Effects of 24-Hour Blood Pressure and Heart Rate Recorded With Ambulatory Blood Pressure Monitoring on Recovery From Acute Ischemic Stroke

Yasuhiro Tomii, MD; Kazunori Toyoda, MD; Rieko Suzuki, MD; Masaki Naganuma, MD; Jun Fujinami, MD; Chiaki Yokota, MD; Kazuo Minematsu, MD

Background and Purpose—This study used ambulatory blood pressure (BP) monitoring to generate BP and heart rate (HR) profiles soon after stroke onset and evaluated the association between determined values and 3-month stroke outcomes.

Methods—We analyzed 24-hour ambulatory BP monitoring records from 104 patients with acute ischemic stroke. Ambulatory BP monitoring was attached at the second and eighth hospitalization days (Days 1 and 7). Both BP and HR were characterized using baseline, mean, maximum, and minimum values and coefficient of variation during 24-hour recording periods. Outcomes at 3 months were assessed as independence according to a modified Rankin Scale score of ≤2 and poor according to the score of ≥5.

Results—Sixty-six (63%) patients achieved independence and 12 (11%) had poor outcomes. Mean ambulatory BP monitoring values changed from 150.5/19.5/85.7/11.3 mm Hg on Day 1 to 139.6/19.3/80.0/11.7 mm Hg on Day 7. After multivariate adjustment, mean values of systolic BP (OR, 0.63; 95% CI, 0.45–0.85), diastolic BP (0.61; 0.37–0.98), pulse pressure (0.55; 0.33–0.85), and HR (0.61; 0.37–0.98) recorded on Day 1 as well as mean HR on Day 7 (0.47; 0.23–0.87) were inversely associated with independence and mean values of systolic BP (1.92; 1.15–3.68), diastolic BP (5.28; 1.92–22.85), and HR (4.07; 1.83–11.88) on Day 1 as well as mean HR on Day 7 (4.92; 1.36–36.99) were positively associated with a poor outcome.

Conclusions—All of systolic BP, diastolic BP, pulse pressure, and HR on Day 1 and HR on Day 7 assessed using ambulatory BP monitoring were associated with outcomes of patients with stroke at 3 months. (Stroke. 2011;42:3511-3517.)

Key Words: ambulatory blood pressure monitoring ■ cerebral infarction ■ hypertension ■ outcome
Table 1. Baseline Characteristics

<table>
<thead>
<tr>
<th></th>
<th>All Patients (n=104)</th>
<th>Independence (n=66)</th>
<th>Poor Outcome (n=92)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Baseline characteristics</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Woman</td>
<td>40 (38%)</td>
<td>22 (33%)</td>
<td>18 (47%)</td>
<td>0.157</td>
</tr>
<tr>
<td>Age, y</td>
<td>71.7±12.5</td>
<td>67.9±12.6</td>
<td>78.1±9.5</td>
<td>&lt;0.001</td>
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<tr>
<td>Hypertension</td>
<td>82 (79%)</td>
<td>52 (79%)</td>
<td>30 (79%)</td>
<td>0.985</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>33 (32%)</td>
<td>22 (33%)</td>
<td>11 (29%)</td>
<td>0.644</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>46 (44%)</td>
<td>31 (47%)</td>
<td>15 (39%)</td>
<td>0.459</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>35 (34%)</td>
<td>18 (27%)</td>
<td>17 (45%)</td>
<td>0.070</td>
</tr>
<tr>
<td>Previous ischemic stroke</td>
<td>29 (28%)</td>
<td>14 (21%)</td>
<td>15 (39%)</td>
<td>0.046</td>
</tr>
<tr>
<td>Current smoking habits</td>
<td>22 (21%)</td>
<td>16 (24%)</td>
<td>6 (16%)</td>
<td>0.340</td>
</tr>
<tr>
<td>Antihypertensive use before onset</td>
<td>53 (51%)</td>
<td>33 (50%)</td>
<td>20 (53%)</td>
<td>0.796</td>
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</table>

**Stroke features and clinical status**

**Subtypes**

<table>
<thead>
<tr>
<th>Subtype</th>
<th>All Patients (n=104)</th>
<th>Independence (n=66)</th>
<th>Poor Outcome (n=92)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardioembolic</td>
<td>37 (36%)</td>
<td>19 (29%)</td>
<td>18 (47%)</td>
<td>0.209</td>
</tr>
<tr>
<td>Atherothrombotic</td>
<td>21 (20%)</td>
<td>15 (23%)</td>
<td>6 (16%)</td>
<td>2.0 (17%)</td>
</tr>
<tr>
<td>Lacunar</td>
<td>15 (14%)</td>
<td>9 (13%)</td>
<td>6 (16%)</td>
<td>1 (8%)</td>
</tr>
<tr>
<td>Other</td>
<td>31 (30%)</td>
<td>23 (35%)</td>
<td>8 (21%)</td>
<td>2 (17%)</td>
</tr>
<tr>
<td>Baseline NIHSS score</td>
<td>4 [1–8]</td>
<td>2 [1–5]</td>
<td>7 [4–18]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Receiving IV rtPA</td>
<td>16 (15%)</td>
<td>4 (6%)</td>
<td>12 (32%)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

**Initiation of antihypertensive therapy**

| By Day 1 ABPM            | 13 (13%)             | 11 (18%)            | 2 (6%)              | 0.086 |
| By Day 7 ABPM            | 34 (33%)             | 23 (37%)            | 11 (31%)            | 0.512 |

Data are expressed as mean±SD, median [interquartile range], or no. (%) as appropriate. Comparisons among groups were performed using χ² test, Student t test, or Mann-Whitney U test as appropriate.

NIHSS indicates National Institutes of Health Stroke Scale; IV rtPA, intravenous recombinant tissue plasminogen activator; ABPM, ambulatory blood pressure monitoring.

*P<0.05 between patients with and without independence; age (67.9±12.6 y versus 78.1±9.5 y, P<0.001), previous ischemic stroke (21% versus 39%, P=0.046), and baseline NIHSS score (2 [1–5] versus 7 [4–18], P<0.001).

†P<0.05 between patients with and without poor outcomes; age (81.8±8.7 y versus 70.3±12.3 y, P<0.001) and baseline NIHSS score (16 [5–24] versus 3 [1–5], P<0.001).

Assessments of BP and HR

Baseline BP and HR values were recorded immediately after arrival at the emergency department (Day 0). Twenty-four-hour ABPM (TM-2431; A&D Company, Ltd) was started at 10 AM of the second and eighth hospitalization days (Days 1 and 7) on the left arm after a relevant difference between the 2 limbs was ruled out by conventional BP checks. Systolic/diastolic BP (SBP/DBP), pulse pressure (PP), and HR were automatically measured every 30 minutes for 24 hours.

We characterized BP and HR profiles by calculating the following values: mean, maximum, minimum, and coefficient of variation (100×SD/mean value) during 24 hours as well as mean values during 16 hours of the day (6 AM to 10 PM) and 8 hours of the night (10 PM to 6 AM). Patients were classified according to a fall (%) in mean SBP during the nighttime compared with the daytime as: dipper (fall ≥10%), nondipper (0%–10%), and riser (nocturnal SBP increased compared with daytime SBP).

Baseline Characteristics

The following baseline characteristics were investigated using the prospective database: sex, age, hypertension (BP ≥140/90 mm Hg before stroke onset or taking antihypertensive agents), diabetes mellitus (fasting blood glucose ≥7.0 mmol/L, hemoglobin A1c ≥6.5%, or taking antidiabetic agents), hyperlipidemia (total cholesterol ≥5.7 mmol/L, triglyceride ≥1.7 mmol/L, or taking antihyperlipidemic agents), atrial fibrillation (documented during hospitalization or history of atrial fibrillation), history of symptomatic ischemic stroke, and current smoking habit. Stroke subtypes were determined according to the Trial of ORG 10172 in Acute Stroke Treatment subtype classification system.10

Outcome

The outcome measurements comprised achieving independent ADL or a poor outcome at 3 months corresponding to modified Rankin Scale scores of ≤2 or ≥5, respectively.

Statistical Analysis

Data were statistically analyzed using JMP 7.0 software (SAS Institute Inc, Cary, NC). Statistical significance for the 2 groups was assessed using Student t test or Mann-Whitney U tests for continuous variables as appropriate and Pearson χ² tests for categorical variables. The 24-hour BP or HR time course between patients with and without each outcome was compared using the 2-way repeated-measures analysis of variance. Predictors for each outcome were determined by multivariate analyses based on the baseline characteristics and the 24-hour BP and HR profiles of the patients. A backward selection procedure was performed for each outcome using P>0.10 of the likelihood ratio test for exclusion. In addition, each
Outcome among quintile groups for mean 24-hour SBP on Day 1 was compared using multivariate analyses to search for the U- or J-shaped phenomenon. A level of $P<0.05$ was considered statistically significant.

**Results**

**Outcomes and Related Factors**

Of a total of 104 eligible patients, 82 (79%) had hypertension and 53 (51%) were treated with antihypertensive agents before stroke onset. Sixty-six (63%) patients reached independent ADL and 12 (11%) had a poor outcome (including death in 1 patient) at 3 months. Table 1 summarizes the baseline characteristics, stroke features, and clinical status. Thirteen and 34 patients were started on antihypertensive therapy on Days 1 and 7, respectively. Thirteen and 34 patients were started on antihypertensive agents before stroke onset. Sixty-six (63%) patients reached independent ADL and 12 (11%) had a poor outcome (including death in 1 patient) at 3 months. Table 1 summarizes the baseline characteristics, stroke features, and clinical status. Thirteen and 34 patients were started on antihypertensive therapy on Days 1 and 7, respectively.

**Whole Day BP/HR Measurements**

At the emergency department on Day 0, SBP/DBP and HR values were $161.3\pm27.3/89.9\pm16.3$ mm Hg and $74.8\pm15.0$ beats/min, respectively. The baseline values of SBP, DBP, PP, or HR were not associated with independent ADL ($P=0.495$, $0.093$, $0.706$, and $0.240$, respectively) or poor outcome ($P=0.770$, $0.710$, $0.513$, and $0.919$, respectively) at 3 months.

Figure 1 shows the 24-hour SBP, DBP, and HR courses on Days 1 and 7 for all of the patients. Mean SBP/DBP and HR on Day 1 were $150.5\pm19.5/85.7\pm11.3$ mm Hg and $68.7\pm11.4$ beats/min, respectively, and $139.6\pm19.3/80.0\pm11.7$ mm Hg and $66.6\pm11.6$ beats/min, respectively, on Day 7. Over the initial week, mean SBP/DBP declined by $10.3\pm16.2/4.8\pm7.8$ mm Hg, but HR did not significantly change. Two-way repeated-measures analysis of variance revealed significant differences in the 24-hour time courses of SBP and DBP between Days 1 and 7 ($P<0.001$ and $P=0.001$, respectively). Thirty patients were excluded from analysis on Day 7; 9 patients left the hospital, 10 refused to undergo further examination, 1 was not examined due to infection with methicillin-resistant *Staphylococcus aureus*, and recordings from 10 others were incomplete.

Figure 2 shows the 24-hour time course of SBP and HR on Days 1 and 7 in patients with independent ADL (black lines). Between patients with and without independent ADL at 3 months, 2-way repeated measures analysis of variance showed significant differences in the 24-hour time course of SBP, PP, and HR on Day 1 ($P<0.001$, $<0.001$, and $0.003$, respectively) and HR on Day 7 ($P<0.001$). After multivariate adjustment, the mean and minimum SBP ($P=0.004$ and $0.035$, respectively), mean DBP ($P=0.044$), mean, minimum, and coefficient of variation of PP ($P=0.010$, $0.010$, and $0.031$, respectively), and mean and maximum HR on Day 1 ($P=0.045$ and $0.045$, respectively) as well as mean HR on Day 7 ($P=0.022$) were inversely associated with independent ADL (Table 2).

Figure 2 also shows the 24-hour time course of SBP and HR on Days 1 and 7 in patients with poor outcomes (gray lines). Two-way repeated-measures analysis of variance revealed significant differences in the 24-hour time course of SBP, DBP, and HR on Day 1 ($P=0.022$, $0.007$, and $<0.001$, respectively) and HR on Day 7 ($P<0.001$) between patients with and without poor outcomes at 3 months. After multivariate adjustment, the mean, maximum, and minimum SBP ($P=0.011$, $0.010$, and $0.012$, respectively), mean and maximum DBP ($P=0.001$ and $0.046$, respectively), and mean, maximum, and minimum HR on Day 1 ($P<0.001$, $0.006$, and $0.007$, respectively) as well as mean HR on Day 7 ($P=0.012$) were positively associated with a poor outcome (Table 2).

Figure 3 shows a comparison of each outcome among quintile groups for mean 24-hour SBP on Day 1. The frequency of patients who achieved independent ADL gradually decreased and that of patients with a poor outcome gradually increased with increasing SBP. Patients who achieved independent ADL were more common in the bottom (SBP $\leq 135$ mm Hg) as compared with the third quintile group (SBP of $145–153$ mm Hg; OR, 9.72; 95% CI, 1.06–191.22; $P=0.044$). Patients with poor outcome were more common in the top (SBP $\geq 169$ mm Hg) as compared with the third quintile group (OR, 17.85; 95% CI, 1.29–649.08; $P=0.030$).

Among the 104 patients, 16 (15%) received intravenous recombinant tissue-type plasminogen activator. Among these, 4 reached independent ADL and 3 had poor outcomes at 3
months. The results were generally similar after excluding these patients; mean SBP on Day 1 was inversely associated with independent ADL (OR, 0.61; 95% CI, 0.42–0.86 per 10-mm Hg increase; \( P < 0.004 \)) and positively associated with a poor outcome (1.97; 1.06–4.79; \( P = 0.031 \)).

**Day and Night BP/HR Measurements**

On Day 1, mean daytime SBP/DBP and HR values were 152.8±19.1/87.0±11.2 mm Hg and 69.8±11.4 beats/min, respectively, and nighttime values were 146.1±22.0/83.4±12.9 mm Hg and 66.6±12.1 beats/min, respectively. After multivariate adjustment, mean levels of daytime SBP, DBP, PP, and HR (\( P = 0.007, 0.047, 0.026, \) and 0.039, respectively) and nighttime SBP, PP, and HR (\( P = 0.025, 0.018, \) and 0.039, respectively) were inversely associated with independent ADL (Table 2). The mean levels of SBP, DBP, and HR both during the daytime (\( P = 0.007, <0.001, \) and 0.001, respectively) and nighttime (\( P = 0.022, 0.004, \) and \( <0.001, \) respectively) were positively associated with a poor outcome. Among the overall patients, 23 (22%) were dippers, 51 (49%) were nondippers, and 30 (29%) were risers (Table 3). Dipper pattern was not associated with either independent ADL or a poor outcome.

Mean daytime SBP/DBP and HR on Day 7 were 142.0±19.8/81.3±11.5 mm Hg and 68.4±11.3 beats/min, respectively, and these nighttime values were 135.5±20.6/76.9±13.1 mm Hg and 63.2±12.9 beats/min, respectively. After multivariate adjustment, the mean levels of both daytime and nighttime HR (\( P = 0.043 \) and 0.033, respectively) were inversely associated with independent ADL (\( P = 0.042 \)) and positively associated with a poor outcome (\( P = 0.002 \)), whereas mean BP profiles were not (Table 2). Among all of the patients, 18 (24%) were dippers, 36 (49%) were nondippers, and 20 (27%) were risers (Table 3). Dipper pattern was not associated once again with either independent ADL or a poor outcome.

**Discussion**

In the present study, we measured BP and HR values during acute stroke using ABPM and determined their association with outcomes at 3 months. The first major finding was that lower BP profiles on Day 1 were independently associated
with better clinical outcomes, whereas those on Day 7 were not. The second major finding was that lower HR profiles on Days 1 and 7 were also independently associated with better outcomes. In addition, we clarified SBP patterns during acute stroke as dipper, nondipper, or riser SBP, although they were not associated with outcomes.

Brain edema, hemorrhagic transformation, recanalization of occluded cerebral arteries, mental stress, and antihypertensive therapy are potential factors that could affect acute-phase BP levels. Of these, mass effect due to brain edema and hemorrhagic transformation causes elevated BP and vice versa. Brain edema and hemorrhagic transformation are key factors to link acute high BP and poor outcomes.4,17–19 The spontaneous decline in BP during the initial hours sometimes reflects the recanalization of occluded cerebral arteries, which often results in favorable outcomes.20,21 Mental stress of hospital admission contributes to elevated BP11; release from the stress can lower BP and possibly improve clinical conditions. Some patients received antihypertensive therapy on the initial day or during the first week, mainly due to having extremely high BP levels or underlying cardiovascular diseases. Such therapy would affect BP and HR levels, although influence of acute BP-lowering on stroke outcomes has not been clarified.22

The present results showed a highly significant association between 3-month outcomes and lower SBP and DBP on Day 1 on any whole day, daytime, or nighttime recording. Figure 3 shows a monotonous linear association between SBP levels with better clinical outcomes, whereas those on Day 7 were not. The second major finding was that lower HR profiles on Days 1 and 7 were also independently associated with better outcomes. In addition, we clarified SBP patterns during acute stroke as dipper, nondipper, or riser SBP, although they were not associated with outcomes.

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The present results showed a highly significant association between 3-month outcomes and lower SBP and DBP on Day 1 on any whole day, daytime, or nighttime recording. Figure 3 shows a monotonous linear association between SBP levels
Table 3. Association Between Fall in BP Between Day and Night and 3-Mo Outcomes

<table>
<thead>
<tr>
<th></th>
<th>Dipper</th>
<th>Nondipper</th>
<th>Riser</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Overall patients</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Day 1</td>
<td>23 (22%)</td>
<td>51 (49%)</td>
<td>30 (29%)</td>
</tr>
<tr>
<td>Patients with independent ADL</td>
<td>14 (21%)</td>
<td>33 (50%)</td>
<td>19 (29%)</td>
</tr>
<tr>
<td>Patients with poor outcome</td>
<td>2 (17%)</td>
<td>6 (50%)</td>
<td>4 (33%)</td>
</tr>
<tr>
<td>Day 7</td>
<td>18 (24%)</td>
<td>36 (49%)</td>
<td>20 (27%)</td>
</tr>
<tr>
<td>Patients with independent ADL</td>
<td>12 (26%)</td>
<td>23 (50%)</td>
<td>11 (24%)</td>
</tr>
<tr>
<td>Patients with poor outcome</td>
<td>0 (0%)</td>
<td>4 (44%)</td>
<td>5 (56%)</td>
</tr>
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</table>

No significantly difference in pattern distribution between patients with or without independent ADL or between those with or without poor outcomes. BP indicates blood pressure; ADL, activities of daily living.
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References
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