Morphological Risk Factors for Rupture of Small (<7 mm) Posterior Communicating Artery Aneurysms

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BACKGROUND: The management of small, unruptured intracranial aneurysms is still controversial. Given the distinctive natural history of aneurysm at different locations, location-specific analysis might be a reasonable approach. This study aimed to investigate morphological discriminators for rupture status by focusing on only posterior communicating artery (PcomA) aneurysms smaller than 7 mm.

METHODS: In 108 small PcomA aneurysms (68 ruptured, 40 unruptured), clinical and morphological characteristics were compared between the ruptured and unruptured groups. Multivariate logistic regression analysis was performed to determine the independent predictors for the rupture status of small PcomA aneurysms.

RESULTS: None of the clinical characteristics were significantly different between the ruptured and unruptured groups (\( P > 0.05 \)). The ruptured group revealed a significantly larger size (\( P = 0.009 \)), aspect ratio (\( P = 0.009 \)), size ratio (\( P = 0.002 \)), dome-to-neck ratio (\( P = 0.002 \)), inflow angle (\( P < 0.001 \)), and proportion of bleb formation (\( P = 0.039 \)). Bottleneck factor (\( P = 0.154 \)), diameter of PcomA (\( P = 0.302 \)), and fetal-type PcomA (\( P = 0.832 \)) showed no significance. With multivariate analyses, size ratio (\( P = 0.012 \)) and inflow angle (\( P = 0.001 \)) were shown to be independently associated with the rupture status of small PcomA aneurysms.

CONCLUSIONS: Morphological characteristics were closely related with the rupture status of small PcomA aneurysms. Size ratio and inflow angle were independent risk factors for rupture and might be useful in clinical risk stratification of small PcomA aneurysms.

INTRODUCTION

Unruptured intracranial aneurysms (IAs) are increasingly detected, and the majority of them are small.1,2 Although the International Study of Unruptured Intracranial Aneurysms trial reported a low rupture rate for unruptured IAs smaller than 7 mm,3 a recent prospective Finnish cohort study showed that 25% of the patients with small (<7 mm) unruptured IAs had an aneurysmal subarachnoid hemorrhage (SAH) during a lifelong follow-up.4 Thus, the effectiveness of aneurysm size as a predictor for rupture remains controversial. Moreover, the correlation between IA rupture with their location has been revealed in various studies.5,6 Compared with other locations, the posterior communicating artery (PcomA) and the anterior communicating artery had a higher incidence of ruptured aneurysms.5 Meanwhile, the percentage of small aneurysms in PcomA aneurysms was particularly high.7 Considering the potential risks of therapy, clinical decision making for unruptured PcomA aneurysms is difficult, especially for those smaller than 7 mm. Therefore, in this study, we reviewed the clinical and morphological characteristics of small PcomA aneurysms (<7 mm) in a single institution to screen for the possible predictors of their rupture.
MATERIALS AND METHODS

Ethics Statement
The Institution Review Board of the Second Military Medical University affiliated with Shanghai Hospital approved this retrospective study, and the requirement for informed consent was waived. The patients’ information was anonymized and de-identified before analysis.

Patients and Clinical Characteristics
We retrospectively reviewed 135 consecutive patients with diagnosed PcomA aneurysms between January 2014 and June 2015 at Shanghai Hospital. All the PcomA aneurysms were determined and measured using three-dimensional rotational angiography (3DRA). After exclusion of patients with multiple aneurysms and PcomA aneurysms larger than 7 mm, 108 PcomA aneurysms were included in the study. Of these PcomA aneurysms, 68 were ruptured with a history of SAH, and 40 were unruptured. For the 40 patients in the unruptured group, 14 exhibited mild headache and 7 suffered from ischemic events, 8 exhibited symptoms of oculomotor nerve palsy, and the other 11 aneurysms were detected incidentally without symptoms of cerebrovascular diseases. The clinical characteristics were collected as the following: age, sex, hypertension, diabetes mellitus, current smoking status, history of familial SAH, and presence of homolateral oculomotor nerve palsy. Hypertension was defined as taking antihypertensive agents, a systolic blood pressure ≥140 mm Hg, or a diastolic blood pressure ≥90 mm Hg. Diabetes mellitus was defined as taking antidiabetic agents, treatment with insulin injections, a fasting plasma glucose level ≥126 mg/dL, a random plasma glucose level of >200 mg/dL, or a hemoglobin A1c level ≥6.5%. Current smoker was defined as those who had smoked at least 100 cigarettes during their lifetime and reported smoking every day or some days before being admitted.

Radiological Findings and Morphological Calculations
The 3DRA was performed using the Artis zee Biplane angiographic system (VC14; Siemens, Erlangen, Germany). All the acquired 3DRA data were transferred to the syngo X Workplace (VB15; Siemens) for reconstruction of the 3D internal carotid artery vessel tree and exported in a stereolithography format to GEOMAGIC STUDIO 9.0 software (Geomagic, Morrisville, North Carolina, USA). First, we defined the neck plane as the location where the aneurysmal sac pouched outward from the parent vessel. Afterward, the models were divided into the aneurysm dome and the inlet and outlet planes of the parent artery, and then exported in stereolithography formats. These formats were imported into Matlab 7.0 (MathWorks, Natick, Massachusetts, USA), which was used to calculate and visualize the morphological parameters.

With this process, we could obtain the morphological parameters of the PcomA aneurysms as defined in previous studies6,9 (Figure 1). The size of the aneurysm dome was defined as the maximum diameter of the aneurysm dome. Dome height was the longest dimension from the neck to the dome tip, and dome width was measured perpendicular to dome height. Aspect ratio (AR) was computed by dividing dome height by neck width. Size ratio (SR) was calculated by dividing size by the average diameter of parent arteries and dome-to-neck ratio (DN) by dividing size by neck width. Bottleneck factor (BN) was defined as the ratio of dome width to neck width. Inflow angle was the angle between inflow and the aneurysm’s main axis from the center of the neck to the tip of the dome. In addition, we evaluated the presence of bleb formation on the aneurysms and whether the PcomA was fetal type. A fetal-type PcomA was defined as a PcomA that has the same or larger caliber as the P2 segment of the posterior cerebral artery, and is associated with an atrophic P1 segment.

Statistical Analysis
Statistical analyses were performed using Microsoft Excel 2003 and SAS 9.1(SAS Institute, Cary, North Carolina, USA). Variables were expressed as median (interquartile range) or number of patients (%) as appropriate. Mann–Whitney U test was used for measurement data, and the γ² test was performed for cross-tabulation. The parameters found to be significant (P < 0.05) in univariate analysis were further analyzed using multivariate logistic regression (backward elimination) to identify those that retained significance when accounting for all relevant parameters; P < 0.05 (two sided) was the criterion for statistical significance.

RESULTS

Univariate Analysis
The baseline and morphological characteristics of the 108 small PcomA aneurysms are shown in Table 1. The patients’ ages ranged from 42 to 82 years, with a median age of 60 years. Twenty-four patients were men, and 84 were women. No baseline variables included in this study showed significant difference (P > 0.05), which indicated that the morphological characteristics of the 2 groups were comparable.

The size of PcomA aneurysms ranged from 1.23 to 6.84 mm, with a median size of 4.36 mm. The ruptured PcomA aneurysms were proved to have a significantly larger size (P = 0.009), AR (P = 0.009), SR (P = 0.002), DN (P = 0.002), and inflow angle (P < 0.001). Bleb formation was observed in a significantly higher
proportion of the ruptured PcomA aneurysms ($P = 0.039$). Other morphological characteristics, including diameter of PcomA ($P = 0.302$), BN ($P = 0.154$), and fetal-type PcomA ($P = 0.832$) were revealed to have no significance between the ruptured and unruptured groups.

### Multivariate Analysis

Multivariate logistic regression was performed to identify the independent risk factors of small PcomA aneurysms rupture using a backward elimination process. All the significant parameters that were significant in univariate analysis were included. The result showed that SR (Odds ratio [OR], 1.67; 95% confidence interval [CI], 1.12–2.50; $P = 0.012$) and inflow angle (OR, 2.01; 95% CI, 1.32–3.05; $P = 0.001$) were independently associated with the rupture status of small PcomA aneurysms (Table 2).

### DISCUSSION

With the wider availability of modern imaging techniques, patients with unruptured IAs are increasingly detected, even with small asymptomatic ones. Previous studies revealed that the size of IA was significantly correlated to their rupture status, and the risk of unruptured IAs smaller than 7 mm was relatively low. However, according to studies depending on the locations, rupture of small anterior circulation aneurysms was the main cause of aneurysmal SAH, which carries a high rate of mortality and morbidity. As a result, clinical decision making for small, unruptured IAs is still difficult for physicians, and reliable predictors for rupture risk are greatly needed.

Various attempts have been made to stratify the rupture risk of intracranial aneurysms. Currently, several clinical, hemodynamic, and morphological variables, including familial SAH history, aneurysm size, and low wall shear stress, have been consistently associated with an increased risk of aneurysm rupture. However, these findings were obtained by analysis of a limited number of parameters with a relatively small sample size. Furthermore, most of these studies were not location specific. In fact, the proportion of small aneurysms and their risk of rupture complications have been revealed to have no significance between the ruptured and unruptured groups.

#### Table 1. Clinical and Morphological Characteristics of Small PcomA Aneurysms

<table>
<thead>
<tr>
<th>Variables</th>
<th>PcomA Aneurysms</th>
<th>Total (n = 108)</th>
<th>Ruptured (n = 68)</th>
<th>Unruptured (n = 40)</th>
<th>$P$ Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical Characteristics</strong></td>
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<tr>
<td>Age (years)</td>
<td>60 (52, 66)</td>
<td>65 (51, 63)</td>
<td>62 (56, 67)</td>
<td>0.056</td>
<td></td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>24 (22.2)</td>
<td>13 (19.1)</td>
<td>11 (27.5)</td>
<td>0.312</td>
<td></td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>53 (49.1)</td>
<td>31 (45.6)</td>
<td>22 (55.0)</td>
<td>0.345</td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus, n (%)</td>
<td>11 (10.2)</td>
<td>4 (5.9)</td>
<td>7 (17.5)</td>
<td>0.054</td>
<td></td>
</tr>
<tr>
<td>Current smoking, n (%)</td>
<td>17 (15.7)</td>
<td>9 (13.2)</td>
<td>8 (20.0)</td>
<td>0.351</td>
<td></td>
</tr>
<tr>
<td>Familial history of SAH, n (%)</td>
<td>9 (8.3)</td>
<td>5 (7.4)</td>
<td>4 (10.0)</td>
<td>0.904</td>
<td></td>
</tr>
<tr>
<td>Oculomotor nerve palsy, n (%)</td>
<td>18 (16.7)</td>
<td>10 (14.7)</td>
<td>8 (20.0)</td>
<td>0.476</td>
<td></td>
</tr>
<tr>
<td><strong>Morphological Characteristics</strong></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Size, mm</td>
<td>4.36 (3.23, 5.47)</td>
<td>4.50 (3.60, 5.696)</td>
<td>3.92 (2.46, 4.72)</td>
<td>0.009</td>
<td></td>
</tr>
<tr>
<td>Diameter of PcomA, mm</td>
<td>1.84 (1.27, 2.25)</td>
<td>1.80 (1.11, 2.18)</td>
<td>1.99 (1.53, 2.50)</td>
<td>0.302</td>
<td></td>
</tr>
<tr>
<td>Aspect ratio (AR)</td>
<td>0.97 (0.75, 1.37)</td>
<td>1.08 (0.84, 1.37)</td>
<td>0.83 (0.66, 1.24)</td>
<td>0.009</td>
<td></td>
</tr>
<tr>
<td>Size ratio (SR)</td>
<td>1.61 (1.20, 1.94)</td>
<td>1.72 (1.30, 2.09)</td>
<td>1.42 (0.90, 1.77)</td>
<td>0.002</td>
<td></td>
</tr>
<tr>
<td>Dome-to-neck ratio (DN)</td>
<td>1.08 (0.91, 1.41)</td>
<td>1.16 (0.96, 1.59)</td>
<td>0.97 (0.86, 1.22)</td>
<td>0.002</td>
<td></td>
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<tr>
<td>Bottleneck factor (BN)</td>
<td>1.13 (0.94, 1.35)</td>
<td>1.18 (1.01, 1.38)</td>
<td>1.09 (0.90, 1.32)</td>
<td>0.154</td>
<td></td>
</tr>
<tr>
<td>Inflow angle, degrees</td>
<td>113 (98, 128)</td>
<td>119 (105, 132)</td>
<td>99 (89, 118)</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Bleb formation, n (%)</td>
<td>49 (45.4)</td>
<td>36 (52.9)</td>
<td>13 (32.5)</td>
<td>0.039</td>
<td></td>
</tr>
<tr>
<td>Fetal type PcomA, n (%)</td>
<td>31 (28.7)</td>
<td>20 (29.4)</td>
<td>11 (27.5)</td>
<td>0.832</td>
<td></td>
</tr>
</tbody>
</table>

Variables are expressed as median (interquartile range), or number of patients (%).

#### Table 2. Independent Risk Factors for Rupture of Small PcomA Aneurysms

<table>
<thead>
<tr>
<th>Variables</th>
<th>P Value</th>
<th>Odds Ratio</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Size ratio</td>
<td>0.012</td>
<td>1.67</td>
<td>1.12–2.50</td>
</tr>
<tr>
<td>Inflow angle</td>
<td>0.001</td>
<td>2.01</td>
<td>1.32–3.05</td>
</tr>
</tbody>
</table>
VARIES IN DIFFERENT LOCATIONS.5,8 THE ANATOMIC GEOMETRY, VESSEL WALL THICKNESS, AND BLOOD FLOW PATTERN OF IAS IN DIFFERENT LOCATIONS ARE DISTINCTIVE, WHICH MIGHT BE THE REASON WHY SOME FINDINGS ARE CONFLICTING. AS A RESULT, LOCATION-SPECIFIC STUDIES MAY BE MORE LIKELY TOACH ACCURATE RESULTS.

WITHOUT CONSIDERING LOCATION, IA SIZE LOSES RELEVANCE TO RUPTURE RISK.24,25 IN THIS STUDY, ALTHOUGH THE ANEURYSM SIZE OF THE RUPTURED GROUP WAS SIGNIFICANTLY LARGER THAN THAT OF THE UNRUPTURED GROUP, IT WAS NOT RETAINED AS AN INDEPENDENT RISK FACTOR THAT DISCRIMINATED THE RUPTURE STATUS OF PCOMA ANEURYSMS. THE VARIABILITY OF THE RUPTURE RISK MIGHT BE RELATED TO THE CALIBER OF THE ORIGINATING OR PARENT VESSEL. SR, A PARAMETER THAT WAS FIRST PROPOSED BY DHAR ET AL.14 AND INCORPORATES THE IA PARENT VESSEL GEOMETRY INTO A MORPHOLOGICAL INDEX, HAS BEEN SHOWN TO BE RELATED WITH ANEURYSM RUPTURE.9,20 KASHIWAZAKI ET AL.19 DEMONSTRATED THAT SR COULD ACCURATELY PREDICT THE RUPTURE RISK OF UIAs, ESPECIALLY SMALL ANEURYSMS (<5 mm). IN ANOTHER PROSPECTIVELY DESIGNED STUDY, RAHMAN ET AL.21 ALSO CONFIRMED THE CORRELATION BETWEEN SR AND ANEURYSM RUPTURE STATUS. IN THE CURRENT STUDY, OUR RESULTS INDICATED SR AS AN INDEPENDENT RISK FACTOR FOR RUPTURE OF SMALL PCOMA ANEURYSMS.


MOST MORPHOLOGICAL STUDIES OF RUPTURE RISK, INCLUDING THE CURRENT ONE, ARE BASED ON THE COMPARISON BETWEEN POST-RUPTURED AND UNRUPTURED ANEURYSMS. WE KNOW THAT THE ANALYSIS OF ANEURYSMS IN “PRE-RUPTURE” STATUS MIGHT BE MORE ACCURATE BECAUSE OF THE POSSIBLE CHANGE OF MORPHOLOGY AFTER RUPTURE.25,26 HOWEVER, IT IS DIFFICULT TO CAPTURE THE SPECIFIC STATUS CLINICALLY TO GAIN A CONSIDERABLE SAMPLE SIZE FOR ACCURATE STATISTICAL ANALYSIS. THEREFORE, CURRENTLY, COMPARISONS BETWEEN POST-RUPTURED AND UNRUPTURED IAS ARE USED AS AN AVAILABLE ALTERNATIVE METHOD, WHICH COULD STILL PROVIDE MEANINGFUL FINDINGS FOR CLINICIANS TO DISCRIMINATE RUPTURE STATUS OF IAS.

LIMITATIONS


CONCLUSIONS

THIS STUDY SHOWED THAT NOT ONLY THE ANEURYSM SIZE, BUT ALSO SR, AR, DN, INFLOW ANGLE, AND BLEB FORMATION WERE SIGNIFICANTLY DIFFERENT BETWEEN RUPTURED AND UNRUPTURED SMALL PCOMA ANEURYSMS. HIGHER SR AND INFLOW ANGLE WERE INDEPENDENT RISK FACTORS FOR PREDICTING THE RUPTURE RISK OF SMALL PCOMA ANEURYSMS.

ACKNOWLEDGEMENTS

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REFERENCES


