Twenty-Four-Hour Variation of Blood Pressure in Vascular Dementia of the Binswanger Type

Hideo Tohgi, MD; Kenichi Chiba, MD; and Munetaka Kimura, MD

Using a noninvasive portable blood pressure recorder, we compared 24-hour variations of blood pressure among 1) 35 patients with Binswanger-type dementia, 2) 43 with lacunar-type dementia, 3) 26 with a single lacunar stroke, and 4) 30 controls. Each group was divided into antihypertensive-treated and -untreated subgroups. Among the untreated subgroups, patients with Binswanger-type dementia had significantly greater 24-hour mean systolic blood pressures, 24-hour systolic blood pressure standard deviations, and maximal systolic blood pressure variations than the controls ($p<0.05$). Among the treated patients, blood pressure variability increased similarly in all subgroups with cerebrovascular lesions compared with the controls ($p<0.05$). The nocturnal blood pressure decreases seen in the controls were absent among both untreated and treated patients with Binswanger- or lacunar-type dementia ($p<0.05$). Our results suggest the importance of hypertension, short-term variations in blood pressure, and a sustained nighttime elevation of blood pressure for the pathogenesis of both Binswanger-type and lacunar-type dementia in patients receiving antihypertensive medication. *(Stroke 1991;22:603-608)*

Vascular dementia of the Binswanger type, also termed subcortical arteriosclerotic encephalopathy, is characterized pathologically by diffuse white matter changes and multiple small infarcts in the cerebral white matter.1-9 Although there has been some debate concerning this disease entity, it is now generally accepted that vascular dementia of the Binswanger type is part of the spectrum of cerebrovascular disease that occurs largely as a result of hypertensive changes in the walls of small penetrating arteries.10

Because the cerebral white matter is located in the end-fields of penetrating arteries, its metabolism may be impaired by wide fluctuations in blood pressure, particularly if cerebrovascular autoregulation is impaired. Previous reports have indicated that patients with impaired blood pressure regulation such as hypertension, labile systolic pressure, and orthostatic hypotension are at high risk for developing Binswanger-type dementia.3-8,10 Such descriptions, however, have been primarily based on casual blood pressure measurements. Admittedly, it is not fully known how blood pressure changes and how low it may fall during the day. Moreover, it remains to be determined whether the significance of such blood pressure abnormalities is the same in the pathogenesis of single lacunar stroke or lacunar states not associated with diffuse white matter changes such as in Binswanger-type dementia. However, it has been demonstrated that ambulatory blood pressure readings correlate more closely with target-organ damage than casual blood pressure readings.11-14 Therefore, using a noninvasive portable blood pressure recorder, we compared 24-hour variations in the blood pressure of patients with lacunar-type dementia, Binswanger-type dementia, a single lacunar stroke, and controls.

Subjects and Methods

The 134 subjects comprised four groups: 1) 30 controls (mean±SD age 69±10 years) with minor neurological or nonneurological diseases who had normal intelligence and whose computed tomograms (CT scans) showed no evidence of vascular lesions, 2) 26 patients with lacunar stroke (mean±SD age 67±8 years) who had normal intelligence but a history of lacunar stroke 1–6 months prior to the present study and showed a single small infarct on CT scans, 3) 43 patients with lacunar-type dementia (mean±SD age 74±9 years) whose CT scans showed multiple lacunes in the basal gray matter and centrum semiovale but did not demonstrate an extensive area of low
density in the periventricular white matter, and 4) 35 patients with Binswanger-type dementia (mean±SD age 73±8 years) (Figure 1). We classified patients as having Binswanger-type dementia if they fulfilled the following criteria: 1) clinical characteristics of vascular dementia according to DSM-III-R14 and Hachinski's ischemic score,16 2) absence of infarcts that alone may produce dementia (large infarcts [≥3 cm in diameter] or infarcts of the thalamus, hippocampus, or cingulate gyrus), 3) presence of an extensive area of low density in the white matter on CT scans (leukoaraiosis)17 usually associated with multiple lacunes10 in the basal gray matter, and 4) absence of other etiologic conditions that may cause diffuse white matter changes (e.g., intoxication or inflammation). The degree of cognitive impairment was assessed with the dementia scale of Hasegawa et al,18 which consists of simple tests of memory, orientation, general knowledge, and calculation (range 0–32.5 points: normal, 31.0–32.5; mildly impaired, 22.0–30.5; moderately impaired, 10.5–21.5; and severely impaired, 0–10.0). Score was <21.5 points in all demented patients. We also divided the subjects into subgroups based on previous diagnosis and treatment of hypertension. Backgrounds of the subjects are shown in Table 1.

Various antihypertensive agents were administered, but calcium antagonists or angiotensin-converting enzyme inhibitors were used in most subjects. The doses of the drugs had been determined to maintain casual blood pressure as appropriate as possible (140–160/70–90 mm Hg) based on the proposal of the Working Group on Hypertension in the Elderly.19 There were no substantial differences among subjects receiving different antihypertensive agents. Subjects not receiving antihypertensive treatment had not been diagnosed as hypertensive based on casual blood pressure measurements but were considered hypertensive if their 24-hour average blood pressure was >130/85 mm Hg based on the results of Drayer et al.20 The proportions of untreated subjects diagnosed in this way as hypertensive are given in Table 1. Informed consent was obtained from all subjects.

All subjects were admitted to the hospital. Bedridden patients were excluded. Blood pressure was monitored using a noninvasive portable recorder (ABPM-630, Colin Medical, Komaki, Japan). The subjects were free to move within the hospital

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>n</th>
<th>Age (mean±SD yr)</th>
<th>Hypertension</th>
<th>Diabetes</th>
<th>Total cholesterol (mean±SD mg/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>No.</td>
<td>%</td>
<td>No.</td>
</tr>
<tr>
<td>Antihypertensive-untreated</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>15</td>
<td>70±9</td>
<td>6</td>
<td>40</td>
<td>0</td>
</tr>
<tr>
<td>Lacunar stroke</td>
<td>16</td>
<td>69±8</td>
<td>8</td>
<td>50</td>
<td>3</td>
</tr>
<tr>
<td>Lacunar-type dementia</td>
<td>24</td>
<td>75±8</td>
<td>10</td>
<td>42</td>
<td>2</td>
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<tr>
<td>Binswanger-type dementia</td>
<td>19</td>
<td>75±8</td>
<td>14</td>
<td>74</td>
<td>0</td>
</tr>
<tr>
<td>Antihypertensive-treated</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>15</td>
<td>68±11</td>
<td>15</td>
<td>100</td>
<td>5</td>
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<tr>
<td>Lacunar stroke</td>
<td>10</td>
<td>64±6</td>
<td>10</td>
<td>100</td>
<td>2</td>
</tr>
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<td>Lacunar-type dementia</td>
<td>19</td>
<td>73±10</td>
<td>19</td>
<td>100</td>
<td>7</td>
</tr>
<tr>
<td>Binswanger-type dementia</td>
<td>16</td>
<td>71±7</td>
<td>16</td>
<td>100</td>
<td>0</td>
</tr>
</tbody>
</table>
TABLE 2. 24-Hour Average, Within-Subject SD, Coefficient of Variation, and Maximal Variation of Systolic Blood Pressure

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>n</th>
<th>24-hr average (mm Hg)</th>
<th>Within-subject SD (mm Hg)</th>
<th>Coefficient of variation (%)</th>
<th>Maximal variation (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Antihypertensive-untreated</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Controls</td>
<td>15</td>
<td>126.0±17.4</td>
<td>15.4±3.7</td>
<td>12.2±2.4</td>
<td>69.3±18.4</td>
</tr>
<tr>
<td>Lacunar stroke</td>
<td>16</td>
<td>132.2±22.7</td>
<td>14.4±3.6</td>
<td>11.1±3.1</td>
<td>74.0±25.3</td>
</tr>
<tr>
<td>Lacunar-type dementia</td>
<td>24</td>
<td>128.7±15.1</td>
<td>15.2±3.8</td>
<td>12.0±3.4</td>
<td>73.0±22.0</td>
</tr>
<tr>
<td>Binswanger-type dementia</td>
<td>19</td>
<td>138.6±19.3*</td>
<td>18.8±6.5*†</td>
<td>13.6±4.5</td>
<td>87.9±32.7*†</td>
</tr>
<tr>
<td><strong>Antihypertensive-treated</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Controls</td>
<td>15</td>
<td>133.2±16.8</td>
<td>15.9±3.4</td>
<td>11.9±2.3</td>
<td>71.7±16.6</td>
</tr>
<tr>
<td>Lacunar stroke</td>
<td>10</td>
<td>138.9±16.8</td>
<td>20.8±7.3†</td>
<td>14.8±4.3†</td>
<td>93.5±25.3†</td>
</tr>
<tr>
<td>Lacunar-type dementia</td>
<td>19</td>
<td>142.5±18.6</td>
<td>18.5±4.4‡</td>
<td>13.1±3.2</td>
<td>83.6±22.7</td>
</tr>
<tr>
<td>Binswanger-type dementia</td>
<td>16</td>
<td>140.4±15.6</td>
<td>19.2±4.8‡</td>
<td>13.7±3.6</td>
<td>87.8±21.7‡</td>
</tr>
</tbody>
</table>

SD, standard deviation. Values are mean±SD.

* p<0.05 different from antihypertensive-untreated controls by one-way ANOVA.
† p<0.05 different from lacunar-type dementia by one-way ANOVA.
‡ p<0.05 different from antihypertensive-treated controls by one-way ANOVA.

During the recording, conforming to the hospital’s mealtime and bedtime schedules. Systolic and diastolic blood pressure, mean arterial blood pressure (diastolic pressure+1/3 pulse pressure), and heart rate were recorded at 30-minute intervals (i.e., 48 times a day). Data were analyzed using an automatic blood pressure measuring device (AA-200, Colin Medical) and a microcomputer (PC-9800, NEC, Tokyo, Japan). Since our subjects demonstrated a far greater fluctuation in systolic than in diastolic pressure, a common finding in the elderly,21-24 we evaluated only the changes in systolic pressure. For evaluating blood pressure variability, we used 1) the within-subject standard deviation (SD) of all systolic readings during 24 hours, 2) the 24-hour SD as a percentage of the 24-hour average (coefficient of variability), and 3) the difference between the maximum and minimum 24-hour systolic blood pressures (maximal variation). We calculated the mean systolic blood pressure and heart rate from 9:00 AM to 8:00 PM for daytime and from 11:00 PM to 4:30 AM for nighttime.

Intergroup differences were tested with one-way analysis of variance (ANOVA). Because we confirmed a normal distribution for within-subject SDs, their group differences were tested using ANOVA and Wilcoxon’s rank sum test. The linear regression coefficients were estimated by least-squares estimators.

**Results**

Among the antihypertensive-untreated subjects, the 24-hour average systolic pressure (Table 2) was significantly higher in patients with Binswanger-type dementia than in the controls (p<0.05). The within-subject SD and maximal variation were also significantly greater in patients with Binswanger-type dementia than in the controls (p<0.05) (Table 2), whereas the coefficient of variation did not differ among subgroups. Even though the night–day difference (nighttime average minus daytime average) of systolic pressure varied widely (Table 3), a negative difference was observed in the controls and patients with lacunar stroke. In contrast, the night–day differ-

TABLE 3. Night–Day Difference of Systolic Blood Pressure and Heart Rate

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>n</th>
<th>Systolic pressure (mm Hg)</th>
<th>Heart rate (beat/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Antihypertensive-untreated</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Controls</td>
<td>15</td>
<td>-8.2±8.8</td>
<td>-13.8±4.9</td>
</tr>
<tr>
<td>Lacunar stroke</td>
<td>16</td>
<td>-1.5±11.25</td>
<td>-11.3±4.9</td>
</tr>
<tr>
<td>Lacunar-type dementia</td>
<td>24</td>
<td>2.9±12.3*</td>
<td>-10.1±4.9</td>
</tr>
<tr>
<td>Binswanger-type dementia</td>
<td>19</td>
<td>1.2±14.0†</td>
<td>-13.2±6.7</td>
</tr>
<tr>
<td><strong>Antihypertensive-treated</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Controls</td>
<td>15</td>
<td>-9.3±12.7</td>
<td>-13.5±6.0</td>
</tr>
<tr>
<td>Lacunar stroke</td>
<td>10</td>
<td>-5.0±18.3</td>
<td>-13.8±7.2</td>
</tr>
<tr>
<td>Lacunar-type dementia</td>
<td>19</td>
<td>6.3±18.4‡</td>
<td>-13.5±10.5</td>
</tr>
<tr>
<td>Binswanger-type dementia</td>
<td>16</td>
<td>1.7±13.4§</td>
<td>-12.4±6.1</td>
</tr>
</tbody>
</table>

Values are mean±SD.

* p<0.01, † p<0.05, respectively, different from antihypertensive-untreated controls by one-way ANOVA.
‡ p<0.01, § p<0.05, respectively, different from antihypertensive-treated controls by one-way ANOVA.
ence in the lacunar-type and Binswanger-type dementia subgroups was slightly positive and differed significantly from that of the controls (p<0.01 and p<0.05, respectively). Heart rate decreased during the nighttime compared with the daytime to similar degrees in the four subgroups.

The lowest and 24-hour average mean arterial blood pressure for each subgroup showed a linear relation, with the lowest value being about 70% of the 24-hour average (Figure 2).

Among the antihypertensive-treated subjects, the 24-hour average systolic pressure (Table 2) did not differ among the four subgroups. In addition, the within-subject SD for the control subgroup did not differ from that for the untreated control subgroup (Table 2). The within-subject SD was significantly greater in the three subgroups with vascular lesions than in the controls (p<0.05), whereas the coefficient of variation was significantly greater only in the lacunar stroke subgroup (Table 2). Maximal variation was significantly greater in the lacunar stroke and Binswanger-type dementia subgroups than in the controls (p<0.05). Similar patterns were observed in the night-day differences of systolic pressure and heart rate in the treated and untreated subgroups (Table 3).

Similar correlations between the 24-hour average and lowest mean arterial blood pressures were obtained for the antihypertensive-treated and untreated subjects (data not shown).

Discussion

Our results demonstrate that patients with Binswanger-type dementia had greater incidences of hypertension (86%, 30 of 35) and undiagnosed hypertension (74%, 14 of 19) than controls, patients with lacunar stroke, and patients with lacunar-type dementia. We thus confirmed the importance of hypertension in the pathogenesis of Binswanger-type dementia.

While blood pressure was lower at night than during the day in the controls, as has been reported previously in normal subjects, average nighttime blood pressure was slightly higher than average daytime blood pressure in both the patients with lacunar-type and Binswanger-type dementia. This elevated nighttime blood pressure has also been found in patients with Shy-Drager syndrome and autonomic failure, which affects the normal circadian rhythm. Similar autonomic dysfunction may exist in dementias of both the lacunar and Binswanger types. Two patterns of diurnal variation have been reported in elderly patients with essential hypertension: blood pressure falling and blood pressure increasing at night, as was seen in about half of our patients with lacunar-type or Binswanger-type dementia. Such a sustained elevation of blood pressure probably contributes substantially to the pathogenesis of vascular lesions in the cerebral white matter and other target organs.

Blood pressure variability was significantly greater in patients with Binswanger-type dementia than in the other untreated subgroups. It is likely that such wide oscillations in systolic blood pressure contributed to the more widespread ischemic changes in the cerebral white matter of patients with Binswanger-type dementia than of those with lacunar stroke because the arterial wall, like physical materials, may
be more susceptible to intermittent stress than to continuous stress and because the cerebral white matter located in the end-fields of penetrating arteries is susceptible to frequent reductions in blood pressure. Our results suggest that the absolute range of variability may be more important than the proportion of variability relative to the average systolic blood pressure. It has been shown that both the 24-hour averages and the variabilities of blood pressure are related to the severity of target-organ damage. The wide blood pressure variability may also be related to fluctuation in cognitive functions, which is the hallmark of multi-infarct dementia.

Although short-term variability in blood pressure is modulated by the autonomic nervous system and probably by the renin–angiotensin system, it has been shown that blood pressure variability is little affected by antihypertensive medications, including those that inhibit the activities of such systems. Our subjects receiving antihypertensive medication showed night–day differences in blood pressure similar to those in untreated subjects. However, the differences among subgroups in blood pressure variability were less distinct among treated than untreated subjects because of the great blood pressure variability in all groups with cerebrovascular lesions. This cannot be explained solely by the elevated blood pressure seen in these subjects because no significant correlation has been found between blood pressure and its variability. We therefore could not find distinct differences in the blood pressure parameters between antihypertensive-treated patients withBinswanger-type dementia and those with lacunar-type dementia.

The lower limit of blood pressure below which cerebral blood flow begins to decrease is linearly correlated with the habitual blood pressure, approximately 70% of the latter. Our results show that in all groups, including the Binswanger-type dementia group, mean arterial blood pressure did not fall far below the lower limit of autoregulation for normal vessels. However, previous autopsy reports have demonstrated severe arteriosclerotic changes in the medullary and basal perforating arteries, suggesting intense pathological response of small vessels to hypertension. Such severe stenosis of the perforating arteries may impair cerebral blood flow, directly exposing the deep white matter to frequent hypotension, even if the lowest blood pressure is above the lower limit of autoregulation for normal vessels. The appropriate therapeutic range for control of hypertension in patients with multi-infarct dementia has been shown to be a systolic blood pressure of 135–150 mm Hg; if systolic blood pressure is reduced below this level, the patients’ cognitive ability deteriorates.

In conclusion, hypertension, variability of blood pressure, and sustained elevation of blood pressure during the night may be important pathogenetic factors, not only for Binswanger-type dementia, but also for lacunar-type dementia among antihypertensive-treated patients.

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