Morphological and clinical risk factors for posterior communicating artery aneurysm rupture

Clinical article

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Object. Recent studies have shown that posterior circulation aneurysms, specifically posterior communicating artery (PCoA) aneurysms, are more likely to rupture than other aneurysms. To date, few studies have investigated the factors contributing to PCoA aneurysm rupture. The authors aimed to identify morphological and clinical characteristics predisposing to PCoA aneurysm rupture.

Methods. The authors retrospectively reviewed 134 consecutive patients with PCoA aneurysms managed at their facility between July 2003 and December 2012. The authors divided patients into groups of those with aneurysmal rupture (n = 39) and without aneurysmal rupture (n = 95) and compared morphological and clinical characteristics. Morphological characteristics were mainly evaluated by 3D CT angiography and included diameter of arteries (anterior cerebral artery, middle cerebral artery, and internal carotid artery), size of the aneurysm, dome-to-neck ratio, neck direction of the aneurysmal dome around the PCoA (medial, lateral, superior, inferior, and posterior), aneurysm bleb formation, whether the PCoA was fetal type, and the existence of other intracranial unruptured aneurysm(s).

Results. Patients with ruptured PCoA aneurysms were significantly younger (a higher proportion were < 60 years of age) and a significantly higher proportion of patients with ruptured PCoA aneurysms showed a lateral direction of the aneurysmal dome around the PCoA, had bleb formation, and the aneurysm was > 7 mm in diameter and/or the dome-to-neck ratio was > 2.0. Multivariate logistic regression analysis showed age < 60 years (OR 4.3, p = 0.011), history of hypertension (OR 5.1, p = 0.008), lateral direction of the aneurysmal dome around the PCoA (OR 6.7, p = 0.0001), and bleb formation (OR 11, p < 0.0001) to be significantly associated with PCoA aneurysm rupture.

Conclusions. The present results demonstrated that lateral projection of a PCoA aneurysm may be related to rupture. (http://thejns.org/doi/abs/10.3171/2013.9.JNS13921)

KEY WORDS • cerebral aneurysm • epidemiology • vascular disorders • posterior communicating artery • risk factors • subarachnoid hemorrhage

Posterior communicating artery (PCoA) aneurysms are one of the most frequent forms of intracranial aneurysms, accounting for approximately 15%–25% of all intracranial aneurysms.⁵,¹⁴ Recent studies on the natural course of unruptured cerebral aneurysms showed that PCoA aneurysms were more likely to rupture.⁵,¹²,¹⁸ The prevalence of small ruptured PCoA aneurysms was particularly high, with 87.5% of aneurysms measuring less than 10 mm in diameter and 40% measuring less than 5 mm in diameter.⁹

Because the PCoA gives rise to many important branches supplying the optic chiasm, oculomotor nerve, mammillary body, tuber cinereum, cerebral crura, ventral thalamus, and rostral portion of the caudate nucleus, interruption of flow through these vessels may result in ischemic damage to the diencephalon with significant morbidity, even after an apparently uneventful surgical procedure.¹⁰,¹⁴ Thus, investigating factors related to the rupture of PCoA aneurysms is clinically meaningful.

We investigated the morphological and clinical characteristics contributing to PCoA aneurysm rupture.
Posterior communicating artery aneurysm rupture

Methods

The study is reported based on criteria from the STROBE (Strengthening the Reporting of Observational Study in Epidemiology) statement, and the study protocol was approved by the institutional ethics committee.

Clinical Characteristics

We retrospectively reviewed a total of 140 consecutive patients diagnosed with PCoA aneurysms between July 2003 and November 2012 at the Department of Neurosurgery at St. Luke’s International Hospital. Of these patients, 6 were excluded because their radiological findings could not be evaluated due to poor quality. We included patients with PCoA aneurysms who were managed with both observation and treatment by coiling and clipping. Among 134 patients, 39 were diagnosed with subarachnoid hemorrhage (SAH) on CT, and 3D CT angiography (CTA) was performed within 2 hours after onset. Ninety-five patients without SAH underwent 3D CTA or MR angiography (MRA) as a medical checkup of the brain for minor symptoms such as headache and were diagnosed with unruptured PCoA aneurysms. All of the patients had no history of SAH. We collected information on the following variables: age; sex; medical history (hypertension, diabetes mellitus, hypercholesterolemia); smoking history (current smoker or not); alcohol consumption status (consuming alcohol > 5 days per week or not); history of familial SAH; presence of the aneurysm-side oculomotor nerve palsy before surgical treatment; use of antiplatelet agents before SAH; and radiological findings. Oculomotor nerve palsy was considered in the presence of the following:

- ptosis
- fixed mydriasis
- diplopia
- complete upward, medial, and downward-gaze palsies

The direction of the dome around the PCoA was classified according to 5 directions: superior, posterior, inferior, medial, and lateral. First, we drew a line through the bifurcation of the ICA and PCoA, which was parallel to the midline (“parallel line”) on the axial plane or the superior view on the 3D CTA, MRA, or DSA image. Next, we drew a line through the bifurcation of the ICA and PCoA, which was perpendicular to the parallel line (“perpendicular line”) (Fig. 1 left). Third, we drew a line through the bifurcation of the ICA and PCoA, which was parallel to the anterior skull base (“horizontal line”) on the sagittal plane or the lateral view on the above images (Fig. 1 right). An aneurysm was defined as having posterior projections according to its positional relationship to the perpendicular line. The projection was said to be either medial or lateral according to its direction relative to the perpendicular line. In addition, the projection was said to be either superior or inferior according to its direction relative to the horizontal line.

Radiological Findings

Three-dimensional CTA is routinely performed in all patients in whom conventional CT confirms the presence of SAH. In screening patients for unruptured PCoA aneurysms we mostly employ MRA, with 3D CTA usually reserved for patients who prefer CT or in whom there are contraindications for MRA such as a pacemaker. In patients with SAH and multiple aneurysms, ruptured aneurysms were identified on the basis of the pattern of hemorrhage on conventional CT scans or from operative data. Radiological findings were reviewed by the same observer (G.A.), who was supervised by an experienced neuroradiologist (A.U.); both radiologists were blinded to clinical information. We measured the diameters of the origin of the anterior cerebral artery and the middle cerebral artery, as well as that of the internal carotid artery (ICA; the diameter at the proximal ICA–PCoA bifurcation), aneurysm size, and dome-to-neck ratio.

In addition, we evaluated the direction of the dome, the presence of bleb formation on the aneurysm, whether the PCoA was fetal type, and the presence of intracranial unruptured aneurysms other than the PCoA aneurysm on 3D CTA, MRA, and/or digital subtraction angiography (DSA). A fetal-type PCoA was defined as a PCoA that has the same caliber as the P2 segment of the posterior cerebral artery and is associated with an atrophic P1 segment. Aneurysm sizes were categorized as ≥ 7 mm or < 7 mm based on the largest diameter of the aneurysm, and dome-to-neck ratio was dichotomized as ≥ 2.0 or < 2.0.

The direction of the dome around the PCoA was classified according to 5 directions: superior, posterior, inferior, medial, and lateral. First, we drew a line through the bifurcation of the ICA and PCoA, which was parallel to the midline (“parallel line”) on the axial plane or the superior view on the 3D CTA, MRA, or DSA image. Next, we drew a line through the bifurcation of the ICA and PCoA, which was perpendicular to the parallel line (“perpendicular line”) (Fig. 1 left). Third, we drew a line through the bifurcation of the ICA and PCoA, which was parallel to the anterior skull base (“horizontal line”) on the sagittal plane or the lateral view on the above images (Fig. 1 right). An aneurysm was defined as having posterior projections according to its positional relationship to the perpendicular line. The projection was said to be either medial or lateral according to its direction relative to the parallel line. In addition, the projection was said to be either superior or inferior according to its direction relative to the horizontal line.

Statistical Analysis

Statistical analysis was performed using SPSS for Macintosh (version 21.0, IBM). The normality of the data was evaluated using the Shapiro-Wilk test. Variables were expressed as mean ± SD, median (IQR 25th–75th percentile), or number of patients (%), as appropriate. Normally distributed variables were compared between patients
with and without PCoA aneurysm rupture using Student t-test; nonnormally distributed variables were compared using the Mann-Whitney U-test. The chi-square test was performed for cross-tabulation. Regarding direction of the aneurysm, we compared one direction with all other directions combined. Multivariate logistic regression analysis was performed using variables that were marginally or significantly associated with PCoA aneurysm rupture on univariate analysis (p < 0.10) and those that were thought to be clinically important for the rupture of such aneurysms. Differences were considered significant at \( p < 0.05 \).

**Results**

The morphological characteristics were evaluated on MRA (n = 101), 3D CTA (n = 89), and/or DSA (n = 50) images. Table 1 shows the clinical characteristics of patients with PCoA aneurysms. Patients with ruptured PCoA aneurysms were significantly younger (a higher proportion were < 60 years of age) and a significantly higher proportion had hypertension. Other baseline characteristics and medical history showed neither marginal nor significant differences between the ruptured and unruptured aneurysm groups (p > 0.10).

Table 2 shows morphological characteristics of patients with PCoA aneurysms. A significantly higher proportion of patients with ruptured PCoA aneurysms had a lateral direction of the aneurysm dome around the PCoA, had bleb formation, and/or had an aneurysm that was > 5 mm in diameter. Other morphological characteristics, except for dome-to-neck ratio > 2.0 (p = 0.052), showed neither marginal nor significant differences between the 2 groups (p > 0.10).

We performed multivariate logistic regression analysis using variables that were marginally or significantly associated with ruptures along with current smoking, which is thought to be an important risk factor for rupture.\(^{16,26}\) The analysis showed that lateral direction of aneurysm dome around the PCoA, age less than 60 years, hypertension, and bleb formation were still significantly associated with PCoA aneurysm rupture (Table 3).

**Discussion**

The PCoA originates from the posterolateral surface of the proximal ICA and gives rise to many important branches supplying the optic chiasm, oculomotor nerve, ventral thalamus, mammillary body, tuber cinereum, hypothalamus, and internal capsule.\(^{11,15}\) A recent study on the natural course of unruptured cerebral aneurysms conducted in a Japanese cohort (Unruptured Cerebral Aneurysm Study [UCAS]) showed that a PCoA aneurysm is more likely to rupture.\(^{28}\) Thus, knowledge of risk factors for rupture is thought to be crucial for managing patients with PCoA aneurysms.

**Projection of Aneurysm and Bleb Formation**

With an enlargement of the aneurysm dome, the aneurysms touch the surrounding intracisternal and juxtacisternal structures (perianeurysmal environment).\(^{33,35}\) including cranial nerves, adjacent brain parenchyma, cranial base bone, dural folds, bridging and surface veins, small arteries, and arachnoid trabecular.\(^{34}\) A PCoA aneurysm projecting laterally will be unable to extend beneath the oculomotor nerve and will compress the superomedial aspect of the oculomotor nerve.\(^{29}\) In addition, when the PCoA aneurysm extends laterally, the aneurysm dome comes into contact with surrounding hard structures such as the tentorial free edge, and deformation may be observed on the dome.\(^{34}\) On the other hand, a recent neuroanatomical study showed that dense fibrous trabeculae differ by location around an anterior commu-

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**TABLE 1: Clinical characteristics of patients with unruptured and ruptured PCoA aneurysms**

<table>
<thead>
<tr>
<th>Variable*</th>
<th>Total (n = 134)</th>
<th>Ruptured (n = 39)</th>
<th>Unruptured (n = 95)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>baseline characteristics</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>mean age, yrs (SD)†</td>
<td>66 (13)</td>
<td>61 (14)</td>
<td>68 (12)</td>
<td></td>
</tr>
<tr>
<td>age &lt;60 yrs†</td>
<td>43 (32)</td>
<td>19 (49)</td>
<td>24 (25)</td>
<td></td>
</tr>
<tr>
<td>male</td>
<td>92 (69)</td>
<td>30 (77)</td>
<td>62 (65)</td>
<td></td>
</tr>
<tr>
<td>current smoking</td>
<td>42 (31)</td>
<td>16 (41)</td>
<td>26 (27)</td>
<td></td>
</tr>
<tr>
<td>daily alcohol consumption</td>
<td>38 (28)</td>
<td>15 (38)</td>
<td>23 (24)</td>
<td></td>
</tr>
<tr>
<td>history of familial SAH</td>
<td>6 (4.5)</td>
<td>3 (7.7)</td>
<td>3 (3.2)</td>
<td></td>
</tr>
<tr>
<td>oculomotor palsy</td>
<td>5 (3.7)</td>
<td>3 (7.7)</td>
<td>2 (2.1)</td>
<td></td>
</tr>
<tr>
<td>antithrombotics</td>
<td>11 (8.2)</td>
<td>2 (5.1)</td>
<td>9 (9.5)</td>
<td></td>
</tr>
<tr>
<td>medical history</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>hypertension†</td>
<td>81 (60)</td>
<td>35 (89)</td>
<td>46 (48)</td>
<td></td>
</tr>
<tr>
<td>hypercholesterolemia</td>
<td>26 (19)</td>
<td>5 (13)</td>
<td>21 (22)</td>
<td></td>
</tr>
<tr>
<td>diabetes mellitus</td>
<td>20 (15)</td>
<td>6 (15)</td>
<td>14 (15)</td>
<td></td>
</tr>
</tbody>
</table>

* Data are expressed as number of patients (%), unless otherwise indicated.
† Variables showing significant difference by univariate analysis (p < 0.05) are indicated by boldface.
From this perspective, the distribution of fibrous trabeculae lateral to the PCoA may be sparse and the lateral direction of the aneurysm dome around the PCoA may indicate a tendency to rupture more easily compared with other directions.

As in previous studies,8,13,24,36 bleb formation was significantly related to PCoA aneurysm rupture in the present study. In a recent study focusing on bleb formation in an effort to gain insight into the mechanisms underlying aneurysm rupture, the highest shear stress values were at or adjacent to the bleb formation.38 Tsukahara et al.41 reported a global rupture rate of 3.42% per year and a rupture rate of 28.3% per year in aneurysms that contained bleb formation at the beginning of the observation period and observed that the likelihood of unruptured aneurysms to rupture was not exceedingly low, even when the aneurysms were smaller than 10 mm in diameter. Any change in the main sac structure introduces the possibility of significant influences of the perianeurysmal environment or other unknown factors.8

Furthermore, the lateral direction may also affect flow dynamics such as wall shear stress, pressure stress, impingement force, and flow rate, all of which have been implicated in aneurysm growth and rupture.7,37 It is presumed that the final shape of the aneurysm is determined by interactions with flow-induced wall injuries, the biochemical response of the aneurysmal wall, and interactions with extravascular structures of the perianeurysmal environment, whereas contact of an aneurysm with the perianeurysmal environment is thought to affect both the growth and rupture of an unruptured aneurysm.34,35 The observed relationship between the lateral direction and rupture may be derived from both extrinsic and intrinsic factors.

### Size of Aneurysm

Although the International Study of Unruptured Intracranial Aneurysms (ISUIA) study gives the impression that small aneurysms have a minimal risk of rupture,45 Forget et al. reviewed the size of ruptured aneurysms and found that 85.6% of these aneurysms were less than 10 mm in diameter. The prevalence of small ruptured PCoA aneurysms was particularly high, with 87.5% of aneurysms measuring less than 10 mm in diameter and 40% measuring less than 5 mm in diameter.9 Similarly, the present results of a multivariate analysis indicated that PCoA aneurysms exceeding 7 mm in diameter were not significantly more common in patients with SAH, an observation supporting previous studies demonstrating that small size was not necessarily an indication of low

### TABLE 2: Imaging findings in patients with unruptured and ruptured PCoA aneurysms

<table>
<thead>
<tr>
<th>Variable</th>
<th>Aneurysms</th>
<th>Ruptured (n = 39)</th>
<th>Unruptured (n = 95)</th>
<th>p Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total (n = 134)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A1 diameter in mm (IQR)</td>
<td>1.7 (1.4–2.1)</td>
<td>1.9 (1.5–2.1)</td>
<td>1.7 (1.4–2.1)</td>
<td>0.33</td>
</tr>
<tr>
<td>M1 diameter in mm (IQR)</td>
<td>2.6 (2.2–3.0)</td>
<td>2.6 (2.3–2.8)</td>
<td>2.6 (2.0–3.1)</td>
<td>0.63</td>
</tr>
<tr>
<td>ICA diameter in mm (IQR)</td>
<td>3.2 (0.61)</td>
<td>3.1 (0.59)</td>
<td>3.2 (0.62)</td>
<td>0.39</td>
</tr>
<tr>
<td>aneurysm size in mm (IQR)</td>
<td>4 (2.5–6.0)</td>
<td>5.9 (4.0–7.5)</td>
<td>3.4 (2.0–5.0)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>size of aneurysm &gt;7 mm†</td>
<td>39 (29)</td>
<td>13 (33)</td>
<td>10 (11)</td>
<td>0.001</td>
</tr>
<tr>
<td>dome-to-neck ratio (IQR)</td>
<td>1.7 (1.3–2.2)</td>
<td>2.0 (1.4–2.6)</td>
<td>1.6 (1.2–2.0)</td>
<td>0.017</td>
</tr>
<tr>
<td>&gt;2.0†</td>
<td>51 (38)</td>
<td>20 (51)</td>
<td>31 (33)</td>
<td>0.052</td>
</tr>
<tr>
<td>direction†</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>medial</td>
<td>13 (9.7)</td>
<td>4 (10)</td>
<td>9 (9.5)</td>
<td>1.0</td>
</tr>
<tr>
<td>lateral</td>
<td>50 (37)</td>
<td>27 (69)</td>
<td>23 (24)</td>
<td>0.0001</td>
</tr>
<tr>
<td>superior</td>
<td>2 (1.5)</td>
<td>1 (2.6)</td>
<td>1 (1.1)</td>
<td>0.49</td>
</tr>
<tr>
<td>inferior</td>
<td>54 (40)</td>
<td>13 (33)</td>
<td>41 (43)</td>
<td>0.34</td>
</tr>
<tr>
<td>posterior</td>
<td>89 (66)</td>
<td>27 (69)</td>
<td>62 (65)</td>
<td>0.69</td>
</tr>
<tr>
<td>bleb†</td>
<td>39 (29)</td>
<td>27 (69)</td>
<td>12 (13)</td>
<td>0.0001</td>
</tr>
<tr>
<td>PCoA fetal type†</td>
<td>47 (35)</td>
<td>17 (44)</td>
<td>30 (32)</td>
<td>0.23</td>
</tr>
<tr>
<td>other intracranial unruptured aneurysm†</td>
<td>39 (29)</td>
<td>13 (33)</td>
<td>26 (27)</td>
<td>0.53</td>
</tr>
</tbody>
</table>

* Variables showing significant difference by univariate analysis (p < 0.05) are indicated by boldface.
† Data are expressed as number of aneurysms (%).

### TABLE 3: Multivariate logistic regression analysis for PCoA aneurysm rupture

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR (95% CI)</th>
<th>p Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>age &lt;60 yrs</td>
<td>4.3 (1.4–13)</td>
<td>0.011</td>
</tr>
<tr>
<td>current smoking</td>
<td>1.0 (0.30–3.5)</td>
<td>0.96</td>
</tr>
<tr>
<td>hypertension</td>
<td>5.1 (1.5–17)</td>
<td>0.008</td>
</tr>
<tr>
<td>lateral projection</td>
<td>6.7 (2.3–19)</td>
<td>0.0001</td>
</tr>
<tr>
<td>bleb</td>
<td>11 (3.3–39)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>size of aneurysm &gt;7 mm†</td>
<td>1.2 (0.29–5.1)</td>
<td>0.77</td>
</tr>
<tr>
<td>dome-to-neck ratio &gt;2.0†</td>
<td>1.5 (0.51–4.7)</td>
<td>0.45</td>
</tr>
</tbody>
</table>

* Variables significantly related to PCoA aneurysm rupture (p < 0.05) are indicated by boldface.
rupture risk. In this respect, we considered specific morphological features such as lateral projection of the aneurysm dome and bleb formation to possibly be more important risk factors for PCoA aneurysm rupture than aneurysm size. If the aneurysm wall structure is weak, even a small PCoA aneurysm will rupture before exposure to the perianeurysmal environment. Emphasis in the current analysis was on the role of morphological characteristics of PCoA aneurysms in the risk of rupture. Whether morphological characteristics contribute independently in aneurysm rupture risk stratification should be assessed in new studies in which these characteristics are determined prospectively.

Clinical Characteristics

Several epidemiological studies have indicated that the actual age-specific incidence rate of SAH has a tendency to increase with increasing age, and some of these studies have demonstrated that SAH continues to increase in frequency as individuals become older. On the other hand, in some studies the incidence of SAH increased with increasing age, reaching the maximum level at the age of 50–70 years but declined after that. Interestingly, in our present study patients with ruptured PCoA aneurysms were younger and the proportion under the age of 60 years was higher than in those without PCoA aneurysm rupture. In a recent study, we investigated factors associated with anterior communicating artery aneurysm rupture and demonstrated that the proportion of patients under the age of 60 years was higher in the SAH group, although the difference did not remain significant in multivariate analysis. Because previous studies did not examine the relationships between age and aneurysm rupture by site of the aneurysm in detail, whether the relationship between age and rupture differs among aneurysm sites is a matter of debate. Among medical history factors, hypertension has been studied as an independent risk factor for aneurysmal SAH and our results are consistent with those of past reports. Smoking was also thought to increase the risk of both aneurysm formation and rupture. In addition, a recent prospective population-based cohort study showed that the tendency of smoking was more prominent in women than men and that at least 1 pathway in the development of SAH requires the presence of both smoking and female sex. In this regard, because the proportion of females did not differ significantly between patients with and without PCoA aneurysm rupture, smoking history might not have been related to PCoA aneurysm rupture in the present study population.

Although oculomotor nerve palsy caused by PCoA aneurysm has been regarded as a warning sign of SAH, oculomotor nerve palsy was not related to SAH in the present study.

Limitations

Certain limitations of this study must be mentioned. First, it was conducted retrospectively at a single institution and the number of patients was too small to draw definite conclusions about morphological and clinical characteristics, possibly leading to selection bias and wide confidence intervals. Second, alcohol consumption and smoking history were not quantitatively evaluated. Third, although intraneurysm hemodynamics characteristics are also believed to be an important factor for aneurysm growth and rupture, direct flow dynamics were not investigated. Fourth, the observed differences may reflect racial differences in the patient population because recent genetic analyses indicated that Japanese and/or Finnish patients are at a higher risk of rupture. Hence, the external validity applies only to a Japanese population and may not be generalizable to other ethnic groups. Finally, we performed 22 univariate analyses, with data presented in Tables 1 and 2. Based on an alpha level of 0.05, the 22 univariate analyses may have led to at least 2 incidental findings throughout the analysis. This number may have led to an overestimation of the precision of the relative risks. To exclude any such limitations in future research, we intend to expand our series and gather data on a larger number of patients with PCoA aneurysms to verify the present findings.

Conclusions

The present study showed that a lateral direction of the aneurysm dome around the PCoA and bleb formation, which was already thought to be related to rupture, are associated with PCoA aneurysm rupture. Lateral projection has never specifically been investigated in prospective cohort studies like UCAS and ISUIA to determine if it is a robust risk factor.

Disclosure

This study was supported by the Japan Heart Foundation Young Investigator’s Research Grant 2012, St. Luke’s Life Science Institute Research Grant for Clinical Epidemiology Research 2012, and a grant from the Smoking Research Foundation. The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper. Author contributions to the study and manuscript preparation include the following. Conception and design: Matsukawa, Fujii, Akaike, Shinoda. Acquisition of data: Matsukawa, Fujii, Akaike, Uemura. Analysis and interpretation of data: Matsukawa, Uemura. Drafting the article: Matsukawa. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Matsukawa. Statistical analysis: Takahashi. Administrative/technical/material support: Niimi. Study supervision: Fujii, Niimi, Shinoda.

References

4. Bonita R, Thomson S: Subarachnoid hemorrhage: epidemiolo-


Accepted September 17, 2013.

Please include this information when citing this paper: published online October 25, 2013; DOI: 10.3171/2013.9.JNS13921.

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