Misery Perfusion, Blood Pressure Control, and 5-Year Stroke Risk in Symptomatic Major Cerebral Artery Disease

Hiroshi Yamauchi, MD, PhD; Shinya Kagawa, MS; Yoshihiko Kishibe, RT; Masaaki Takahashi, RT; Tatsuya Higashi, MD, PhD

Background and Purpose—The benefit of strict blood pressure (BP) control in high-risk patients with symptomatic major cerebral artery disease and misery perfusion (MP) is controversial. Our purposes were (1) to determine whether MP is a predictor of a 5-year risk of subsequent stroke and (2) to investigate the relationships among BP during follow-up, MP, and the stroke risk.

Methods—We studied 130 nondisabled patients with symptomatic major cerebral artery disease. Baseline hemodynamic measurements were obtained from 15O-gas positron emission tomography, and patients received medical treatment and they were followed for 5 years or until stroke recurrence or death.

Results—During 5 years, strokes occurred in 6 of 16 patients with MP and in 15 of 114 without MP (log-rank test; P<0.01).

Conclusion—Patients with MP showed a high-5-year stroke recurrence, but a large part of the 5-year stroke risk disappeared after 2 years. Aggressive BP control may be hazardous in patients with impaired perfusion, including MP.

Key Words: blood pressure ■ cerebrovascular disease ■ positron emission tomography ■ prognosis

Chronic hemodynamic compromise, as indicated by increased oxygen extraction fraction (OEF; misery perfusion [MP])

on positron emission tomography, is a risk factor for subsequent strokes in patients with atherosclerotic internal carotid artery (ICA) or middle cerebral artery occlusive diseases. However, the benefit of bypass surgery or strict control of blood pressure (BP) for reducing the stroke risk in MP patients is controversial.

Bypass surgery has been proven to improve MP. The Carotid Occlusion Surgery Study (COSS) in patients with recent symptomatic ICA occlusion and MP failed to show that surgery compared with medical therapy reduces the risk of ipsilateral ischemic stroke in 2 years. However, it was criticized that although the Kaplan–Meier curves at 2 years were not different, a continuation of the curves could result in a crossover showing a benefit to surgery. Although patients with symptomatic ICA occlusion show a decrease in stroke rate over time, it is unclear whether this is true for MP patients.

BP lowering may increase the stroke risk in patients with impaired perfusion, as indicated by a decreased cerebral blood flow [CBF]/cerebral blood volume [CBV] ratio on positron emission tomography. In our previous study, the relationship between BP and a 2-year stroke risk was different between patients with impaired perfusion (including MP) and those without impaired perfusion. The stroke risk was high in patients with lower BP with impaired perfusion and in higher BP patients without impaired perfusion. However, a recent evaluation of nonsurgical controls from the COSS reported a contradictory finding, a lower stroke risk was associated with lower BP in patients with ICA occlusion and MP.

Our study purposes were (1) to determine whether MP is a predictor of a 5-year risk of subsequent stroke and (2) to investigate the relationships among BP during follow-up, MP, and the 5-year stroke risk.

Methods

We enrolled 130 nondisabled, medically treated patients with symptomatic occlusion of the extracranial ICA or occlusion or stenosis (>50% diameter reduction) of the intracranial ICA or middle cerebral artery in our observational study, as previously reported. This included 103 men and 27 women aged 44 to 90 years (mean±SD, 64±8 years; Table I in the online-only Data Supplement). The ethics
Results

Sixteen patients (12%) had MP and 114 did not have MP (Table I in the online-only Data Supplement). No patient characteristics significantly differed between the groups. Twenty-three patients had a decreased CBF/CBV ratio and normal OEF, 16 had a normal CBF/CBV ratio and increased OEF, and 75 had a normal CBF/CBV ratio and normal OEF. All patients, except 2, were treated with antiplatelet therapy.

All patients, except 4, were followed up for 5 years until stroke recurrence or death. None underwent vascular reconstruction surgery. One patient with MP and 3 patients without MP were lost to follow-up at 25 months and at 25, 40, and 43 months, respectively.

In patients with and without MP, the 5-year incidence of all strokes occurred in 6 (including 1 hemorrhage; 37.5%) and 15 (including 3 hemorrhages; 13.1%), respectively (hazard ratio [HR], 3.5; 95% confidence interval [CI], 1.4–8.9; P<0.01), and the incidence of ipsilateral ischemic stroke occurred in 4 (25%) patients and 4 (3.5%) patients, respectively (HR, 7.9; 95% CI, 1.9–31.9; P<0.05; Figure 1; Table II in the online-only Data Supplement). In patients with and without MP, the incidence of any ischemic strokes occurred in 5 (33.3%) and 12 (11.5%), respectively (HR, 3.4; 95% CI, 1.2–9.8; P<0.05). Beyond 2 years, there was only 1 ipsilateral ischemic stroke in patients without MP, whereas strokes elsewhere occurred in 2 patients with MP (1 hemorrhage) and in 5 patients without MP (1 hemorrhage). Death occurred in 3 patients with MP and in 7 patients without MP.

In patients with and without a decreased CBF/CBV ratio (impaired perfusion), the 5-year incidence of all strokes occurred in 9 of 39 (23.0%) patients and 12 of 91 (13.1%) patients, respectively (HR, 1.9; 95% CI, 0.8–4.6; P=0.13), and the incidence of ipsilateral ischemic stroke occurred in 6 (15.3%) and 2 (2.1%), respectively (HR, 7.7; 95% CI, 1.5–38.3; P<0.05). Death occurred in 4 patients with a decreased CBF/CBV ratio and in 6 patients without a decreased CBF/CBV ratio. In patients with an increased OEF but a normal CBF/CBV ratio, no stroke occurred.

Overall, there was a negative relationship between the SBP categories and the risk of ipsilateral ischemic stroke (Tables II and III in the online-only Data Supplement); the HR per 20 mm Hg was 0.26 (95% CI, 0.07–0.91; P<0.05). Alternatively, there was a positive relationship between the SBP categories and the risk of stroke in territories other than the diseased artery; the HR per 20 mm Hg was 4.5 (95% CI, 2.2–9.2; P<0.0001).

In the subgroup comparisons of the total stroke recurrence rate with SBP, a high-stroke risk was observed in patients with lower BP with MP and in higher BP patients without MP (interaction, P<0.01). The interaction was more apparent when the relationship was compared between patients with a decreased CBF/CBV ratio and those without a decreased CBF/CBV ratio (P<0.005; Figure 2).

In patients with a decreased CBF/CBV ratio (including MP), the normal SBP (<130 mm Hg) was significantly associated with an increased risk of ipsilateral ischemic stroke (log-rank test, P<0.05; Figure 3). In patients with a normal CBF/CBV ratio and increased OEF, the normal SBP was also associated with an increased risk of ipsilateral ischemic stroke.
CBV ratio, the SBP outside the 130 to 149 mm Hg range was significantly associated with an increased risk of all strokes (Fisher exact test, P<0.0005).

In multivariate analysis using the Cox proportional hazard model, MP and a normal SBP (<130 mm Hg) were independently associated with an increased risk of ipsilateral ischemic stroke. The adjusted HRs conferred by the presence of MP and a normal SBP were 6.1 (95% CI, 1.5–25.3; P<0.05) and 6.8 (95% CI, 1.3–34.6; P<0.05), respectively. Alternatively, the adjusted HRs conferred by the presence of a decreased CBF/CBV ratio and a normal SBP were 7.6 (95% CI, 1.5–37.9; P<0.05) and 8.2 (95% CI, 1.6–40.9; P<0.05), respectively. The risk of all strokes was independently associated with MP (adjusted HR, 2.9; 95% CI, 1.1–7.5; P<0.05) and SBP (range, 130–149 mm Hg; adjusted HR, 0.26; 95% CI, 0.08–0.78; P<0.05).

In 61 patients with ICA occlusion, all 4 ipsilateral ischemic strokes occurred only in patients with a normal SBP (<130 mm Hg); 2 in 12 MP patients, 0 in 9 with an increased OEF and a normal CBF/CBV ratio, 1 in 10 with a normal OEF and a decreased CBF/CBV ratio, and 1 in 30 with a normal OEF and a normal CBF/CBV. Four strokes (3 hemorrhages) in the other vascular territories occurred only in patients without a normal SBP; 1 with MP, 1 with a normal OEF and a decreased CBF/CBV ratio, and 2 with a normal OEF and a normal CBF/CBV ratio.

**Discussion**

In patients with symptomatic major cerebral arterial disease, MP was an independent predictor of a subsequent stroke risk during a 5-year follow-up period. The 5-year incidence of ipsilateral ischemic stroke (25%) and all strokes (37.5%) was higher in patients with MP than in those without MP (3.5% and 13.1%, respectively). The risk of ipsilateral ischemic stroke declined markedly after 2 years, and only 1 occurred in a patient without MP. Thus, a large part of the 5-year stroke risk in patients with MP disappeared after 2 years.

We provided data that showed a major decrease in the rate of ipsilateral ischemic stroke after 2 years in patients with MP, as shown in our previous study. Thus, continuing COSS for an additional 3 years would not have shown a significant benefit for surgery, and the surgical complication rates would have needed to be low. One possible explanation for this is that unstable MP may become stabilized or attenuated over time in relation to the development of collaterals or the reduced metabolic demand because of ischemic neuronal damage.

This study also demonstrated that the relationship between the follow-up BP and stroke risk differs between patients with and without impaired perfusion. All patients with MP had a decreased CBF/CBV ratio. In patients with impaired perfusion, a normal SBP (<130 mm Hg) was associated with an increased risk of ipsilateral ischemic stroke. In patients without impaired perfusion, an SBP outside of the 130 to 149 mm Hg range was associated with an increased risk of all stroke. In patients with impaired perfusion, including those with MP, an aggressive reduction of BP may be hazardous, especially during the first 2 years after presentation.

Powers et al evaluated 91 nonsurgical controls from the COSS. All patients had an increased OEF ratio ipsilaterally to recent symptomatic carotid occlusion. They reported a reduced risk of ipsilateral ischemic stroke in patients with a mean SBP during follow-up of ≤130/85 mm Hg, which is inconsistent with our results. Several factors may contribute to this difference. First, COSS studied only ICA occlusion. In our patients with ICA occlusion, ipsilateral ischemic stroke occurred only in patients with a normal SBP (<130 mm Hg). Second, in the COSS, it is unclear whether the patients had impaired perfusion. In our study, a lower BP was associated with an increased stroke risk in patients with a decreased CBF/CBV ratio, but not in patients with an increased OEF and a normal CBF/CBV ratio. Thirdly, the target goal for BP was 130/85 mm Hg in the COSS. In such patients with an increased OEF and a higher BP, a higher BP may barely maintain the CBF. Thus, patients with an increased OEF and a higher BP may be more susceptible to low-flow infarcts because of a reduction in BP than in those with a lower BP, which may cause stroke before BP can reach the target (130/85 mm Hg). The COSS surgical group showed a low postoperative stroke rate after the improvement of the OEF ratio, despite a BP distribution similar to the nonsurgical group, which suggests that an interaction between an increased

**Figure 3.** Kaplan–Meier cumulative failure curves for ipsilateral ischemic stroke in patients with and without normal systolic blood pressure (SBP), with a decreased cerebral blood flow (CBF)/cerebral blood volume (CBV) ratio (upper), for all strokes in patients with or without SBP within the range of 130 to 149, and for patients without a decreased CBF/CBV ratio (lower).
OEF and an aggressive reduction in BP may cause a high-stroke rate in the nonsurgical group. In our cohort, the BP was mildly controlled depending on the level of BP in each patient. Finally, recurrent thromboembolic stroke may occur more frequently in carotid occlusion patients with a higher BP than in those with a lower BP. Derdeyn et al. reported that most recurrent strokes were thromboembolic in patients with ICA occlusion and an increased OEF ratio. In our cohort, subcortical infarcts were a major type of recurrent ipsilateral strokes, in which the thromboembolic mechanism was less likely.

Both BP studies were post hoc analyses of observational studies based on a small number of events in a small sample. A randomized, controlled trial is needed to determine the level at which the BP should be lowered to achieve maximal benefits in patients with or without hemodynamic compromise. We must establish strategies for selecting treatments based on hemodynamic measurements in atherosclerotic major cerebral artery disease.

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Disclosures
None.

References
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SUPPLEMENTAL MATERIAL

Title:
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Supplemental Methods

Materials and methods

Patients
We analyzed data collected from 130 medically treated patients enrolled in our observational study. We investigated the relationship between hemodynamic compromise and stroke risk in symptomatic patients with atherosclerotic occlusive disease of the major cerebral arteries other than extracranial ICA stenosis. Patients were first referred to the PET unit at Shiga Medical Center from the outpatient clinic or other hospitals in the Shiga Prefecture to undergo hemodynamic parameter evaluation as part of a clinical assessment to determine the need for extracranial-to-intracranial (EC-IC) bypass.

Inclusion criteria for the observational study were as follows: 1) occlusion of the extracranial ICA or occlusion or stenosis (>50% diameter reduction) of the intracranial ICA or MCA as documented by conventional or magnetic resonance angiography; 2) the ability to independently perform daily life activities (modified Rankin scale score <3); and 3) history of transient ischemic attack (TIA) or complete stroke involving the relevant ICA or MCA territory at any time before PET examination. TIA was defined as the development of focal symptoms of presumed ischemic cerebrovascular origin lasting <24 h. The exclusion criteria were as follows: 1) history of vascular reconstruction surgery; or 2) the presence of potential sources of cardiogenic embolism. Overall, 35 of the 165 patients enrolled in the study underwent bypass surgery due to hemodynamic impairment observed on PET and were excluded from the present study.

Hypertension, diabetes mellitus, ischemic heart disease, and hypercholesterolemia were judged as present based on treatment history at the time of PET examination. The ethics committee of our center approved the study protocol, and all patients provided written informed consent prior to participation.

Positron emission tomography measurements
All patients underwent PET scans with a whole-body Advance PET scanner (General Electric Medical System, Wauwatosa, WI, USA), which permits simultaneous acquisition of 35 image slices with inter-slice spacing of 4.25 mm. The intrinsic scanner resolutions were 4.6–5.7 mm and 4.0–5.3 mm in the transaxial and axial directions, respectively. As part of the scanning procedure, but before tracer administration, 68Ge/68Ga transmission scanning was performed for 10 min for attenuation correction. Functional images were reconstructed as 128 × 128 pixels, with each pixel representing an area of 2.0 × 2.0 mm.

A series of 15O-gas studies was also performed. C15O2 and 15O2 were inhaled continuously through a mask. The total scan time was 5 min. Bolus inhalation of C15O with 3-min scanning was used to measure CBV. Arterial samples were manually obtained during the scanning.

The CBF, cerebral metabolic rate of oxygen, and oxygen extraction fraction (OEF) were calculated based on the steady-state method. The ratio of CBF to CBV was calculated pixel-by-pixel as an indicator of the cerebral perfusion pressure.

Data analysis
We analyzed 10 tomographic planes from 46.25–84.5 mm above and parallel to the orbitomeatal line, which corresponded to the levels from the basal ganglia and thalamus to the centrum semiovale. The region of interest (ROI) was placed on the CBF images. Each image was examined by placing 10–12 circular ROIs (16 mm in diameter) compactly over the grey matter of the outer cortex in each hemisphere. According to the atlas, the ROIs in all 10 images covered the distribution of the MCA and the watershed areas. The same ROIs were transferred to the other images. The mean hemispheric
values in each hemisphere were calculated as the average of the values of all circular ROIs. In patients with cerebral cortex infarction, the circular ROIs that overlapped low-intensity areas on T1-weighted magnetic resonance imaging (MRI) scans were excluded from analysis using a simple method of correlating the PET scans with the MRI scans.\textsuperscript{6}

Normal control values of the $^{15}$O-gas PET variables were obtained from seven normal volunteers (4 men, 3 women) aged 47 ± 7 years old (mean ± standard deviation [SD]) who underwent normal routine neurological examinations and MRI scans. The mean OEF value obtained from these 14 control hemispheres was 44.5% ± 3.8%. Hemispheric OEF values defined beyond the upper 95% limit in normal subjects (>52.9%) represented increased OEF. Comparative values for CBF and the CBF/CBV ratio in normal controls were 44.6 ± 4.5 and 11.4 ± 1.8, respectively. Hemispheric CBF and CBF/CBV ratio values <35.0 mL/100 g/min and 7.6/min, respectively, were considered abnormal.

Patients with an increased OEF, decreased CBF, and decreased CBF/CBV ratio in hemispheres with arterial disease were categorized as having MP, while patients with a decreased CBF/CBV ratio were categorized as having decreased cerebral perfusion pressure (i.e., impaired perfusion). Patients were categorized by an investigator who was blinded to their clinical status.

**Follow-up and outcomes**

Attending physicians were informed of the PET findings, but treatment of risk factors and the use of drugs was left to their clinical judgment. All patients were examined at 1- or 2-month intervals after undergoing PET studies in the outpatient clinic of our center or of related hospitals in the Shiga Prefecture. At each visit, an interim history was obtained, BP was measured, and a neurological examination was performed. Patients were followed for 5 years or until stroke recurrence or death. Recurrent ischemic stroke was defined as the acute onset of a new focal neurological deficit of cerebral origin persisting for >24 h without primary intracranial hemorrhage on CT or MRI scan.

**Statistical analysis**

The patients’ clinical backgrounds were compared between the groups using Student’s t tests or chi-squared tests, as appropriate; significance was established at $p < 0.05$. The incidence of recurrent stroke was compared between the groups using Mantel-Cox log-rank statistics and the Kaplan-Meier survival curves. Survival analysis of the subsequent endpoints began on the day of PET examination, which was considered the date of study entry. Multivariate analysis using the Cox proportional hazards model was used to test the effect of multiple variables on stroke recurrence. Covariate selection was performed by including the following covariates in a stepwise model: age, sex, recurrent symptoms (i.e., recurrent episodes of ischemic attack prior to PET scan or after angiographic demonstration of arterial disease), the time between the last symptoms and the PET scan, symptomatic arterial occlusion, extracranial ICA occlusion, complications (e.g., hypertension, diabetes mellitus, prior ischemic heart disease, hypercholesterolemia), smoking habit, BP during follow-up (categorization or normal BP), and misery perfusion or decreased CBF/CBV ratio. A forward stepwise selection was performed, and covariates were included and selected based on a significant relationship ($p < 0.05$) with an outcome event to enter into the model so that $p < 0.05$ remained in the model. The selected covariates were then included in a final model for analysis. The differences in the relationship between the follow-up BP with recurrent strokes in the subgroups were evaluated by adding an interaction term to the model.
References


### Supplemental Tables

#### Supplemental Table I. Characteristics of patients with and without misery perfusion

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Categorizations</th>
<th>Present</th>
<th>Absent</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Misery perfusion</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of patients</td>
<td></td>
<td>16</td>
<td>114</td>
</tr>
<tr>
<td>Age, mean ± SD, y</td>
<td></td>
<td>65 ± 9</td>
<td>64 ± 8</td>
</tr>
<tr>
<td>Sex, male/female, No.</td>
<td></td>
<td>15/1</td>
<td>88/26</td>
</tr>
<tr>
<td>Diagnosis, No.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TIA (amaurosis/hemispheric)</td>
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<td>0 (0/0)</td>
<td>21 (2/19)</td>
</tr>
<tr>
<td>Minor stroke</td>
<td></td>
<td>16</td>
<td>93</td>
</tr>
<tr>
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<td>44</td>
</tr>
<tr>
<td>After demonstration of arterial disease</td>
<td></td>
<td>2</td>
<td>23</td>
</tr>
<tr>
<td>No. of months between the last symptom and PET, mean ± SD</td>
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<td>15 ± 22</td>
<td>8 ± 15</td>
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<tr>
<td>Symptomatic qualifying artery, No</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Occlusion/stenosis</td>
<td></td>
<td>14/2</td>
<td>72/42</td>
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<tr>
<td>Extracranial ICA occlusion</td>
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<td>12</td>
<td>49</td>
</tr>
<tr>
<td>Intracranial ICA (occlusion/stenosis)</td>
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<td>1 (0/1)</td>
<td>13 (1/12)</td>
</tr>
<tr>
<td>MCA (occlusion/stenosis)</td>
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<td>3 (2/1)</td>
<td>52 (22/30)</td>
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<td>Other medical illness, No</td>
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<td></td>
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<tr>
<td>Hypertension</td>
<td></td>
<td>9</td>
<td>69</td>
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<tr>
<td>Diabetes mellitus</td>
<td></td>
<td>7</td>
<td>40</td>
</tr>
<tr>
<td>Ischemic heart disease</td>
<td></td>
<td>6</td>
<td>21</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td></td>
<td>4</td>
<td>36</td>
</tr>
<tr>
<td>Smoking habit (current and former), No</td>
<td></td>
<td>6</td>
<td>40</td>
</tr>
</tbody>
</table>

SD, standard deviation; ICA, internal carotid artery; MCA, middle cerebral artery; PET, positron emission tomography; TIA, transient ischemic attack.
**Supplemental Table II. Univariate analysis of recurrent stroke risk factors**

<table>
<thead>
<tr>
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<th>Arterial territory</th>
<th>Other territory</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>No. of patients</td>
<td>8</td>
<td>122</td>
</tr>
<tr>
<td>Age, mean ± SD, y</td>
<td>67 ± 6</td>
<td>64 ± 8</td>
</tr>
<tr>
<td>Sex, male, No(%)</td>
<td>7(87)</td>
<td>96(78)</td>
</tr>
<tr>
<td>Recurrent symptoms</td>
<td>4(50)</td>
<td>48(39)</td>
</tr>
<tr>
<td>After demonstration of arterial disease</td>
<td>2(25)</td>
<td>23(19)</td>
</tr>
<tr>
<td>No. of months between last symptom and PET, mean ± SD</td>
<td>20 ± 22</td>
<td>8 ± 15</td>
</tr>
<tr>
<td>Recurrent (6 m or less)</td>
<td>4(50)</td>
<td>96(78)</td>
</tr>
<tr>
<td>Arterial occlusion</td>
<td>4(50)</td>
<td>82(67)</td>
</tr>
<tr>
<td>Extracranial ICA occlusion</td>
<td>4(50)</td>
<td>57(46)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>7(87)</td>
<td>71(58)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>4(50)</td>
<td>43(35)</td>
</tr>
<tr>
<td>Ischaemic heart disease</td>
<td>4(50)</td>
<td>23(19)</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>2(25)</td>
<td>38(31)</td>
</tr>
<tr>
<td>Smoking (current and former)</td>
<td>4(50)</td>
<td>42(34)</td>
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<tr>
<td>Decreased CBF/CBV</td>
<td>6(75)</td>
<td>33(27)</td>
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<tr>
<td>Misery perfusion SBP</td>
<td>4(50)</td>
<td>12(10)</td>
</tr>
<tr>
<td>Categorisation</td>
<td>1.3 ± 0.7</td>
<td>2.0 ± 0.8</td>
</tr>
<tr>
<td>Normal BP</td>
<td>6(75)</td>
<td>29(23)</td>
</tr>
</tbody>
</table>

BP = blood pressure; CBF = cerebral blood flow; CBV = cerebral blood volume; ICA = internal carotid artery; PET = positron emission tomography; SBP = systolic blood pressure

Categorisation = 1, <130; 2, 130–149; 3, 150–169; and 4, ≥170 mm Hg;
# Supplemental Table III. Five-year stroke occurrence and SBP

<table>
<thead>
<tr>
<th>Ischemic stroke in the territory</th>
<th>SBP, mmHg</th>
<th>&lt;130</th>
<th>130–149</th>
<th>150–169</th>
<th>&gt;170</th>
</tr>
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<tr>
<td>Total (n = 130)</td>
<td></td>
<td>6/36 (16.6%)</td>
<td>1/60 (1.7%)</td>
<td>1/29 (3.4%)</td>
<td>0/5 (0%)</td>
</tr>
<tr>
<td>With misery perfusion* (n = 16)</td>
<td></td>
<td>3/7 (42.9%)</td>
<td>0/5 (0%)</td>
<td>1/3 (33.3%)</td>
<td>0/1 (0%)</td>
</tr>
<tr>
<td>Decreased CBF/CBV, normal OEF (n = 23)</td>
<td></td>
<td>1/5 (20%)</td>
<td>1/11 (9.0%)</td>
<td>0/7 (0%)</td>
<td>0/0 (0%)</td>
</tr>
<tr>
<td>Normal CBF/CBV, increased OEF (n = 16)</td>
<td></td>
<td>0/4 (0%)</td>
<td>0/11 (0%)</td>
<td>0/1 (0%)</td>
<td>0/0 (0%)</td>
</tr>
<tr>
<td>Normal CBF/CBV, normal OEF (n = 75)</td>
<td></td>
<td>2/20 (10%)</td>
<td>0/33 (0%)</td>
<td>0/18 (0%)</td>
<td>0/4 (0%)</td>
</tr>
<tr>
<td>Any ischemic stroke</td>
<td></td>
<td>7/36 (19.4%)</td>
<td>3/60 (5%)</td>
<td>6/29 (20.6%)</td>
<td>1/5 (20%)</td>
</tr>
<tr>
<td>With misery perfusion* (n = 16)</td>
<td></td>
<td>3/7 (42.9%)</td>
<td>1/5 (20%)</td>
<td>1/3 (33.3%)</td>
<td>0/1 (0%)</td>
</tr>
<tr>
<td>Decreased CBF/CBV, normal OEF (n = 23)</td>
<td></td>
<td>1/5 (20%)</td>
<td>2/11 (19.0%)</td>
<td>0/7 (0%)</td>
<td>0/0 (0%)</td>
</tr>
<tr>
<td>Normal CBF/CBV, increased OEF (n = 16)</td>
<td></td>
<td>0/4 (0%)</td>
<td>0/11 (0%)</td>
<td>0/1 (0%)</td>
<td>0/0 (0%)</td>
</tr>
<tr>
<td>Normal CBF/CBV, normal OEF (n = 75)</td>
<td></td>
<td>3/20 (15%)</td>
<td>0/33 (0%)</td>
<td>5/18 (27%)</td>
<td>1/4 (25%)</td>
</tr>
<tr>
<td>Stroke in other vascular territory</td>
<td></td>
<td>1/36 (2.7%)</td>
<td>3/60 (5.0%)</td>
<td>5/29 (17.2%)</td>
<td>4/5 (80%)</td>
</tr>
<tr>
<td>With misery perfusion* (n = 16)</td>
<td></td>
<td>0/7 (0%)</td>
<td>2/5 (40%)</td>
<td>0/3 (0%)</td>
<td>0/1 (0%)</td>
</tr>
<tr>
<td>Decreased CBF/CBV, normal OEF (n = 23)</td>
<td></td>
<td>0/5 (0%)</td>
<td>1/11 (9.0%)</td>
<td>0/7 (0%)</td>
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</tr>
<tr>
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<td></td>
<td>0/4 (0%)</td>
<td>0/11 (0%)</td>
<td>0/1 (0%)</td>
<td>0/0 (0%)</td>
</tr>
<tr>
<td>Normal CBF/CBV, normal OEF (n = 75)</td>
<td></td>
<td>1/20 (5%)</td>
<td>0/33 (0%)</td>
<td>5/18 (27%)</td>
<td>4/4 (100%)</td>
</tr>
<tr>
<td>All stroke Total (n = 130)</td>
<td></td>
<td>7/36 (19.3%)</td>
<td>4/60 (6.7%)</td>
<td>6/29 (20.6%)</td>
<td>4/5 (80%)</td>
</tr>
<tr>
<td>With misery perfusion* (n = 16)</td>
<td></td>
<td>3/7 (42.9%)</td>
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<td>0/33 (0%)</td>
<td>5/18 (27%)</td>
<td>4/4 (100%)</td>
</tr>
</tbody>
</table>

CBF, cerebral blood flow; CBV, cerebral blood volume; OEF, oxygen extraction fraction; SBP, systolic blood pressure

*Misery perfusion or decreased CBF/CBV in the territory.
증상성 주요 대뇌동맥질환 환자에서의 극단적 관류 저하, 혈압 조절 및 5년 뇌졸중 위험성

Misery Perfusion, Blood Pressure Control, and 5-Year Stroke Risk in Symptomatic Major Cerebral Artery Disease

Hiroshi Yamauchi, MD, PhD; Shinya Kagawa, MS; Yoshihiko Kishibe, RT; Masaaki Takahashi, RT; Tatsuya Higashi, MD, PhD

Abstract 7

배경과 목적
중상성대뇌동맥질환 및 극단적 관류저하(misery perfusion, MP)가 있는 고위험 환자에서, 엄격한 혈압(blood pressure, BP) 조절의 유용성은 아직 논란의 여지가 있다. 연구자들은 (1) MP가 5년 뇌졸중 위험도의 예측 인자인지, (2) 추적 관찰 기간의 BP, MP 및 뇌졸중 위험도 사이의 상호 관계를 분석하고자 하는 목적을 갖고 본 연구를 진행하였다.

방법
중상성 주요 대뇌동맥 질환이 있고 어느 정도 일상 생활이 가능한 130명의 환자를 수집하였다. 초기 혈류학적 측정은 ¹⁸F-가체 양전자발산단층촬영(positron emission tomography)을 이용하여 측정하였으며, 대상 환자들은 의학적 치료를 받으며 5년 간 혹은 뇌졸중 재발 또는 사망이 발생할 시점까지 추적 관찰하였다.

결과
5년의 추적 관찰 기간 동안, 뇌졸중은 MP가 있는 환자 16명 중 6명 그리고 MP가 없는 환자 114명 중 15명에서 발생하였다(로그-순위 검정: P<0.01). MP가 있는 환자에서 4건(25%)의 동측 혈압 저하 뇌졸중이 발생하였고, MP가 없는 환자에서는 4건이 발생하였다 (P<0.001). 동측의 혈압저하증 발생 위험은 2년이 지나면서 급격히 감소하였고, MP가 없는 환자에서는 단 한 건의 동측 혈압저하증만 발생하였다. 관류가 저하된 환자(MP 포함)에서 정상적인 수축기 BP(<130 mmHg)를 유지할 때 동측 혈압저하증의 위험이 증가하였으나, MP가 없는 환자에서 수축기 BP가 130–149 mmHg 범위 밖으로 유지되면 모든 종류의 뇌졸중 위험도가 증가하였다.

결론
MP가 있는 환자는 5년 뇌졸중 재발 위험도가 증가하는데, 그러한 추가 위험의 상당수는 2년이 지나면서 감소한다. MP를 바탕하여 관류가 저하된 환자에서 적극적인 BP 조절은 위험을 없릴 가능성이 있다.
뇌혈종이 발생한 후에 깊은 정맥혈전증 예방을 위한 항응고요법을 하는 것이 혼란의 뇌혈종예방이란 가? 

Is Prophylactic Anticoagulation for Deep Venous Thrombosis Common Practice After Intracerebral Hemorrhage?

Shyam Prabhakaran, MD, MS; Patricia Herbers, MS; Jane Khoury, PhD; Opeolu Adeoye, MD; Pooja Khatri, MD; Simona Ferioli, MD; Dawn O. Kleindorfer, MD

(Stroke. 2015;46:369-375.)

Key Words: anticoagulants ■ pulmonary embolism ■ thromboembolism

배경과 목적
뇌혈종(intracerebral hemorrhage, ICH) 이후 깊은 정맥혈전증 예방을 위해 항응고요법을 하는 것은 안전하다. 현재의 전단지침은 혈종이 가진 것이 명주면 예방적 항응고요법을 할 것을 권고한다. 이 연구는 ICH 발생 이후의 깊은 정맥혈전증 예방에 대한 전국적인 동향을 평가하려고 하였다.

방법
Premier 데이터베이스를 분석하여 2006년부터 2010년 사이에 입원하여 이를 이상 생존한 성인 ICH(국제신경병리학 6판 코드 431)환자를 찾아냈다. 외상이 있거나 개두습, 혈관조영술을 받은 환자는 제외하였다. 연구대상은 지방형 항응고제의 종류와 처방 투여한 날짜를 조사하였다. 단변량 통계와 다변수 로지스틱 회귀분석을 이용하여 ICH 이후 예방적 항응고요법을 하게 되는 것과 관련이 있는 인자를 조사하였다.

결과
32680명(평균 나이, 69.7세; 남자, 50.1%)의 자발성 ICH 환자 중에서, 5395명(16.5%)이 입원 중에 예방적 항응고요법을 받았다. 이 중에서, 2416명(44.8%)은 2일 이내에 예방적 항응고요법을 받았다. 가장 흔히 사용한 약물은 헤파린(71.1%), 에녹사판린(enoxaparin, 27.5%), 달테판린(dalteparin, 1.4%)이었다. 예방적 항응고요법을 받은 환자의 비율은 연구 기간 동안 14.3%에서 18.0%로 약간 증가하였다(P<0.01 for trend). 미국 내에서 지리적인 지역의 차이에 따라 예방적 항응고요법의 사용은 차이가 나서(P<0.001) 북동부(23.2%), 남부(19.0%), 중서부(10.8%), 서부(9.8%)의 순이었다. 다변수 분석에서 지리적인 지역은 예방적 항응고요법의 독립적인 예측 인자였다.

결론
미국의 ICH 환자 중 20%가 안 되는 비율에서 깊은 정맥혈전증 예방을 위한 항응고요법을 받는다. 사용하는 경우 아울러 이내에 시작하는 비용은 절반을 차지할 것이다. 이후의 연구는 전문의 변화에 대해 이해하는데 집중하고 진료지침에 근거한 치료를 강조해야 한다.