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Impact of bifurcation angle and inflow coefficient on the rupture risk of bifurcation type basilar artery tip aneurysms

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OBJECTIVE Risk factors for aneurysm rupture have been extensively studied, with several factors showing significant correlations with rupture status. Several studies have shown that aneurysm shape and hemodynamics change after rupture. In the present study the authors investigated a static factor, the bifurcation angle, which does not change after rupture, to understand its effect on aneurysm rupture risk and hemodynamics.

METHODS A hospital database was retrospectively reviewed to identify patients with cerebral aneurysms treated surgically or endovascularly in the period between 2008 and 2015. After acquiring 3D rotational angiographic data, 3D stereolithography models were created and computational fluid dynamic analysis was performed using commercially available software. Patient data (age and sex), morphometric factors (aneurysm volume and maximum height, aspect ratio, bifurcation angle, bottleneck ratio, and neck/parent artery ratio), and hemodynamic factors (inflow coefficient and wall shear stress) were statistically compared between ruptured and unruptured groups.

RESULTS Seventy-one basilar tip aneurysms were included in this study, 22 ruptured and 49 unruptured. Univariate analysis showed aspect ratio, bifurcation angle, bottleneck ratio, and inflow coefficient were significantly correlated with a ruptured status. Logistic regression analysis showed that aspect ratio and bifurcation angle were significant predictors of a ruptured status. Bifurcation angle was inversely correlated with inflow coefficient ($p < 0.0005$), which in turn correlated directly with mean ($p = 0.028$) and maximum ($p = 0.014$) wall shear stress (WSS) using Pearson's correlation coefficient, whereas aspect ratio was inversely correlated with mean (0.012) and minimum ($p = 0.018$) WSS.

CONCLUSIONS Bifurcation angle and aspect ratio are independent predictors for aneurysm rupture. Bifurcation angle, which does not change after rupture, is correlated with hemodynamic factors including inflow coefficient and WSS, as well as rupture status. Aneurysms with the hands-up bifurcation configuration are more prone to rupture than aneurysms with other bifurcation configurations.

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KEY WORDS aneurysm; aspect ratio; basilar artery; bifurcation; rupture; vascular disorders

Cerebral aneurysms have a prevalence of approximately 2%–5% in the general population[18] but represent a serious health care issue, with 30-day mortality rates after rupture of up to 50%–60%[1] and dependence rates among survivors of 30%–40%.[1] Advances in noninvasive imaging techniques and greater awareness of the risks posed by aneurysms have resulted in the identification of more and more unruptured aneurysms, but 50%–80% of all aneurysms do not rupture during an individual's lifetime.[4] Consequently, questions such as

ABBREVIATIONS AUC = area under the curve; HD = hands-down; HN = hands-neutral; HU = hands-up; ROC = receiver operating characteristic; WSS = wall shear stress.

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whether all unruptured aneurysms should be treated on diagnosis or whether aneurysms with a low risk of rupture can be identified and excluded from treatment are controversial and much debated. The treatment of unruptured aneurysms is not a 100% risk-free option, with 3% mortality and 15% morbidity rates for surgical treatment and 2% morbidity and 5% mortality rates for endovascular intervention.[18] However, the occurrence of subarachnoid hemorrhage results in high risks to patients and greatly increased economic burdens.[19] Therefore, the ideal procedure will allow us to identify aneurysms that will rupture and thus to focus resources on the optimum treatment. However, this ideal is far from practical reality as the factors governing aneurysm rupture are complex and intertwined and not fully understood.

Several studies have attempted to unravel the complex nature of aneurysm microbiology and the hemodynamics that influence aneurysm growth and rupture, including patient,[3,11] anatomical,[10,15] and/or hemodynamic factors,[13] with varying degrees of emphasis. Several patient-specific parameters such as age, ethnicity, and smoking have been proven to be associated with rupture.[7,11] In addition, morphometric parameters such as aspect ratio,[1,14] bottleneck ratio,[10] bleb formation,[24] neck deviation,[1,14] inflow angle,[2] and aneurysm volume/ostium ratio[21] can be used to discriminate ruptured from unruptured aneurysms.

In the present study we analyze the factors that may influence rupture in bifurcation-type basilar tip aneurysms, propose a classification for bifurcation types (which do not change after rupture), evaluate how the bifurcation geometry and angle affect the hemodynamics inside the aneurysm, and analyze the significance of predicting the rupture of bifurcation aneurysms.

Methods

Patient Selection

Our hospital database was reviewed to identify patients with cerebral aneurysms treated surgically or endovascularly in the period between 2008 and 2015. Cases with aneurysms associated with rudimentary or duplicated posterior cerebral artery, multiple aneurysms in the vertebrobasilar system, asymmetrical posterior cerebral arteries with differential diameters exceeding 50%, and poor image quality preventing model construction, as well as previously treated aneurysms, were excluded. The institutional review board of Kohnan Hospital, Sendai, Japan, approved the design of this study.

Aneurysm Model Creation

Conventional digital subtraction and 3D rotational angiography had been performed using standard transfemoral catheterization with a biplanar unit (Innova 3131, GE Healthcare Japan). Images had been obtained during a 6-second injection of contrast agent and a 200° rotation, with imaging at 30 frames per second for 5 seconds. The 150 projection images were reconstructed into a 3D data set of 512 × 512 × 512 isotropic voxels covering a field of view of 200 mm in all 3 directions.

The 3D data set obtained from rotational angiography was exported to a personal computer to form a 3D iso-

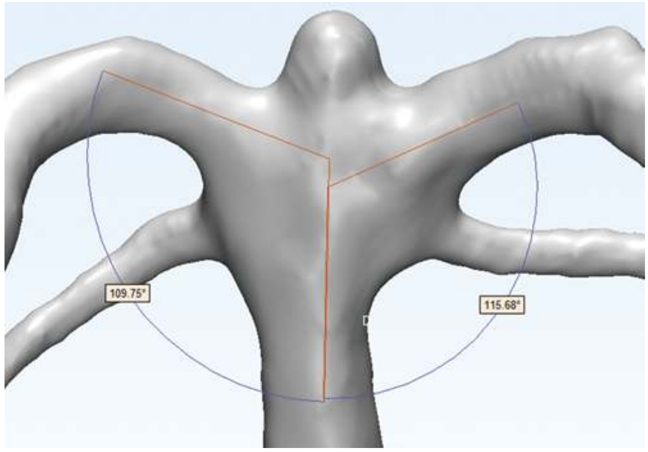

FIG. 1. Screenshot showing the method of measuring the angle of bifurcation using 3-matic Research. The angle of bifurcation is the caudal angle formed between the intersection of the center lines of the basilar artery and the bilateral posterior cerebral arteries. The sum of both angles was used for statistical analysis. Figure is available in color online only.

surface model of the aneurysms. The 3D surface was extracted using VMTK 1.2 (http://www.vmtk.org) according to the instructions and was then displayed on the native axial, coronal, and sagittal slices of the original 3D data set and adjusted to achieve visual matching of the luminal boundary of all regions of interest. The segmented 3D surface was then processed with commercial software (3-matic Research 9.0, Materialise) to smooth the fine irregularities, to obtain planes for inlets and outlets, and to clear small branches from the regions of interest. The rate of volume change was suppressed to ≤ 5% during the smoothing process. The output data were processed in stereolithography format.

Morphometric Analysis

Measurements were taken using 3-matic Research 9.0. Aneurysm height, width, and neck diameter; basilar artery diameter; and bifurcation angle were all measured manually. Aspect ratio (aneurysm height/neck diameter), bottleneck ratio (aneurysm width/neck diameter), neck/parent artery ratio (aneurysm neck diameter/basilar artery diameter), and bifurcation angle (sum of both basilar artery–P_1 angles) were calculated for all aneurysms. The bifurcation angle was defined as the angle formed between the intersection of the center lines of the basilar artery and the bilateral posterior cerebral arteries (Fig. 1). These manually calculated angles were also confirmed using Hemoscope computational fluid dynamic software (v1.4, EBM Corp.).

Hemodynamic Analysis

Hemodynamic analysis was conducted using Hemoscope, which allowed us to automate the following processes. First, these vascular geometries were filled with unstructured cells. The shape mainly consisted of hexahedrons, with a size of approximately 0.25 mm in the far-wall region and 0.125 mm (width) and 0.05 mm (height) in the near-wall region. Near-wall meshes consisted of 3 layers. The inlet and outlet vessels were extended by 5 and 10 times greater than the measured diameters, respectively. The blood density (ρ) and viscosity (μ) were set at 1050 kg/m^3 and 0.004 Pa·s, respectively. The boundary conditions were determined in accordance with the constant wall shear stress (WSS) theory. In other words, the flow rates of inlet and outlet vessels were calculated using the following equation: $Q = (\tau\pi/32\mu) \times D^3$, where Q, τ, μ, and D are flow rate, WSS, fluid viscosity, and vascular diameter, respectively. The equation is the well-known theoretical basis for fully developed laminar pipe flow. In this study, the WSS (τ) was set at 1.5 Pa.[23] After calculating total inflow at an inlet vessel, the amount of inflow was distributed to each outlet vessel according to the above equation, and the specified boundary conditions of the inlet and outlet vessels were the pressure and velocity boundary condition, respectively. The present computation adopted steady flow, so the inlet pressure was set at 100 mm Hg.

Computation

Governing equations of fluid flow were solved in the 3D unsteady state using the finite volume method. Blood was assumed to be an incompressible and Newtonian fluid, and the nature of flow was allowed to have transient behaviors. The Euler and second-order upwind schemes were adopted for discretizing unsteady and convective acceleration terms. The convergent criteria were set at 10^{-4}.

Postprocessing

Computed velocity information allowed us to visualize the aneurysm flow structures with streamlines, and the inflow environment was characterized by the aneurysm inflow rate. The aneurysm inflow rate was the net flow rate entering the aneurysm through a user-defined aneurysm neck. To quantify the strength of inflow, the aneurysm inflow rate coefficient was defined as $\Phi = Qa/Qb$, where Qa and Qb were aneurysm inflow rate and basilar artery flow rate, respectively.

Statistical Analysis

SPSS version 20 (IBM Corp.) was used to analyze the data. For univariate analysis, Pearson's chi-square test was used for nominal data and the Student t-test for numeric data. The receiver operating characteristic (ROC) curve was used to identify the correct thresholds and cutoff points for the parameters that were significantly different on univariate analyses. For multivariate analysis, logistic regression or stepwise linear regression was used according to the type of data (categorical or ordinal, respectively). Pearson's correlation coefficient was used to test for correlations between hemodynamic and morphometric parameters. A $p \leq 0.05$ was considered statistically significant.

Results

Seventy-one basilar tip aneurysms were examined in total, 22 ruptured and 49 unruptured. Sixteen females and 6 males, with a mean age of 57.5 ± 12.746 years, harbored the ruptured aneurysms; and 38 females and 11 males, with a mean age of 62.86 ± 11.642 years, harbored unruptured aneurysms.

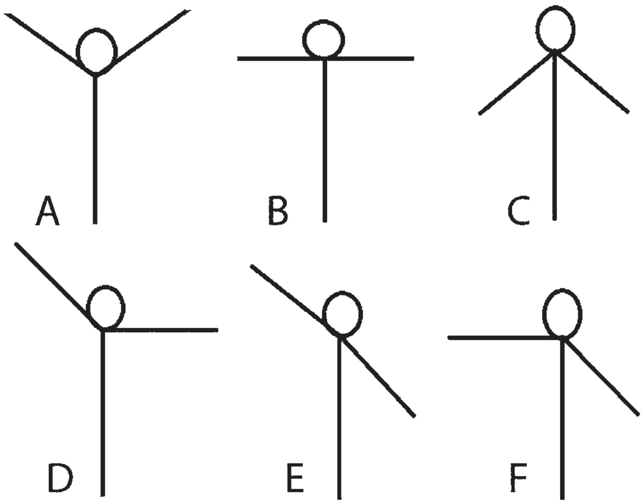

FIG. 2. Schematic of the bifurcation classifications used in this study: hands-up (HU) configuration (**A**), hands-neutral (HN) configuration (**B**), hands-down (HD) configuration (**C**), HU/HN configuration (**D**), HU/HD configuration (**E**), and HN/HD configuration (**F**).

We classified bifurcation into 6 types including 3 pure types—hands-up (HU; both parent-daughter artery angles are above 100°), hands-neutral (HN; both parent-daughter artery angles are between 80° and 100°), and hands-down (HD; both parent-daughter artery angles are below 80°)—and 3 mixed types (HU/HN, HU/HD, and HN/HD; Fig. 2).

Statistical analysis was performed using rupture status and bifurcation configuration as dependent factors. Both factors were plotted against the obtained morphometric and hemodynamic data.

Factors Correlated With Rupture Status

Univariate analysis demonstrated that bifurcation type was significantly different between ruptured and unruptured aneurysms: the HU and HU/HN configurations were significantly associated with ruptured as opposed to unruptured status ($p = 0.007$, OR 6.0923 and $p = 0.025$, OR 3.548, respectively), whereas the HU/HD and HN configurations were significantly associated with an unruptured status ($p = 0.049$, OR 0.0947 and $p = 0.008$, OR 0.145, respectively; Table 1). The HD, HU/HN, and HN/HD configurations showed no significant difference. Univariate analysis also showed that the bifurcation angle ($p = 0.003$), aspect ratio ($p < 0.0005$), bottleneck ratio ($p = 0.002$, and inflow coefficient ($p = 0.025$) were significantly associated with ruptured rather than unruptured status. Age, sex, aneurysm volume and maximum height, neck/parent artery ratio, and WSS values were all nonsignificant.

The ROC curve was plotted to determine the best cutoff values for inflow coefficient, aspect ratio, bottleneck ratio, and bifurcation angle. The cutoff values correlated with ruptured aneurysm were inflow coefficient ≤ 0.5 (area under the curve [AUC] = 0.31, $p = 0.043$, chi-square test with cutoff value, OR 3.0145), aspect ratio > 1 (AUC = 0.779, $p < 0.0005$, OR 9.18), bottleneck ratio > 1.25 (AUC = 0.714, $p = 0.001$, OR 6.525), and bifurcation angle ≥ 200° (AUC = 0.79, $p < 0.0005$, OR 7.3846).

Logistic regression analysis was used to test the vari-

TABLE 1. Factors correlated with aneurysm rupture status

Factor	Ruptured Aneurysm	Unruptured Aneurysm	p Value	OR
Patient data				
Total no.	22	49		
Mean age (yrs)	57.5 ± 12.746	62.86 ± 11.642	0.086	
Sex			0.765	
F	16	38		
M	6	11		
Bifurcation factors				
Bifurcation type				
HU	9 (40.9%)	5 (10.2%)	0.007*	6.0923
HD	1 (4.5%)	3 (6.1%)	1	
HN	2 (9.1%)	20 (40.8%)	0.008*	0.145
HU/HD	0 (0%)	9 (18.4%)	0.049*	0.0947
HU/HN	9 (40.9%)	8 (16.3%)	0.025*	3.548
HN/HD	1 (4.5%)	4 (8.2%)	1	
Mean bifurcation angle (°)	208.1 ± 39.261	182.67 ± 28.047	0.002*†	
No. w/ bifurcation angle ≥200°	16 (72.7%)	13 (26.5%)	<0.0005*	7.3846
Other morphometric factors				
Mean max aneurysm height (mm)	4.99 ± 3.61	5.56 ± 2.41	0.433	
Mean aneurysm vol (mm^3)	163.8855 ± 340.39	172.79 ± 213.296	0.894	
Mean aspect ratio	1.3282 ± 0.358	0.9969 ± 0.297	<0.0005*†	
No. w/ aspect ratio >1	19 (86.4%)	20 (40.8%)	<0.0005*	9.18
Mean bottleneck ratio	1.5 ± 0.467	1.196 ± 0.303	0.002*	
No. w/ bottleneck ratio >1.25	18 (81.8%)	20 (40.8%)	0.001*	6.525
Mean neck/parent artery ratio	1.634 ± 0.8577	1.974 ± 0.608	0.061	
Hemodynamic factors				
Mean inflow coefficient	0.37718 ± 0.297	0.54273 ± 0.275	0.025*	
No. w/ inflow coefficient ≤0.5	16 (72.7%)	23 (46.9%)	0.043*	3.0145
Mean WSS (Pa)	0.592 ± 0.5798	0.627 ± 0.683	0.719	
Mean min WSS (Pa)	0.0265 ± 0.0579	0.05946 ± 0.128	0.254	
Mean max WSS (Pa)	6.148 ± 3.668	5.919 ± 5.1938	0.853	

Means are presented ± SD.
* Statistical significance on univariate analysis.
† Statistical significance on logistic regression analysis.

ables that were significant on univariate analyses. Aspect ratio (p = 0.002) and bifurcation angle (p = 0.034) retained statistical significance.

Correlation of Bifurcation Angle With Other Parameters

Aneurysms were classified into 2 groups based on the ROC curve parameters as described above (Table 2). The first group had a bifurcation angle ≥ 200° and the second an angle < 200°. Univariate analysis was used to analyze the correlation of bifurcation angles with other variables such as aneurysm volume and maximum height, bottleneck ratio, neck/parent artery ratio, inflow coefficient, and WSS values. Aneurysm volume (p = 0.001) and maximum height (p < 0.0005), neck/parent artery ratio (p < 0.0005), and inflow coefficient (p < 0.0005) were all significantly associated.

Factors that were statistically significant on univariate analysis were tested with stepwise linear regression analysis using the actual values of bifurcation angles in all aneurysms as continuous variables. Only inflow coefficient and neck/parent artery ratio were strong predictors of the bifurcation angle. The best model (F = 34.853, p < 0.0005) included inflow coefficient as the only predictor (p < 0.0005). The second best model (F = 20.367, p < 0.0005) included both the inflow coefficient (p = 0.037) and the neck/parent artery ratio (p = 0.043).

How Individual Factors Interact

To understand the relationships between the hemodynamic and morphometric parameters, Pearson's correlation coefficient was calculated between inflow coefficient, bifurcation angle, aneurysm volume, maximum aneurysm height, aspect ratio, and WSS values (mean, maximum, and minimum; Table 3). Bifurcation angle was inversely correlated with inflow coefficient (p < 0.0005), as well as aneurysm volume (p < 0.0005) and maximum height (p < 0.0005). Inflow coefficient was inversely correlated with bifurcation angle (p < 0.0005) and directly correlated with mean and maximum WSS (p = 0.028 and 0.014, respectively) and aneurysm volume (p < 0.0005) and maximum

TABLE 2. Correlation of bifurcation angle with other parameters

Factor	Angle ≥200°	Angle <200°	p Value
No.	29	42	
Mean max aneurysm height (mm)	3.84 ± 1.44	6.45 ± 3.1	<0.0005*
Mean aneurysm vol (mm³)	49.165 ± 41.787	253.486 ± 306.557	0.001*
Mean bottleneck ratio	1.398 ± 0.0.514	1.259 ± 0.339	0.205
Mean neck/parent artery ratio	1.38 ± 0.46	2.2 ± 0.65	<0.0005*†
Mean inflow coefficient	0.29 ± 0.19	0.63 ± 0.265	<0.0005*†
Mean WSS (Pa)	0.54 ± 0.49	0.67 ± 0.739	0.391
Max WSS (Pa)	5.576 ± 3.368	6.276 ± 5.526	0.545
Min WSS (Pa)	0.0676 ± 0.162	0.0366 ± 0.0557	0.253

Means are presented ± SD.
* Statistical significance on univariate analysis.
† Statistical significance on linear regression analysis.

height ($p < 0.0005$). Aspect ratio was inversely correlated with mean ($p = 0.012$) and minimum ($p = 0.018$) WSS and directly correlated with aneurysm volume ($p = 0.01$) and maximum height ($p < 0.0005$).

Discussion

The present study demonstrated that bifurcation angle, which does not significantly change after rupture, was significantly predictive of aneurysm rupture. Moreover, bifurcation angle was strongly correlated with inflow coefficient, which in turn significantly correlated with WSS. Therefore, measuring the simple bifurcation configuration may be a useful predictor of a cerebral aneurysm's hemodynamics and tendency to rupture.

Few studies have investigated the impact of bifurcation angle on the risk of aneurysm rupture. A study of the bifurcation angle together with other morphometric parameters in middle cerebral artery aneurysms revealed significant correlations between bifurcation angle and rupture status on both univariate ($p = 0.03$) and multivariate ($p = 0.004$) analysis.[12] Other significant factors were aspect ratio and aneurysm angle.[12] Another investigation on the impact of the P_1-P_1 angle and bifurcation angle, among other factors, on rupture status in basilar tip aneurysms demonstrated that the bifurcation angle approached significance ($p = 0.063$), but only the P_1-P_1 angle maintained significance after multivariate analysis.[9] That study provided insight into the impact of bifurcation angle and parent vessel–daughter vessel–aneurysm relationships on rupture risk, but the relationship was not explained, and neither was the correlation of bifurcation with the other hemodynamic and morphometric factors tested.

Interpretation of these findings must consider the important fact that aneurysm shape changes after rupture.[5,6,16] Follow-up of 9 aneurysms from before to after rupture showed that the hemodynamics had changed in 6 of the 9 cases and that the shape had changed in 7 of 9 cases.[6] A study of 4 posterior communicating artery aneurysms before and after rupture revealed that all aneurysms had increases in size, volume, and surface area and that morphology changed in both high and low WSS areas.[5] Interpretation of these findings requires care as a size change may not be directly attributable to rupture but rather to the dynamic nature of aneurysm growth given the long latency between initial imaging and rupture in these studies (years in some cases). However, these studies provide important insights into the dynamic nature of aneurysms and their changes over time, as well as the potential effects on the results of computational fluid dynamic analysis and the conclusions drawn. The relation between hemodynamics and geometry involves a complex of cause-effect interactions as the hemodynamics are affected by the geometry of the parent artery, aneurysm, and branches and, over time, cause changes in the biology of the aneurysm wall via different mechanisms, resulting in aneurysm growth, lobulation, or bleb formation.[13,24] Such changes in aneurysm geometry will in turn affect the hemodynamic phenomena inside the aneurysm.[24] To date, all large population studies attempting to understand the factors related to aneurysm rupture have been retrospective;[3,7,11] thus, accurate understanding the morphometric parameters that govern aneurysm rupture remains difficult because we cannot determine whether the final geometry is the cause or the result of rupture. Therefore, studying static morphometric parameters and understanding their causality in aneurysm rupture may prove valuable and excludes any bias in study-

TABLE 3. Pearson's correlation coefficient between the hemodynamic and morphometric parameters

Parameter	Inflow Coefficient	Aspect Ratio	Bifurcation Angle	Aneurysm Vol	Max Aneurysm Height	Mean WSS	Min WSS	Max WSS
Inflow coefficient								
Pearson's correlation	1	−0.72	−0.677	0.608	0.661	0.260	−0.112	0.289
p value		0.552	<0.0005*	<0.0005*	<0.0005*	0.028*	0.351	0.014*
Aspect ratio								
Pearson's correlation	−0.072	1	0.025	0.304	0.478	−0.297	−0.281	−0.078
p value	0.552		0.838	0.01*	<0.0005*	0.012*	0.018*	0.516
Bifurcation angle								
Pearson's correlation	−0.667	0.025	1	−0.66	−0.659	−0.171	0.123	−0.157
p value	<0.0005*	0.825		<0.0005*	<0.0005*	0.154	0.306	0.192

* Significant correlation.

ing a single time point in the dynamic aneurysm geometry, which with time may change before rupture.[16] In the present study, we focused on the bifurcation angle and its impact on aneurysms, as this angle would not change much with aneurysm growth or after rupture, and thus could provide information about the pre-rupture environment inside aneurysms.

The impact of bifurcation angle on rupture and intraaneurysmal hemodynamics can be understood by its effect on the inflow coefficient. In this study, the HU configuration was related to a lower inflow coefficient, and inflow increased as the angle of bifurcation shifted more toward the HD configuration. This effect is caused by a split in blood flow between the bilateral posterior cerebral arteries and the aneurysm in the HU configuration, causing a lower inflow coefficient, which in turn was correlated with lower WSS in the aneurysm (Fig. 3A and B), and consequently promoting rupture. On the other hand, a smaller bifurcation angle was related to a greater inflow coefficient and, consequently, higher WSS. This observation indicates that, in the HD bifurcation types, blood flows directly from the parent artery to the aneurysm and then outflows to the daughter arteries (Fig. 3C). We postulate that this type of flow creates a steadier hemodynamic environment inside the aneurysm and so delays rupture. This relationship was delineated by the calculation of Pearson's correlation coefficient (Table 3). Bifurcation angle was inversely correlated with inflow coefficient ($p < 0.0005$). In turn, the inflow coefficient was directly correlated with mean ($p = 0.028$) and maximum WSS ($p = 0.014$). These findings indicate that a larger bifurcation angle is associated with lower inflow into the aneurysm, which leads to lower WSS and predisposes the aneurysm to rupture.

Further interesting correlations were found between bifurcation angle and aneurysm volume, maximum aneurysm height, and inflow coefficient. Bifurcation angle was inversely correlated with volume and maximum height and inflow coefficient, suggesting that a larger bifurcation angle (HU configuration) causes aneurysms to rupture at a smaller size as compared with a smaller bifurcation angle (HD configuration). A higher inflow coefficient was directly correlated with larger aneurysm volumes. Overall, a larger bifurcation angle causes a lower inflow coefficient, so the aneurysm ruptures at a smaller size, as compared with a smaller bifurcation angle, because of the unstable biological environment resulting from lower WSS as a consequence of the lower inflow in the aneurysm. Our comparison between aneurysms with bifurcation angles ≥ 200° and < 200° shows this finding clearly (Table 2). Aneurysm volume and maximum height were statistically different between these 2 groups ($p = 0.001$ and $p < 0.0005$, respectively). Aneurysms with a bifurcation angle ≥ 200° had significantly smaller volumes and maximum heights, as well as significantly lower inflow coefficients ($p < 0.0005$). This bifurcation configuration is more common among ruptured aneurysms, suggesting that these aneurysms ruptured at a smaller size than aneurysms with other bifurcation configurations.

Aspect ratio was inversely correlated with mean ($p = 0.012$) and minimum ($p = 0.018$) WSS, suggesting that a larger aspect ratio resulted in lower WSS, which may explain why a larger aspect ratio is related to the rupture

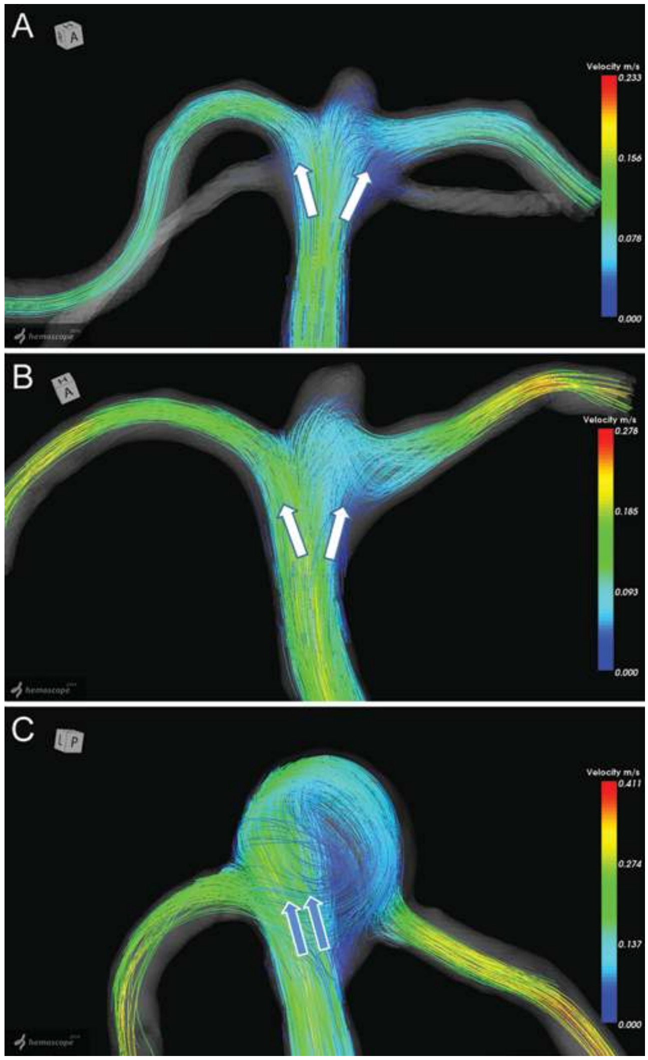

FIG. 3. Postsimulation processing showing streamline distributions inside aneurysms with HU (**A** and **B**) and HD (**C**) configurations. The streamlines in the pictured HU configurations are split between the aneurysm and the 2 posterior cerebral arteries, leading to a lower inflow coefficient (0.12 and 0.18, respectively). Most flow goes into the aneurysm first and then exits from the aneurysm into the posterior cerebral arteries in the HD configuration. This led to a higher inflow coefficient (0.86) and a more stable intraaneurysmal hemodynamic environment.

of aneurysms. Other authors have reported a similar correlation between aspect ratio and WSS.[17] In the present study, as shown on logistic regression analysis, aspect ratio and bifurcation angle had the strongest effects on rupture status mediated via WSS lowering inside the aneurysm, whether as a direct consequence in the case of the aspect ratio or via the effect on inflow in the case of the bifurcation angle. Given our results, the presence of an HU configuration and/or aspect ratio more than 1.6 should prompt immediate treatment in patients with bifurcation aneurysms.[17] Aspect ratio has been widely studied and its relation to WSS is well understood,[17] but findings in the present study emphasize the effects of bifurcation angle on aneurysm inflow and hemodynamics. Our results agree with previously reported data, especially in terms of aspect ratio[1,8,22] and bifurcation angle.[13] The importance of considering bifurcation type as a risk for aneurysm rupture is based on the fact that the bifurcation will not significantly change like several other aneurysmal characteristics do after rupture.[6,16] Moreover, the effects of bifurcation angle on inflow and ultimately on intraaneurysmal hemodynamics will not change greatly after rupture, as other parameters of aneurysmal geometry will. Our results also favor low WSS as the predisposing factor leading to aneurysm rupture[13,17,20] and demonstrate that low WSS is partly caused by the configuration of the bifurcation as well as the aspect ratio.

This study is limited by its retrospective nature, small number of aneurysms selected for evaluation, which may not represent the general population, and our focus on one type of aneurysm (basilar tip). The latter was selected to standardize most factors other than the aneurysm and must be considered when applying the same principle to other bifurcation type aneurysms such as middle cerebral artery and internal carotid artery terminus aneurysms because the studied parameters may be unique to the basilar artery. We also acknowledge that we assumed a static nature of the bifurcation angle. This assumption requires further study since no studies to date have examined this aspect of aneurysm morphology over time. Our computational simulations unified inlet parameters and did not consider the differences between patients in terms of blood pressure, pulse rate, and blood chemistry and viscosity that may affect the aneurysms. These conditions were chosen to unify the parameters for studying the geometry and its effect, and these choices should be remembered while interpreting the results of this study.

Conclusions

Aspect ratio and bifurcation angle are strong predictors for the rupture of bifurcation type aneurysms. This effect on aneurysm pathophysiology is attributable to their effects on WSS and aneurysm hemodynamics. Bifurcation configuration should be considered in the assessment of aneurysm rupture risk because of its considerable effects on aneurysm hemodynamics and inflow.

Acknowledgments

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References

1. Amenta PS, Yadla S, Campbell PG, Maltenfort MG, Dey S, Ghosh S, et al: Analysis of nonmodifiable risk factors for intracranial aneurysm rupture in a large, retrospective cohort. **Neurosurgery 70:**693–701, 2012
2. Baharoglu MI, Schirmer CM, Hoit DA, Gao BLL, Malek AM: Aneurysm inflow-angle as a discriminant for rupture in sidewall cerebral aneurysms: morphometric and computational fluid dynamic analysis. **Stroke 41:**1423–1430, 2010
3. Brinjikji W, Zhu YQ, Lanzino G, Cloft HJ, Murad MH, Wang Z, et al: Risk factors for growth of intracranial aneurysms: a systematic review and meta-analysis. **AJNR Am J Neuroradiol** [epub ahead of print], 2015
4. Brisman JL, Song JK, Newell DW: Cerebral aneurysms. **N Engl J Med 355:**928–939, 2006
5. Chien A, Sayre J: Morphologic and hemodynamic risk factors in ruptured aneurysms imaged before and after rupture. **AJNR Am J Neuroradiol 35:**2130–2135, 2014
6. Cornelissen BM, Schneiders JJ, Potters WV, van den Berg R, Velthuis BK, Rinkel GJ, et al: Hemodynamic differences in intracranial aneurysms before and after rupture. **AJNR Am J Neuroradiol 36:**1927–1933, 2015
7. Greving JP, Wermer MJ, Brown RD Jr, Morita A, Juvela S, Yonekura M, et al: Development of the PHASES score for prediction of risk of rupture of intracranial aneurysms: a pooled analysis of six prospective cohort studies. **Lancet Neurol 13:**59–66, 2014
8. Hassan T, Timofeev EV, Saito T, Shimizu H, Ezura M, Matsumoto Y, et al: A proposed parent vessel geometry-based categorization of saccular intracranial aneurysms: computational flow dynamics analysis of the risk factors for lesion rupture. **J Neurosurg 103:**662–680, 2005
9. Ho AL, Mouminah A, Du R: Posterior cerebral artery angle and the rupture of basilar tip aneurysms. **PLoS One 9:**e110946, 2014
10. Hoh BL, Sistrom CL, Firment CS, Fautheree GL, Velat GJ, Whiting JH, et al: Bottleneck factor and height-width ratio: association with ruptured aneurysms in patients with multiple cerebral aneurysms. **Neurosurgery 61:**716–723, 2007
11. Juvela S, Porras M, Poussa K: Natural history of unruptured intracranial aneurysms: probability of and risk factors for aneurysm rupture. **J Neurosurg 108:**1052–1060, 2008
12. Lin N, Ho A, Gross BA, Pieper S, Frerichs KU, Day AL, et al: Differences in simple morphological variables in ruptured and unruptured middle cerebral artery aneurysms. **J Neurosurg 117:**913–919, 2012
13. Meng H, Tutino VM, Xiang J, Siddiqui A: High WSS or low WSS? Complex interactions of hemodynamics with intracranial aneurysm initiation, growth, and rupture: toward a unifying hypothesis. **AJNR Am J Neuroradiol 35:**1254–1262, 2014
14. Nikolic I, Tasic G, Bogosavljevic V, Nestorovic B, Jovanovic V, Kojic Z, et al: Predictable morphometric parameters for rupture of intracranial aneurysms—a series of 142 operated aneurysms. **Turk Neurosurg 22:**420–426, 2012
15. Prestigiacomo CJ, He W, Catrambone J, Chung S, Kasper L, Pasupuleti L, et al: Predicting aneurysm rupture probabilities through the application of a computed tomography angiography-derived binary logistic regression model. **J Neurosurg 110:**1–6, 2009
16. Schneiders JJ, Marquering HA, van den Berg R, VanBavel E, Velthuis B, Rinkel GJ, et al: Rupture-associated changes of cerebral aneurysm geometry: high-resolution 3D imaging before and after rupture. **AJNR Am J Neuroradiol 35:**1358–1362, 2014
17. Shojima M, Oshima M, Takagi K, Torii R, Hayakawa M, Katada K, et al: Magnitude and role of wall shear stress on cerebral aneurysm: computational fluid dynamic study of 20 middle cerebral artery aneurysms. **Stroke 35:**2500–2505, 2004
18. Vlak MH, Algra A, Brandenburg R, Rinkel GJ: Prevalence of unruptured intracranial aneurysms, with emphasis on sex, age, comorbidity, country, and time period: a systematic review and meta-analysis. **Lancet Neurol 10:**626–636, 2011
19. Wiebers DO, Torner JC, Meissner I: Impact of unruptured intracranial aneurysms on public health in the United States. **Stroke 23:**1416–1419, 1992
20. Xiang J, Natarajan SK, Tremmel M, Ma D, Mocco J, Hopkins LN, et al: Hemodynamic-morphologic discriminants for intracranial aneurysm rupture. **Stroke 42:**144–152, 2011
21. Yasuda R, Strother CM, Taki W, Shinki K, Royalty K, Pulfer

K, et al: Aneurysm volume-to-ostium area ratio: a parameter useful for discriminating the rupture status of intracranial aneurysms. **Neurosurgery 68:**310–318, 2011
22. You SHH, Kong DSS, Kim JSS, Jeon P, Kim KH, Roh HK, et al: Characteristic features of unruptured intracranial aneurysms: predictive risk factors for aneurysm rupture. **J Neurol Neurosurg Psychiatry 81:**479–484, 2010
23. Zarins CK, Zatina MA, Giddens DP, Ku DN, Glagov S: Shear stress regulation of artery lumen diameter in experimental atherogenesis. **J Vasc Surg 5:**413–420, 1987
24. Zhang Y, Mu S, Chen J, Wang S, Li H, Yu H, et al: Hemodynamic analysis of intracranial aneurysms with daughter blebs. **Eur Neurol 66:**359–367, 2011

Disclosures

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Author Contributions

Conception and design: Niizuma, Rashad, Sugiyama. Acquisition of data: Rashad, Sugiyama, Sato, Endo, Matsumoto. Analysis and interpretation of data: Niizuma, Rashad, Sugiyama. Drafting the article: Niizuma, Rashad. Critically revising the article: Niizuma, Omodaka, Fujimura, Tominaga. Reviewed submitted version of manuscript: Niizuma, Sugiyama, Sato, Endo, Omodaka, Matsumoto, Fujimura, Tominaga. Statistical analysis: Niizuma, Rashad. Study supervision: Tominaga.

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