Moyamoya Disease-Related Versus Primary Intracerebral Hemorrhage
Location and Outcomes Are Different

Hyun-Wook Nah, MD; Sun U. Kwon, MD; Dong-Wha Kang, MD; Jae-Sung Ahn, MD; Byung-Duk Kwon, MD; Jong S. Kim, MD

Background and Purpose—The purpose of our study was to compare lesion location between moyamoya disease-related intracerebral hemorrhage (MMD-ICH) and primary intracerebral hemorrhage (P-ICH).

Methods—Ninety-three patients each with MMD-ICH and P-ICH were compared. In patients with MMD-ICH, angiographic findings were assessed with special attention to the prominent anterior choroidal artery. Follow-up data were obtained through clinical visit and telephone interview.

Results—The location of hemorrhage was different between MMD-ICH and P-ICH, the most frequent one being intraventricular region (37.6%) in the former and putaminal region (46.2%) in the latter (P<0.001). Intraventricular hemorrhage was more frequent in MMD-ICH than P-ICH (80.6% versus 20.4%, P<0.001). In MMD-ICH, primary intraventricular hemorrhage was more closely associated with prominent ipsilateral anterior choroidal artery than ICHs without intraventricular hemorrhage (75.0% versus 16.7%, P<0.001). Higher rates of rebleeding and infarction were observed in MMD-ICH than in age- and sex-matched patients with P-ICH.

Conclusions—MMD-ICH may differ from P-ICH in hemorrhage location, generally presenting with intraventricular hemorrhage with or without ICH, which may be due to a prominent anterior choroidal artery. Patients with MMD may be more likely to experience recurrent bleeding and infarction. (Stroke. 2012;43:1947-1950.)

Key Words: intracranial hemorrhage • moyamoya

Because the mechanisms of moyamoya disease-related intracranial hemorrhage (MMD-ICH) differ from those of primary intracerebral hemorrhage (P-ICH), their lesion locations and rate of recurrent bleeding may also differ. We attempted to compare lesion locations and clinical outcomes in patients with MMD-ICH and P-ICH and investigated the angiographic findings to elucidate the mechanism underlying the preferential hemorrhage location.

Methods
We reviewed the medical records of patients who were admitted to Asan Medical Center between January 2000 and December 2010. MMD diagnosis was based on previous guidelines,2 and any intracranial hemorrhage in these patients was identified. P-ICH was defined as any intracranial hemorrhage without a secondary cause such as berry aneurysm, vascular malformations, bleeding diathesis, trauma, tumor, hemorrhagic infarction, and venous thrombosis. Two control subjects were included: Control I, a patient with P-ICH admitted just before each patient with MMD-ICH, and Control II, a patient with P-ICH matched to each patient with MMD-ICH by age (±5 years) and sex.

Hemorrhage locations were assessed by CT or MRI. The volume of intraparenchymal hemorrhage was measured. Because previous reports suggested a higher prevalence of anterior choroidal artery (AchA) dilatation in hemorrhagic MMD,3 we assessed the status of the AchA in patients with MMD in whom angiographic analysis was available. Because the mean length of the AchA in normal subjects is 25 mm,4 and an AchA 40 to 50 mm long was classified as “well visualized,”5 we defined any AchA >40 mm as “prominent AchA,” which was assessed by an investigator blinded to the hemorrhage location. MMD-ICH was divided into ICH without intraventricular hemorrhage (IVH), ICH+IVH, and IVH only, and the prevalence of a prominent AchA ipsilateral to the hemorrhage was compared. Follow-up data were obtained by hospital recording or telephone interview regarding rebleeding, infarction, and mortality.

For statistics, categorical variables and continuous variables were analyzed using Pearson χ² or Fisher exact and t test or Mann-Whitney U test, respectively (PASW 18.0, a probability value <0.05 considered significant). The Kaplan–Meier method was applied to calculate the times to rebleeding and infarction in each group with the curves compared using the log rank test.

Results
During the study period, there were 581 patients with MMD, 93 (16%) presenting with ICH, and 1954 patients with P-ICH. Approximately 90% of patients with P-ICH were hypertensive. Patients with MMD-ICH were younger, more often female, and had fewer vascular risk factors (Table).

The location of lesion was different between MMD-ICH and P-ICH (P<0.001), the most frequent location being the intraventricular (37.6%) followed by lobar and putaminal regions in the
former, whereas it was the putamen (46.2%) followed by thalamus and pons in the latter (Figure 1). The prevalence of any IVH was higher ($P<0.001$), and the prevalence of accompanying IVH in putaminal or lobar ICH was also higher in patients with MMD-ICH than in patients with P-ICH (69.8% versus 1.9%, $P<0.001$). The volume of ICH did not differ between the 2 groups.

For Control II, 81 patients were matched in each group, and 12 young patients with MMD-ICH were excluded. A comparison with Control II subjects showed that risk factors were still more prevalent in patients with P-ICH, and lesion locations and the prevalence of any IVH also differed significantly (Table, right column).

Of the 93 patients with MMD, 85 were available for angiographic review. Prominent AchAs were found in 69 patients, 31 on the left and 28 on the right side. They were located ipsilateral to the lesions in 43 and contralateral in 25 patients. When ICH without IVH, ICH+IVH, and primary IVH were compared, there were significant differences in the prevalence of ipsilesional prominent AchA (16.7%, 45.7%, and 75.0%, respectively; $P<0.001$), whereas the prevalence of contral-esimal prominent AchA did not differ (27.8%, 25.7%, and 34.4%, respectively; $P=0.729$). Patients with MMD-ICH and Control II subjects were followed for a mean duration of 48 months (median, 38 months; range, 0–136 months). Although mortality within 1 month did not differ (4.9% versus 7.4%, $P=0.514$), clinical event-free survival was shorter in patients with MMD-ICH than in patients with P-ICH ($P=0.005$; Figure 2A). Rebleeding-free survival ($P=0.043$; Figure 2B) and infarction-free survival ($P=0.037$; Figure 2C) were also shorter in patients with MMD-ICH. In patients with MMD-ICH, 8 of the 9 (88.9%) infarctions developed within 1 month after onset.

### Discussion

In contrast to P-ICH, MMD-ICH usually presented with IVH with or without ICH; 74% of intraparenchymal hemorrhages

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### Table. Characteristics of MMD-ICH and P-ICH

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>MMD-ICH (n=93)</th>
<th>P-ICH (n=93)</th>
<th>$P$ Value</th>
<th>MMD-ICH* (n=81)</th>
<th>P-ICH* (n=81)</th>
<th>$P$ Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>40.3±12.5</td>
<td>58.6±13.3</td>
<td>&lt;0.001</td>
<td>43.0±10.4</td>
<td>43.1±10.1</td>
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<td>Female sex</td>
<td>65 (68.9)</td>
<td>30 (32.3)</td>
<td>&lt;0.001</td>
<td>55 (67.9)</td>
<td>55 (67.9)</td>
<td>0.999</td>
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<td>Hypertension</td>
<td>21 (22.6)</td>
<td>82 (88.2)</td>
<td>&lt;0.001</td>
<td>20 (24.7)</td>
<td>66 (81.5)</td>
<td>&lt;0.001</td>
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<tr>
<td>Diabetes</td>
<td>3 (3.2)</td>
<td>17 (18.3)</td>
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<td>3 (3.7)</td>
<td>12 (14.8)</td>
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<td>Smoking</td>
<td>16 (17.2)</td>
<td>26 (28.0)</td>
<td>0.114</td>
<td>16 (19.8)</td>
<td>18 (22.2)</td>
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<td>Alcohol drinking</td>
<td>29 (31.2)</td>
<td>48 (51.6)</td>
<td>0.007</td>
<td>28 (34.6)</td>
<td>35 (43.2)</td>
<td>0.334</td>
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<tr>
<td>Use of antithrombotics</td>
<td>4 (4.3)</td>
<td>8 (8.6)</td>
<td>0.233</td>
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<td></td>
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<tr>
<td>Hemorrhage location</td>
<td></td>
<td></td>
<td>&lt;0.001</td>
<td></td>
<td></td>
<td>&lt;0.001</td>
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<tr>
<td>Putaminal</td>
<td>21 (22.6)</td>
<td>43 (46.2)</td>
<td>26 (19.8)</td>
<td>37 (45.7)</td>
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<td></td>
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<tr>
<td>Thalamic</td>
<td>5 (5.4)</td>
<td>18 (19.4)</td>
<td>5 (6.2)</td>
<td>15 (18.5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lobar</td>
<td>22 (23.7)</td>
<td>9 (9.7)</td>
<td>20 (24.7)</td>
<td>12 (14.8)</td>
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<tr>
<td>Caudate</td>
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<td>2 (2.5)</td>
<td>1 (1.2)</td>
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<tr>
<td>Pontine</td>
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<tr>
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<td>4 (4.9)</td>
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<tr>
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<td>30 (37.0)</td>
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<tr>
<td>Callosal</td>
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<td>SAH</td>
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<td>Any IVH</td>
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<td>19 (20.4)</td>
<td>&lt;0.001</td>
<td>63 (77.8)</td>
<td>18 (22.2)</td>
<td>&lt;0.001</td>
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<td>1/43 (2.3)</td>
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<td>10/18 (55.6)</td>
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<tr>
<td>Cerebellar</td>
<td>2/4</td>
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<td></td>
<td></td>
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</tr>
<tr>
<td>Primary IVH</td>
<td>35/35</td>
<td>2/2</td>
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<tr>
<td>Callosal</td>
<td>4/4</td>
<td></td>
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<td>ICH volume, mL</td>
<td>17.8±18.1</td>
<td>13.0±16.3</td>
<td>0.156</td>
<td>17.8±18.1†</td>
<td>14.5±17.3†</td>
<td>0.378</td>
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</table>

Values are no. (percent) or mean±SD. MMD-ICH indicates moyamoya disease-related intracerebral hemorrhage; P-ICH, primary intracerebral hemorrhage; IVH, intraventricular hemorrhage; SAH, subarachnoid hemorrhage. *After matching for age and sex. †Supratentorial ICH volume (in 44 patients with MMD-ICH and 72 patients with P-ICH).
were accompanied by IVH. Because the prevalence of caudate or thalamic hemorrhage, which usually empties into the ventricle, was low in MMD-ICH, and ICH volume did not differ between MMD-ICH and P-ICH, the high prevalence of IVH in MMD may be due to vascular pathology occurring near the ventricle. This hypothesis is supported by our finding that both primary IVH and ICH+IVH were significantly associated with ipsilesionally prominent AchA, suggesting that rupture of focal protrusions or microaneurysm formation in the abnormally dilated AchA branches may produce preferential development of IVH in MMD.6

We also found that recurrent bleeding was more frequent in MMD-ICH than in P-ICH. Our observations agree with previous results showing that the incidence of rebleeding was relatively high in MMD-ICH.7 Interestingly, patients with MMD-ICH also had a higher risk of cerebral infarction, most (88.9%) occurring within 1 month of the hemorrhage. This result agrees with previous reports showing development of early cerebral infarction after MMD-ICH.8 Perhaps, hemodynamic alterations, vasospasms, or blood pressure-lowering treatments may predispose hemodynamically unstable patients with MMD to develop early ischemic strokes.

In summary, despite limitations such as small sample size, use of P-ICH instead of all causes of ICH as controls, the lack of pathological data, and the heterogeneous follow-up duration, our findings suggest that location of hemorrhage and natural course are different between MMD-ICH and P-ICH.

Figure 1. Representative patients with moyamoya disease-related hemorrhage. A, Primary IVH; B, lobar hemorrhage with IVH; C, putaminal hemorrhage with IVH; D, callosal hemorrhage with IVH. IVH indicates intraventricular hemorrhage.

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Disclosures
None.

References
Figure 2. Kaplan–Meier curves for clinical events (A), rebleeding (B), and infarction (C).
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The version of the article, “Moyamoya Disease-Related Versus Primary Intracerebral Hemorrhage Location and Outcomes Are Different” by Nah et al that published ahead-of-print on June 12, 2012 and appeared in the July issue of the journal (Stroke. 2012;43:1947–1950) contained an error in the title. It should read, “Moyamoya Disease-Related Versus Primary Intracerebral Hemorrhage: Location and Outcomes Are Different”. The title has been corrected in the online version of the article.