Acute Blood Pressure Levels and Neurological Deterioration in Different Subtypes of Ischemic Stroke

Kazunori Toyoda, MD; Shigeru Fujimoto, MD; Masahiro Kamouchi, MD; Mitsuo Iida, MD; Yasushi Okada, MD

Background and Purpose—The purpose of this study was to determine at which time points acute blood pressure (BP) was associated with neurological deterioration at 3 weeks in patients with ischemic stroke as a whole and in patients with different subtypes.

Methods—BP was measured every 6 hours for the first 36 hours of emergent hospitalization in 565 consecutive patients (347 men, 70±11 years in age) presenting within 24 hours of an acute ischemic stroke. Neurological deterioration was defined as a ≥2-point increase in the National Institutes of Health stroke scale (NIHSS) score at 3 weeks compared to the admission score.

Results—At 3 weeks, 64 patients (11.3%) had deteriorated neurologically. For the group as a whole, high systolic BP (SBP) values measured at 12, 18, 24, and 36 hours postadmission were independently related to neurological deterioration after adjustment for age, sex, and known predictors, including admission NIHSS score, admission blood glucose level, and large infarct size. At 24 hours, the odds of neurological deterioration increased by 20% per 10-mm Hg increase in SBP. For cardioembolic stroke patients, high SBP values measured at 12 through 36 hours were independently related to neurological deterioration after multivariate adjustment. For patients having stroke other than cardioembolism, no SBP values at any time point were related to neurological deterioration.

Conclusions—Acute SBP values between 12 and 36 hours postadmission, but not those on admission or at 6 hours, were predictive of neurological deterioration within the initial 3 weeks of ischemic stroke, particularly for cardioembolic stroke patients. (Stroke. 2009;40:2585-2588.)

Key Words: cerebral infarction ■ blood pressure ■ hypertension ■ stroke outcome ■ stroke scale ■ cardioembolism

High blood pressure (BP) is common during acute ischemic stroke and is associated with subsequent death, dependency, or clinical deterioration.1 The BP value is generally highest on hospital admission, and then falls over the initial hours and days.1–3 Of 32 studies included in a systematic review on acute BP and stroke outcomes, 18 assessed the usefulness of admission BP as an indicator.1 More recent studies also used admission BP to determine the relationship between acute BP and stroke outcomes.3,4 However, admission BP may not appropriately reflect stroke patients’ acute condition, because it is often affected by the mental stress of hospital admission, a full bladder, nausea, and pain, which can resolve within hours.

The goal of this study was to determine at which time points during the initial 36 hours after admission acute BP values could be used to predict the neurological deterioration of stroke patients within the initial 3 weeks.
studied. Of them, hypertension was defined as systolic BP (SBP) ≥140 or diastolic BP (DBP) ≥90 mm Hg before stroke or history of antihypertensive medication.

BP was measured on admission and every 6 hours during the initial 36 hours, with 1 hour error in the daytime and 2 hours error in the nighttime. BP was measured by trained nurses using a mercury sphygmomanometer after the patients had rested in the supine position; the average of 2 consecutive measurements was used for analysis. Antihypertensive agents were given intravenously for patients with an extremely high BP according to the guidelines; nicardipine, diltiazem, or nitroglycerine were primarily used. Labetalol is not commercially used in Japan.

Blood tests on admission

<table>
<thead>
<tr>
<th>Test</th>
<th>Total (n=565)</th>
<th>Deteriorated (n=64)</th>
<th>Nondeteriorated (n=501)</th>
<th>Odds Ratio for Deterioration</th>
<th>95% CI</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood glucose, mmol/L</td>
<td>7.2±2.9</td>
<td>8.3±3.9</td>
<td>7.0±2.8</td>
<td>1.09†</td>
<td>1.00–1.19</td>
<td>0.048</td>
</tr>
<tr>
<td>LDLoxid cholesterol, mmol/L</td>
<td>3.00±0.94</td>
<td>2.73±0.87</td>
<td>3.04±0.94</td>
<td>0.79†</td>
<td>0.56–1.12</td>
<td>0.193</td>
</tr>
<tr>
<td>HDL cholesterol, mmol/L</td>
<td>1.27±0.41</td>
<td>1.22±0.49</td>
<td>1.27±0.39</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Triglyceride, mmol/L</td>
<td>1.32±0.78</td>
<td>1.12±0.72</td>
<td>1.34±0.78</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urea nitrogen, mmol/L</td>
<td>5.71±2.99</td>
<td>6.49±3.62</td>
<td>5.61±2.91</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Creatinin, mmol/L</td>
<td>82.3±92.7</td>
<td>91.2±106.7</td>
<td>81.1±90.9</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hematocrit, g/dL</td>
<td>39.6±5.8</td>
<td>38.2±6.3</td>
<td>39.8±5.7</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Platelet, ×10^12/μL</td>
<td>217±74</td>
<td>219±83</td>
<td>217±73</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White blood cell, ×10^3/μL</td>
<td>7.8±4.6</td>
<td>9.3±6.0</td>
<td>7.6±4.4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>hs-CRP, mg/dL*</td>
<td>1.16±3.15</td>
<td>3.28±6.84</td>
<td>0.84±2.13</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Stroke features

<table>
<thead>
<tr>
<th>Type</th>
<th>Total (n=565)</th>
<th>Deteriorated (n=64)</th>
<th>Nondeteriorated (n=501)</th>
<th>Odds Ratio for Deterioration</th>
<th>95% CI</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardioembolism</td>
<td>183 (32.4)</td>
<td>31 (48.4)</td>
<td>152 (30.3)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Large artery atherosclerosis</td>
<td>106 (18.8)</td>
<td>10 (15.6)</td>
<td>96 (19.2)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Small artery disease</td>
<td>174 (30.8)</td>
<td>10 (15.6)</td>
<td>164 (32.7)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other etiology</td>
<td>102 (18.1)</td>
<td>13 (20.3)</td>
<td>89 (17.8)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vertebralbasilar territory infarct</td>
<td>151 (26.7)</td>
<td>11 (17.2)</td>
<td>140 (27.9)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diameter &gt;15 mm</td>
<td>281 (49.7)</td>
<td>50 (78.1)</td>
<td>231 (46.1)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Admission NIHSS score, median (IQR)</td>
<td>4 (2–8)</td>
<td>10.5 (4–20)</td>
<td>4 (2–7)</td>
<td>2.24†</td>
<td>1.50–3.39</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Values are median and interquartile range (IQR) for NIHSS score and No. (percentage) or mean±SD for other items.

*Highly sensitive C-reactive protein (hs-CRP) was measured for only 338 patients who were admitted to our center after November 2002.

Statistics

All analyses were performed using JMP 7 statistical software (SAS Institute Inc). Multiple logistic regression analysis was performed to identify predictors of neurological deterioration. For the analysis, variables listed on the Table were automatically selected in a stepwise selection method. To determine the association of the BP values with neurological deterioration, the identified predictors, as well as sex and age, were used to adjust the BP effect estimates at each time point. Two-way repeated-measures analysis of variance was performed to compare the 36-hour BP time course between patients with and without neurological deterioration. A probability value <0.05 was considered statistically significant.
Blood Pressure and Neurological Deterioration in Different Stroke Subtypes

Of 183 patients having cardioembolic stroke, 31 (16.9%) showed neurological deterioration, including 14 deaths. After multivariate adjustment, high SBP values at all time points between 12 and 36 hours were significantly related to neurological deterioration (Figure 2, right top). From 12 through 36 hours, odds of progression increased by \( \approx 30\% \) per 10-mm Hg increase in SBP. In addition, high DBP values between 18 and 36 hours were significantly related to deterioration (figure not shown). Of the remaining 382 patients, 33 (8.6%) showed neurological deterioration, including: 10 of 174 lacunar patients (5.8%), 10 of 106 patients with large-artery atherosclerosis (9.4%), and 13 of 102 patients having stroke of other determined or undetermined etiology (12.8%). After multivariate adjustment, none of the SBP or DBP values within the initial 36 hours were related to neurological deterioration for the noncardioembolic patients as a whole or for patients with each subtype (Figure 2, right bottom).

Discussion

The major finding of this study was that high SBP values measured at 12 through 36 hours postadmission, but not on admission or at 6 hours, were independently related to neurological deterioration within 3 weeks poststroke. Because several factors, including mental stress, which do not necessarily correlate with stroke severity or arteriosclerotic conditions, affect cardiovascular modulation during the initial several hours, BP values at this time point do not seem to be appropriate for predicting stroke outcomes. The GAIN International Trial\(^7\) also failed to find an association between baseline BP and stroke outcome, and stressed the relationship between the BP course over the initial 2.5 days and the neurological deterioration.

After adjustment for sex, age, blood glucose, infarct \( >15 \) mm, and admission NIHSSS, high SBP values at 12, 18, 24, and 36 hours were significantly related to neurological deterioration (Figure 2, left). At 24 hours, the odds of progression increased by 20% per 10 mm Hg increase in SBP. In contrast, any DBP values were not related to deterioration.

Blood Pressure and Neurological Deterioration in Different Stroke Subtypes

Of 183 patients having cardioembolic stroke, 31 (16.9%) showed neurological deterioration, including 14 deaths. After multivariate adjustment, high SBP values at all time points between 12 and 36 hours were significantly related to neurological deterioration (Figure 2, right top). From 12 through 36 hours, odds of progression increased by \( \approx 30\% \) per 10-mm Hg increase in SBP. In addition, high DBP values between 18 and 36 hours were significantly related to deterioration (figure not shown). Of the remaining 382 patients, 33 (8.6%) showed neurological deterioration, including: 10 of 174 lacunar patients (5.8%), 10 of 106 patients with large-artery atherosclerosis (9.4%), and 13 of 102 patients having stroke of other determined or undetermined etiology (12.8%). After multivariate adjustment, none of the SBP or DBP values within the initial 36 hours were related to neurological deterioration for the noncardioembolic patients as a whole or for patients with each subtype (Figure 2, right bottom).

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outcome. Another study reported the significance of the initial 24-hour SBP as a predictor for long-term mortality. Elevated baseline or acute BP values have been reported to be associated with subsequent development of brain edema and hemorrhagic transformation. Massive edema and hemorrhagic transformation are characteristic findings of cardioembolic stroke, and they were reported to have a relationship with higher 24-hour BP in cardioembolic stroke. These findings may explain the relationship between high SBP values measured at 12 through 36 hours and poor outcome in the present cardioembolic patients. In contrast, because atherothrombotic stroke patients often have a hemodynamic crisis, and maintenance of collateral blood flow to the ischemic penumbra is necessary during acute days, elevated BP may be protective against ischemic lesions. Because lacunar stroke is often nonprogressive, and because stroke of other etiology is heterogeneous, the relationship between BP and outcome may not be clear.

The limitations of the present study include the fact that NIHSSS at 36 hours was not assessed for all the patients. Thus, it is difficult to discuss whether BP courses during the initial 36 hours were associated with neurological deterioration during the same period or they influence neurological deterioration during the later period. The second limitation was that NIHSS subscore was not assessed. Thus, it is difficult to discuss whether neurological deterioration resulted from the additional damage of the initial infarction or from recurrent stroke in a new territory. Third, definition of neurological deterioration as a ≥2-point NIHSSS increase may inappropriately label some patients as having deteriorated because of the intraindividual variability in the NIHSS, and ≥4-point increase may be more usual and appropriate definition. Fourth, hs-CRP was not measured for all patients and was not used in the multivariate analysis. Fifth, other than age, admission NIHSS score, admission blood glucose level, and large infarct size, there seems to be some more established predictors for neurological deterioration, and our selection of the above variables using a stepwise selection method may not be perfect. However, even if the other characteristics were selected as variables, the present results were almost identical.

In conclusion, acute SBP values at 12 through 36 hours, but not those on admission or at 6 hours, were predictive of neurological deterioration within the initial 3 weeks of ischemic stroke, particularly in cardioembolic patients. There is insufficient evidence to evaluate the effect of altering BP on outcome during acute stroke. Encouraged by the success of the ACCESS study, several studies dealing with antihypertensive therapy for acute ischemic stroke are ongoing. To choose patients eligible for antihypertensive therapy, acute BP levels other than those measured immediately after admission may be appropriate. Hyperacute BP lowering therapy solely based on the admission BP value may not be appropriate.

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**Disclosures**

None.

**References**

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