Posterior Cerebral Artery Laterality on Magnetic Resonance Angiography Predicts Long-Term Functional Outcome in Middle Cerebral Artery Occlusion

Masahiko Ichijo, MD; Kazunori Miki, MD, PhD; Satoru Ishibashi, MD, PhD; Makoto Tomita, PhD; Tomoyuki Kamata, MD, PhD; Hiroto Fujigasaki, MD, PhD; Hidehiro Mizusawa, MD, PhD

Background and Purpose—Prominent posterior cerebral artery (PCA) laterality upon 3-dimensional time-of-flight magnetic resonance angiography is often encountered in patients with middle cerebral artery occlusion. We hypothesized that this sign is correlated with improved functional outcome in patients with middle cerebral artery occlusion treated with intravenous recombinant tissue plasminogen activator.

Methods—Fifty acute ischemic stroke patients with middle cerebral artery occlusion were treated with intravenous recombinant tissue plasminogen activator from April 2007 to October 2009. All patients routinely underwent initial (first 3 hours) magnetic resonance scans on admission, and additional follow-up (14–21 days after stroke onset) computed tomography scans. Two film readers blinded to all clinical information assessed the presence or absence of PCA laterality on magnetic resonance angiography. We retrospectively analyzed the clinical and radiologic data on all patients.

Results—Out of 50 patients, 20 showed PCA laterality on magnetic resonance angiography. National Institute of Health Stroke Scale score 7 days after stroke onset was significantly lower (P=0.007), and infarct volume on follow-up computed tomography was significantly smaller (P=0.009) in patients with PCA laterality than in patients without this sign. Multivariate logistic regression analyses showed an adjusted odds ratio of 8.49 for a favorable outcome (modified Rankin Scale score 0–1 at 6 months) in patients with PCA laterality (95% CI: 1.82 to 55.8, P=0.005).

Conclusions—The presence of PCA laterality on magnetic resonance angiography before intravenous recombinant tissue plasminogen activator can be used as a predictor of favorable functional outcome in patients with middle cerebral artery occlusion, probably due to improvement of recanalization rate. (Stroke. 2013;44:512-515.)

Key Words: acute stroke ■ collateral circulation ■ tissue plasminogen activator

Subjects and Methods
For detailed methods, see the online-only Data Supplement. Briefly, this retrospective case-control study was performed on all acute ischemic stroke patients that received tissue plasminogen activator (tPA).

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ischemic stroke patients admitted to our hospital from April 2007 to October 2009. We selected acute proximal MCA occlusion patients who were treated with IV rtPA within 3 hours of symptom onset.

All patients underwent brain magnetic resonance imaging (MRI; Signa HDxt 1.5T Optima Edition, GE Healthcare, Milwaukee, WI) before rtPA administration, and follow-up brain CT 14 to 21 days after stroke onset. Collected data included demographic and clinical parameters, radiological data, the National Institutes of Health Stroke Scale (NIHSS), and the modified Rankin Scale (mRS), which is included in our standard protocol for all stroke patients.

To assess the presence of PCA laterality, laterality of either PCA on MRA was considered to be present if 1 or more segmental extents were observable on axial stereoscopic images (Figure). If the signal from either PCA ended in the same segment, laterality was defined as negative. The site of proximal MCA occlusion, the status of posterior communicating (PCOM) artery, or recanalization status was also assessed by MRA. The Alberta Stroke Program Early CT Score (ASPECTS) was used to evaluate the final infarct extent.7

Univariable parametric and nonparametric comparisons of clinical characteristics were performed as appropriate. To identify independent predictors of favorable outcome, we performed multivariate logistic regression analyses using age, sex, baseline NIHSS score, risk factors, and PCA laterality.

Results

Fifty-six patients were examined for inclusion in this study; 6 of these patients were excluded because of motion artifacts on MRI. Among the 50 patients who met the inclusion criteria,

| Table 1. Characteristics of Patients With and Without PCA Laterality on MRA |
|-----------------|-----------------|-----------------|-----------------|-----------------|
| With PCA Laterality | Without PCA Laterality | P Value |
| (n=20) | (n=30) | (n=20) | (n=30) |
| Age, years (median, IQR)  | 79 (70–82) | 77 (61–84) | 0.714 |
| No. of women | 8 | 10 | 0.765 |
| mRS 0–1 before stroke | 18 | 28 | 1.000 |
| Hypertension | 11 | 18 | 0.776 |
| Diabetes mellitus | 4 | 5 | 0.327 |
| Hyperlipidemia | 5 | 6 | 0.736 |
| Atrial fibrillation | 14 | 13 | 0.086 |
| Congestive heart failure | 2 | 6 | 0.450 |
| Previous stroke | 4 | 6 | 1.000 |
| Smoking | 5 | 10 | 0.754 |
| Antiplatelet therapy at stroke onset | 6 | 10 | 0.001 |
| Anticoagulant therapy at stroke onset | 2 | 5 | 0.687 |
| Antihypertensive therapy at stroke onset | 11 | 14 | 0.773 |
| Statin therapy at stroke onset | 5 | 5 | 0.494 |
| Dominant ipsilateral PCOM† | 5 | 6 | 0.736 |
| CRP (median, IQR) | 0.54 (0.09–1.95) | 0.345 (0.09–1.14) | 0.870 |
| Blood glucose, mg/dL (median, IQR) | 110 (94–140) | 118 (106.5–134.75) | 0.335 |
| Systolic blood pressure (median, IQR) | 158.5 (135–178.75) | 162 (149–175.5) | 0.470 |
| Initial NIHSS (median, IQR) | 13.5 (9–25) | 16.5 (10–23) | 0.565 |
| Initial GCS (median, IQR) | 14 (10–15) | 10 (14–15) | 0.103 |
| 7 days NIHSS (median, IQR) | 2.5 (1–8) | 11.5 (4–20) | 0.007* |
| Follow-up CT ASPECTS | 8.5 (7–10) | 6.5 (4–9) | 0.009* |
| mRS 0–1 at 6 months | 15 | 11 | 0.008* |

GCS indicates Glasgow Coma Scale; IQR, interquartile range; NIHSS, National Institutes of Health Stroke Scale; mRS, modified Rankin Scale; PCA, posterior cerebral artery; PCOM, posterior communicating artery.

For continuous variables, the median and P values from the Mann–Whitney U test are shown.

The resulting proportions and P values from Fisher’s exact test are shown.

*P<0.05 considered to be significant.

†If diameter of PCOM was equal to or larger than that of ipsilateral P1, we classified dominant ipsilateral PCOM.
36% were women. The median age was 77.5 (range 40 to 96) years, and the median initial NIHSS score was 14.5 (range 4 to 32). Thirty-three patients were found to have MCA M1 occlusion, and 17 patients, M2 occlusion.

PCA laterality on MRA was observed in 20 patients (40%). The signal extent of the PCA in all of these patients was confined to the ipsilateral side of the ischemic hemisphere. Demographic data and clinical parameters, status of PCOM did not differ significantly between the groups (Table 1). The median initial NIHSS score did not differ significantly between the groups (13.5 with laterality versus 16.5 without laterality; interquartile range [IQR], 9 to 25 versus 10 to 23; \( P = 0.565 \)). The NIHSS score 7 days after admission was significantly lower in patients with PCA laterality than in those without it (2.5 versus 11.5; IQR, 1 to 8 versus 4 to 20; \( P = 0.007 \)). Follow-up CT ASPECTS was significantly higher in patients with PCA laterality than in those without it (8.5 versus 6.5; IQR, 7 to 10 versus 4 to 9; \( P = 0.009 \)), indicating a smaller infarct extent (Table 1). Successful recanalization was achieved in 73% (19 out of the 26 patients with available follow-up MRA) after rtPA thrombolysis treatment. Recanalization rate was significantly higher in patients with PCA laterality (\( P = 0.006 \); Table S1 in the online-only Data Supplement). Significantly more of the patients positive for PCA laterality (15 of 20 patients) had a favorable clinical outcome (mRS score of 0–1 at 6 months) than did laterality-negative patients (11 of 30 patients; \( P = 0.008 \); Table 1). Multivariate logistic regression analysis was performed to further evaluate independent predictors of clinical outcome. PCA laterality (OR, 8.49; 95% CI, 1.82 to 55.8; \( P = 0.005 \)) was independently associated with favorable outcome, after adjustment for other variables (Table 2).

### Discussion

This study demonstrated that increased signal extent of the ipsilateral PCA on 3-dimensional time-of-flight MRA, namely PCA laterality, was significantly associated with smaller ischemic region volume, better recanalization rate, and lower NIHSS score 7 days after stroke onset, and with better long-term functional outcome, in patients with MCA occlusion who were treated with rtPA.

PCA laterality is rarely observed in nonstroke patients, supporting the view that laterality of the PCA is a unique finding in MCA occlusion. PCA laterality on MRA indicates the presence of collateral flow via the LMAs from the ipsilateral PCA to the MCA in patients with proximal occlusion of the MCA.

In our preliminary study of patients with PCA laterality, the ischemic regions on follow-up CT were confined primarily to the basal ganglia or insular cortex, and, to a lesser extent, the cortical ischemic regions within the MCA territory. Indeed, the extent of infarction in the cortical regions (M1 to M6 in ASPECTS; total score 6) was significantly smaller in patients with PCA laterality than in those without it (ASPECTS score 5.3 versus 3.3, \( P < 0.01 \)), but no significant differences were observed in other ASPECT regions, such as the insular cortex, basal ganglia, and internal capsule (ASPECTS

### Table 2. Factors Associated With Favorable Clinical Outcome

<table>
<thead>
<tr>
<th></th>
<th>mRS Score 0–1 at 6 Months</th>
<th>Estimated OR</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes (n=26)</td>
<td>No (n=24)</td>
</tr>
<tr>
<td>Age, years (median, IQR)</td>
<td>76 (68–81)</td>
<td>79 (66–84)</td>
</tr>
<tr>
<td>No. of women</td>
<td>9</td>
<td>9</td>
</tr>
<tr>
<td>Hypertension</td>
<td>16</td>
<td>13</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>8</td>
<td>5</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>7</td>
<td>4</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>15</td>
<td>12</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Previous stroke</td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>Smoking</td>
<td>6</td>
<td>9</td>
</tr>
<tr>
<td>Antiplatelet therapy at stroke onset</td>
<td>9</td>
<td>7</td>
</tr>
<tr>
<td>Anticoagulant therapy at stroke onset</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Antihypertensive therapy at stroke onset</td>
<td>15</td>
<td>10</td>
</tr>
<tr>
<td>Statin therapy at stroke onset</td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>Blood glucose, mg/dL (median, IQR)</td>
<td>111 (98–136)</td>
<td>121 (109–137)</td>
</tr>
<tr>
<td>Systolic blood pressure (median, IQR)</td>
<td>159 (147–174)</td>
<td>165 (148–176)</td>
</tr>
<tr>
<td>Initial NIHSS score (median, IQR)</td>
<td>11 (8–14)</td>
<td>22 (16–26)</td>
</tr>
<tr>
<td>Positive PCA laterality</td>
<td>15</td>
<td>5</td>
</tr>
</tbody>
</table>

For continuous variables, the median and \( P \) values from the Mann–Whitney U test are shown. The resulting proportions and \( P \) values from Fisher’s exact test are shown. OR indicates odds ratio. \( * P < 0.05 \) considered to be significant.
score 2.8 versus 2.9, \( P=0.91 \); Table S2 in the online-only Data Supplement). In a previous study including patients with proximal MCA occlusion, all patients with prominent collateral flow from the PCA to the MCA via the LMAs also had angiographic collateral flow from the ipsilateral ACA to the MCA. In our study, the presence of PCA laterality was significantly associated with the appearance of collateral flow signals on MRI in the ipsilateral MCA territory (Table S3 in the online-only Data Supplement). In contrast to the rtPA treatment group, the neurological and radiological outcome in the no rtPA group did not differ with or without PCA laterality analyzed by database in this study (Table S4 in the online-only Data Supplement). In this sense, PCA laterality on MRA may be associated with the development of collateral circulation via the LMAs from the territories of both the ACA and the PCA, which can preserve penumbral blood flow prior to recanalization, resulting in a smaller extent of cortical infarction after rtPA administration in patients with MCA occlusion.

In a previous angiographic study of endovascular therapy for acute ischemic stroke, the presence of well-developed collaterals before recanalization was significantly associated with better outcomes, such as high incidence of reperfusion, small infarct volume, and low rate of symptomatic hemorrhagic transformation. Therefore, pretreatment evaluation of cerebral collaterals should be useful for identifying patients who have the best chance of benefitting from recanalization therapy. We found here that patients with PCA laterality in the setting of thrombolysis for acute MCA occlusion had a smaller infarct volume, better recanalization rate, and better long-term neurological outcome. This MRA finding might therefore be an important discriminating marker of leptomeningeal collateral status and might be useful in guiding decision-making in terms of the use of aggressive thrombolytic therapy after stroke.

This study had several limitations. It was a single-center, retrospective study and was limited by a small sample size. A longitudinal study investigating the correlation between PCA laterality and outcome after thrombolysis is required to confirm and extend our findings.

**Disclosures**

None.

**References**

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Supplemental Methods

This retrospective case-control study was performed on all patients admitted to our hospital from April 2007 to October 2009 who were clinically diagnosed with acute ischemic stroke by neurologists and managed in the stroke care unit. The inclusion criteria were as follows: (1) presentation within 3 h of symptom onset and treatment with IV rtPA according to Japanese guidelines; and (2) acute ischemic regions within the MCA territory on diffusion-weighted imaging (DWI), or occlusion of the MCA on MRA. All patients underwent brain MR imaging (MRI) (Signa HDxt 1.5 T Optima Edition, GE Healthcare, Milwaukee, WI) before rtPA administration. The MRI included the following sequences acquired in the axial plane: spin-echo DWI, T2- fluid attenuated inversion recovery (FLAIR), and three-dimensional time-of-flight (3D-TOF) MRA. Follow-up brain CT was performed on all patients 14 to 21 days after stroke onset.

Demographic data, as well as information on cardiovascular risk factors, medical history, and the results of diagnostic tests, including routine blood tests, were collected at the time of admission. According to our institution's standard protocol for ischemic stroke patients, neurological deficits were evaluated by using the National Institutes of Health Stroke Scale (NIHSS) on admission and 7 days after admission. The modified Rankin Scale (mRS) score was assessed on admission and at 6 months after the onset of symptoms (by follow-up visit or phone call). Favorable clinical outcome was defined as a mRS score of 0-1 at 6 months.

Film readers blinded to all clinical information assessed the presence of PCA laterality and the site of occlusion of the MCA. To assess PCA laterality, we used Zeal and Rhoton’s classification of each segment. Laterality of either PCA on MRA was considered to be present if 1 or more segmental extents were observable on axial stereoscopic images (Figure 1). We considered P2a (anterior ambient segment) and P2p (posterior ambient segment) to be different segments. If the signal from either PCA ended in the same segment, laterality was defined as negative. To evaluate collaterals in the ipsilateral MCA territory, we also assessed the hyperintense vessels (HV) on FLAIR, of which usefulness in assessing collateral flow has been reported recently.
images, HV signals were defined as focal, linear or serpentine, hyperintense signals relative to gray matter in the distal to Sylvian fissure corresponding to the M3 or distal segments of the MCA. We blinded to clinical data independently assessed the presence and the location of HV using initial FLAIR MRI in this study. We assessed the status of posterior communicating (PCOM) artery using initial MRA. If the diameter of PCOM was equal to or larger than that of ipsilateral P1, we classified it as dominant ipsilateral PCOM. We defined proximal MCA occlusion as M1 or M2 segment occlusion on the basis of the MRA findings. M1 occlusion was defined as main MCA trunk occlusion before the bifurcation, and M2 occlusion was defined as branch occlusion after the bifurcation. Patients who underwent follow-up MRA within 7 days from admission, recanalization status were assessed by a modified grading system based on thrombolysis in myocardial infarction (TIMI) grade using MRA. TIMI 2 and 3 was regarded as successful recanalization, and TIMI 0 and 1 as poor recanalization. The Alberta Stroke Program Early CT Score (ASPECTS) was used to evaluate the final infarct extent on follow-up CT scan.

Univariable parametric and nonparametric comparisons of clinical characteristics were performed with the Mann–Whitney U test, the chi-squared test with or without Yates’s correction, and Fisher’s exact test, as appropriate. To identify independent predictors of favorable outcome in patients treated with rtPA, first we performed univariate analyses to detect the factors having a significant relationship with favorable clinical outcome. Then, with respect to these factors, we performed multivariate logistic regression analyses using age, gender, baseline NIHSS score, history of smoking, and PCA laterality. All statistical analyses were performed with JMP software (Version 9.02; SAS Institute Inc, Cary, NC), under the direction of statistician (M.K.).

Supplemental References


### Supplemental Table S1. Comparison of ischemic region volume, and clinical outcome by recanalization status in patients with middle cerebral artery M1 or M2 occlusion

<table>
<thead>
<tr>
<th></th>
<th>Recanalization</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Success (n = 19)</td>
<td>Poor (n = 7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Initial NIHSS</td>
<td>14.1 ± 8.9</td>
<td>16.7 ± 6.4</td>
<td>0.401</td>
<td></td>
</tr>
<tr>
<td>7 days NIHSS</td>
<td>4.7 ± 4.4</td>
<td>16.4 ± 9.5</td>
<td>0.008*</td>
<td></td>
</tr>
<tr>
<td>mRS 0-1 at 6 month</td>
<td>14</td>
<td>2</td>
<td>0.069</td>
<td></td>
</tr>
<tr>
<td>Follow-up CT ASPECTS</td>
<td>8.1 ± 1.9</td>
<td>5.6 ± 3.4</td>
<td>0.107</td>
<td></td>
</tr>
<tr>
<td>PCA laterality positive</td>
<td>12</td>
<td>0</td>
<td>0.006*</td>
<td></td>
</tr>
</tbody>
</table>

Data are mean ± SD; For continuous variables, P values from the Mann–Whitney U test are shown. The resulting proportions and the P values from Fisher’s exact test (with Yates’s correction when appropriate) are shown.

* P<0.05 was considered significant; ASPECTS, Alberta Stroke Program Early CT Score; mRS, modified Rankin Scale

NIHSS, National Institutes of Health Stroke Scale; PCA, posterior cerebral artery

### Supplemental Table S2. Comparison of ischemic region on follow-up CT in patients with middle cerebral artery M1 or M2 occlusion

<table>
<thead>
<tr>
<th></th>
<th>With PCA laterality (n = 20)</th>
<th>Without PCA laterality (n = 30)</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Follow-up CT ASPECTS</td>
<td>8.4 ± 1.8</td>
<td>6.2 ± 2.8</td>
<td>0.004*</td>
<td></td>
</tr>
<tr>
<td>M1 to M6 area in ASPECTS</td>
<td>5.3 ± 1.1</td>
<td>3.3 ± 2.1</td>
<td>0.002*</td>
<td></td>
</tr>
<tr>
<td>C, I, L, IC area in ASPECTS</td>
<td>2.8 ± 1.1</td>
<td>2.9 ± 0.6</td>
<td>0.906</td>
<td></td>
</tr>
</tbody>
</table>

Data are mean ± SD; For continuous variables, P values from the Mann–Whitney U test are shown. The resulting proportions and the P values from Fisher’s exact test (with Yates’s correction when appropriate) are shown.

* P<0.05 was considered significant; ASPECTS, Alberta Stroke Program Early CT Score; PCA, posterior cerebral artery

M1, anterior MCA; M2, lateral MCA; M3, posterior MCA; M4, superior M1; M5, superior M2; M6, superior M3

C, caudate nucleus; I, Insular cortex; L, Lenticular nucleus; IL, Internal capsule
Supplemental Table S3. Relationship of the location of HV on FLAIR and PCA laterality on MRA

<table>
<thead>
<tr>
<th>Location of HV on FLAIR</th>
<th>With PCA laterality (n = 20)</th>
<th>Without PCA laterality (n = 30)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>HV in frontal-parietal lobes†</td>
<td>18 (90%)</td>
<td>7 (23%)</td>
<td>&lt; 0.001*</td>
</tr>
<tr>
<td>HV in temporal-occipital junction‡</td>
<td>20 (100%)</td>
<td>19 (63%)</td>
<td>0.002*</td>
</tr>
</tbody>
</table>

The resulting proportions and the P values from Fisher’s exact test (with Yates’s correction when appropriate) are shown. *P<0.05 was considered significant.

FLAIR, fluid-attenuated inversion recovery; HV, hyperintense vessels.
† HV in frontal-parietal lobes represent MCA collaterals predominantly from PCA via LMA.
‡ HV in temporal-occipital junction represent MCA collaterals predominantly from ACA via LMA.

Supplemental Table S4. Comparison of ischemic region volume, and clinical outcome in patients with middle cerebral artery M1 or M2 occlusion (non-rtPA group)

<table>
<thead>
<tr>
<th></th>
<th>With PCA laterality (n = 12)</th>
<th>Without PCA laterality (n = 15)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial NIHSS</td>
<td>9.3 ± 11.6</td>
<td>9.9 ± 8.9</td>
<td>0.695</td>
</tr>
<tr>
<td>7 days NIHSS</td>
<td>6.9 ± 8.9</td>
<td>9.4 ± 8.7</td>
<td>0.508</td>
</tr>
<tr>
<td>Follow-up CT ASPECTS</td>
<td>7.8 ± 1.7</td>
<td>7.3 ± 1.9</td>
<td>0.686</td>
</tr>
<tr>
<td>mRS 0-1 at 6 month</td>
<td>4</td>
<td>6</td>
<td>0.722</td>
</tr>
</tbody>
</table>

Data are mean ± SD; For continuous variables, P values from the Mann–Whitney U test are shown. The resulting proportions and the P values from Fisher’s exact test (with Yates’s correction when appropriate) are shown.

NIHSS, National Institutes of Health Stroke Scale; PCA, posterior cerebral artery.
ASPECTS, Alberta Stroke Program Early CT Score; mRS, modified Rankin Scale.