</th>
<th>%</th>
<th>UR</th>
<th>%</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>6</td>
<td>50%</td>
<td>6</td>
<td>50%</td>
<td>12</td>
</tr>
<tr>
<td>B</td>
<td>15</td>
<td>68%</td>
<td>7</td>
<td>32%</td>
<td>22</td>
</tr>
<tr>
<td>C</td>
<td>2</td>
<td>33%</td>
<td>4</td>
<td>67%</td>
<td>6</td>
</tr>
<tr>
<td>Total</td>
<td>23</td>
<td>58%</td>
<td>17</td>
<td>42%</td>
<td>40</td>
</tr>
</tbody>
</table>

In these results, the two ruptured aneurysms with a pathological reduction of the lumen proximal to the aneurysms and a consequent extremely elevated wall shear stress were excluded.

Table 3
Maximum Wall Shear Stress Averaged over Flow Type for Ruptured (R) and Unruptured (UR) Aneurysms

<table>
<thead>
<tr>
<th>Type</th>
<th>R</th>
<th>Range</th>
<th>UR</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>89</td>
<td>35–200</td>
<td>68</td>
<td>10–150</td>
</tr>
<tr>
<td>B</td>
<td>226</td>
<td>50–600</td>
<td>175</td>
<td>10–570</td>
</tr>
<tr>
<td>C</td>
<td>165</td>
<td>160–170</td>
<td>93</td>
<td>10–40</td>
</tr>
<tr>
<td>Mean</td>
<td>188</td>
<td>35–600</td>
<td>118</td>
<td>10–570</td>
</tr>
</tbody>
</table>

In these results, the two ruptured aneurysms with a pathological reduction of the lumen proximal to the aneurysms and a consequent extremely elevated wall shear stress were excluded. If they were included, the average wall shear stress of the ruptured group would be 271 dyn/cm².

In these results, the two ruptured aneurysms with a pathological reduction of the lumen proximal to the aneurysms and a consequent extremely elevated wall shear stress were excluded. If they were included, the average wall shear stress of the ruptured group would be 271 dyn/cm².
Table 2. The group with the largest number of ruptured aneurysms was flow Type B, which accounted for 65% of all ruptured aneurysms. In this group, 68% (15) of aneurysms were ruptured, whereas 32% (7) were unruptured. In groups A and C, the majority of aneurysms were unruptured, accounting for 50% (6) and 67% (4) of aneurysms in these groups, respectively.

The averages of MWSS over each flow type for ruptured and unruptured aneurysms are presented in Table 3. It was found that for all flow types the MWSS for ruptured aneurysms was higher than for unruptured aneurysms. The group that had the highest MWSS was Type B, which as mentioned previously, had the largest percentage of ruptured aneurysms. Group B was followed by groups C and A, which had lower values of MWSS and smaller percentages of ruptured aneurysms.

Examples of the wall shear stress distributions at peak systole for ruptured and unruptured aneurysms in each flow category are presented in Figure 4. Corresponding visualizations of the flow patterns are presented in Figure 5. This visualizations help understanding the relationship between the flow patterns and the wall shear stress values. In flow type A, the flow from the parent vessel splits toward the daughter vessels before reaching the aneurysm, and thus enters the aneurysm with a diffuse inflow jet that produces relatively low values of wall shear stress. In contrast, in type B, the flow splits right at the neck of the aneurysm and the inflow jet “slides” along the aneurysm wall, creating a region of elevated wall shear stress. Finally, in type C, the flow enters the aneurysm, travels toward the dome and splits inside the aneurysm. In this case, the inflow jet is diffused as it travels toward the dome of the aneurysm and produces a region of elevated wall shear stress at the impaction zone in the dome. However, the values of WSS tend to be smaller than those observed in type B.

CONCLUSION

Cerebral aneurysms are pathological dilations of the arterial wall frequently located near arterial bifurcations in the circle of Willis (25–27). The most serious consequence is their rupture and intracranial hemorrhage, with an associated high mortality and morbidity rate (28–31). Intracranial aneurysms are particularly difficult to treat, and often do not produce symptoms before they rupture (32). Improvements of neuroradiological techniques have resulted in more frequent detection of unruptured aneurysms. Because prognosis of subarachnoid hemorrhage is still poor, preventive surgery is increasingly considered as a therapeutic option. But every treatment carries a risk, which sometimes matches or exceeds the yearly risk of aneurysm rupture. Therefore, the best patient care would be to treat only those patients who are likely to rupture (33–35).

Previous studies based on patient-specific computational models have suggested that aneurysms with concentrated inflow jets that hit the aneurysm wall at a small impingement region and create a complex and unstable intra-aneurysmal
flow pattern are more likely to rupture (12). In addition, it has been shown that elevated wall shear stress produced by different flow patterns may be related to the rupture of aneurysms of the anterior communicating artery (13). Therefore, the aim of this study was to extend these results to cerebral aneurysms of terminal morphologies.

Although the number of aneurysms considered in this study was limited, interesting observations linking hemodynamic characteristics and aneurysm rupture were made. In particular, it was found that ruptured aneurysms had larger maximum wall shear stress values than unruptured aneurysms, and that different flow types had in average different WSS values. These observations are consistent with previous findings on ACoA aneurysms and add further evidence that high WSS may be responsible for the local weakening of the arterial wall and progression to rupture. If statistically confirmed with larger samples, this three-way relationship between flow type, wall shear stress, and aneurysm rupture may potentially be useful for assessing the risk of rupture of cerebral aneurysms.

There are several limitations to our computational methodology that could affect the results of computational fluid dynamics simulations. However, previous sensitivity analyses (11) indicated that using patient-specific vascular geometries the hemodynamic patterns of cerebral aneurysms were not strongly dependent on non-Newtonian viscosity characteristics, moderate changes in the inflow rates, inclusion of small vessel branches proximal of the aneurysm (but away from the neck), and outflow boundary conditions. Patient-specific flow conditions were not available for this study; therefore, “typical” flow waveforms measured in normal subjects were used to prescribe pulsatile flow boundary conditions. However, these flow conditions were scaled with the area of the vessels so that all patients had the same WSS at the inflow of the internal carotid artery and basilar artery, as reported in experimental studies (36, 37). This allows us to compare magnitudes of hemodynamic variables such as wall shear stress. Additionally, in this study, images of ruptured aneurysms were acquired after the rupture, and it was assumed that the hemodynamic characteristics determined from these images were close to those just before rupture. Most studies of cerebral aneurysms investigating their rupture suffer from the same limitation because unruptured aneurysms are seldom followed until they rupture. Despite this limitation, the hemodynamic classification proposed in our previous work (13) and applied here, which is based on the flow division characteristics, is unlikely to strongly depend on the exact shape of the aneurysms which most probably changes—if it changes—at the dome after rupture. This issue, however, deserves further investigation.

The results presented in this work suggest that aneurysms with high values of peak wall shear stress may be more likely to have ruptured than those with lower wall shear stress magnitudes. In turn, the magnitude of the maximum wall shear stress in the aneurysm is associated to the different manners in which the blood flow in the parent artery splits,
enters the aneurysm, and bifurcates to the daughter branches. In particular, aneurysms with an inflow jet that splits into two secondary jets at the aneurysm neck (flow Type B) have the highest wall shear stress and are most likely to have ruptured. This finding is in agreement with a previous work in which only anterior communicating artery aneurysms were investigated. The significance of these findings is that if they are statistically confirmed with larger number of cases, flow types could be directly observed during angiographic examinations and linked to wall shear stress categories that may help evaluate which aneurysms are more likely to rupture.

REFERENCES