The effects of 24-hour blood pressure and heart rate recorded with ambulatory blood pressure monitoring on recovery from acute ischemic stroke

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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 mm Hg on Day 1 to 139.6/19.3/80.0 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

An acute hypertensive response occurs in up to 80% of all patients with acute stroke, but management of hypertension remains controversial because of the paucity of reliable evidence from randomized clinical trials. Data from observational studies have suggested that high blood pressure (BP) is related to a poor outcome, whereas BP elevation during the acute phase might help to maintain cerebral perfusion pressure. Elevated BP generally falls and returns to prestroke levels during the initial days without therapeutic intervention. One systematic review found that the admission BP value was a useful indicator of stroke outcomes. On the other hand, admission BP might be unreliable or misleading, because BP can transiently elevate or decline within several hours after stroke onset depending on the level of consciousness, physical activity, and mental stress of hospital admission. Thus, consecutive BP monitoring during the initial hours or days might be a better prognostic predictor than admission BP values alone.

Compared with casually recorded BP, ambulatory BP monitoring (ABPM) has been proposed as a way to accurately evaluate clinical status, because a large number of records can be generated. However, whether BP profiles using ABPM during the acute phase are associated with stroke outcomes remains unclear.

The aim of this study was to evaluate the association of BP and heart rate (HR) profiles using ABPM devices early after stroke onset with 3-month outcomes.

Patients and Methods

Patient Population

We registered 136 consecutive Japanese patients with ischemic stroke who were admitted to our stroke care unit within 24 hours of symptom onset between January and December 2008. Of these, we excluded 6 patients who were dependent on activities of daily living (ADL) corresponding to a modified Rankin Scale ≥3 before stroke onset, 2 with severe subcutaneous hemorrhage in the arm, 3 infected with neurovirus, 7 who did not provide informed consent (principally...
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.16

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 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 variable was included in each model to determine its individual influence on the outcome.
At the emergency department on Day 0, SBP/DBP and HR values were 161.3 ± 16.3 mm Hg and 74.8 ± 15.0 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 ± 19.5/85.7 ± 11.3 mm Hg and 68.7 ± 11.4 beats/min, respectively, and 139.6 ± 19.3/80.0 ± 11.7 mm Hg and 66.6 ± 11.6 beats/min, respectively, on Day 7. Over the initial week, mean SBP/DBP declined by 10.3 ± 16.2/4.8 ± 7.8 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, and 1 was not examined due to infection with methicillin-resistant Staphylococcus aureus, and recordings from 10 others were incomplete.

Figure 2 also 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 3 shows a comparison of 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.

#### Whole Day BP/HR Measurements

At the emergency department on Day 0, SBP/DBP and HR values were 161.3 ± 27.3/89.9 ± 16.3 mm Hg and 74.8 ± 15.0 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 ± 19.5/85.7 ± 11.3 mm Hg and 68.7 ± 11.4 beats/min, respectively, and 139.6 ± 19.3/80.0 ± 11.7 mm Hg and 66.6 ± 11.6 beats/min, respectively, on Day 7. Over the initial week, mean SBP/DBP declined by 10.3 ± 16.2/4.8 ± 7.8 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, and 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-meiasures 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 ≤ 135 mm Hg) as compared with the third quintile group (SBP of 145–153 mm Hg; OR, 9.72; 95% CI, 1.06–169 mm Hg; OR, 9.72; 95% CI, 1.06–169 mm Hg; OR, 9.72; 95% CI, 1.06–169 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 ≥ 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 ± 19.8/87.0 ± 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.\(^4\),\(^7\)–\(^9\) 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 BP\(^11\); 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

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<th>Table 2. Association of BP and HR With 3-Mo Outcomes</th>
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<td>SBP Mean 24-h SBP</td>
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<td>Mean daytime SBP</td>
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<td>Mean nighttime SBP</td>
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<tr>
<td>Maximum 24-h SBP</td>
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<tr>
<td>Minimum 24-h SBP</td>
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<tr>
<td>CV of 24-h SBP</td>
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<tr>
<td>DBP Mean 24-h DBP</td>
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<td>Mean daytime DBP</td>
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<td>Maximum 24-h DBP</td>
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<td>CV of 24-h PP</td>
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<td>HR Mean 24-h HR</td>
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<tr>
<td>CV of 24-h HR</td>
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<td>Dipper pattern</td>
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OR and 95% CI for increase of 10 mm Hg or 10 beats/min as appropriate based on variables appearing in backward selection model. BP indicates blood pressure; HR, heart rate; SBP, systolic blood pressure; CV, coefficient of variation; DBP, diastolic blood pressure; PP, pulse pressure; NIHSS, National Institutes of Health Stroke Scale; OR, odds ratio; CI, confidence interval.

*Statistically significant difference (P<0.05).
†Independence analysis, adjusted for age, previous ischemic stroke, and baseline NIHSS score.
‡Poor outcome analysis, adjusted for age, previous ischemic stroke, current smoking habits, and baseline NIHSS score.
Night and 3-Mo Outcomes

Table 3. Association Between Fall in BP Between Day and Night and 3-Mo Outcomes

<table>
<thead>
<tr>
<th>Day 1</th>
<th>Dipper</th>
<th>Nondipper</th>
<th>Riser</th>
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<tbody>
<tr>
<td>Overall patients</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>
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<table>
<thead>
<tr>
<th>Day 7</th>
<th>Dipper</th>
<th>Nondipper</th>
<th>Riser</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall patients</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>
</tbody>
</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.

Figure 3. Multivariate-adjusted ORs and 95% CIs for 3-month outcomes among quintiles for mean 24-hour SBP levels on Day 1. Adjusted for age, previous ischemic stroke, and baseline NIHSS score. SBP indicates systolic blood pressure; NIHSS, National Institutes of Health Stroke Scale; mRS, modified Rankin Scale.

Several factors can cause hypertensive response during acute stroke, including inadequately treated or undetected chronic hypertension before stroke onset, increased sympathoadrenal tone with subsequent renin release and vasoconstriction because of impaired cardiac baroreceptor sensitivity, and stress responses to hospitalization, urinary retention, or conscious disturbance; some of these do not last long. In our cohort, any components of admission BP or HR did not predict chronic outcomes. Thus, BP should be frequently and consecutively measured to minimize the influence of unexpected factors and to accurately assess the clinical significance of acute BP levels. ABPM appears to be a practical and appropriate method for such assessment. A systematic review involving 20 studies with 5683 patients shows the advantage of ABPM over routine clinical BP measurement as a diagnostic tool for hypertension and suggests that ABPM leads to more appropriate targeting of antihypertensive treatment than the routine measurement. In a general population from the Ohasama study, ABPM had stronger predictive power for stroke risk than did screening routine BP measurement. Thus, ABPM may also have the strong predictive power for stroke outcomes. A randomized trial to control acute BP and HR levels is warranted to determine whether low BP and HR levels can directly improve outcomes or whether patients with predicted improved outcomes tend to have low BP and HR levels.
Sources of Funding
This study was supported in part by a Research Grant for Cardiovascular Diseases (21A-4), Intramural Research Fund (22-4-1) for Cardiovascular Disease of National Cerebral and Cardiovascular Center, Grants-in-Aid (H20-Junkanki-Ippan-019, H23-Junkanki-Ippan-010) from the Ministry of Health, Labour and Welfare, Japan, and a Grant-in-Aid for Scientific Research (C, 20591039) from the Japan Society for the Promotion of Science.

Disclosures
K.M. receives research support from the Ministry of Health, Labour and Welfare, Japan, the Mihara Cerebrovascular Disorder Research Promotion Fund, Research Grants for Cardiovascular Diseases, Grant-in-aid, the Foundation for Biomedical Research and Innovation, Mitsubishi Tanabe Pharma Corporation, Kyowa Hakko Kirin Pharma, Inc, and Hitachi Medical Corporation, K.T. receives research support from Grants-in-Aid from the Ministry of Health, Labour and Welfare, Japan.

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*Stroke*. 2011;42:3511-3517; originally published online September 29, 2011; doi: 10.1161/STROKEAHA.111.628586

*Stroke* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0039-2499. Online ISSN: 1524-4628

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