Decrease in Cerebral Blood Flow With Blood Pressure Reductions in Patients With Chronic Stroke

Sakan Mori, MD; Seizo Sadoshima, MD; Kenichiro Fujii, MD; Setsuro Ibayashi, MD; Kozo Iino, MD; Masatoshi Fujishima, MD

Background and Purpose: Possible effects of changes in blood pressure on the cerebral circulation were studied in patients with chronic stroke and age-matched nonstroke control subjects at 28±10 months (mean±SD) (range, 18 to 54 months) and 27±6 months (range, 19 to 44 months), respectively, after the first measurement.

Methods: Cerebral blood flow was measured by the 133Xe inhalation method in 55 patients (mean±SD age, 62±11 years; 39 with brain infarction and 16 with hemorrhage) and 10 control subjects (mean±SD age, 61±9 years). Correlations between changes in cerebral blood flow and blood pressure were evaluated.

Results: Among brain infarctions, average cerebral blood flow did not change from the first study; however, changes in cerebral blood flow in each individual were closely related to changes in systolic and mean arterial blood pressures (P<.01 and P<.05, respectively). Of these, in 10 patients with cerebral blood flow decreased more than 15% from the initial levels, systolic and mean arterial blood pressures decreased by 25±32 mm Hg and 16±14 mm Hg (P<.05 and P<.005, respectively). In contrast, in 29 patients with unchanged or increased cerebral blood flow, changes in systolic (0±19 or −2±12 mm Hg, respectively) and mean arterial blood pressures (3±22 or −1±11 mm Hg, respectively) were not significant, and their systolic blood pressure levels were maintained above 110 mm Hg.

Conclusions: Blood pressure importantly correlates with cerebral circulatory changes among patients with chronic brain infarction. Early detection of cerebral hemodynamic changes should be useful for determining the most favorable levels of blood pressure and for selecting appropriate therapy. (Stroke. 1993;24:1376-1381.)

Key Words: blood pressure • cerebral blood flow • cerebral infarction

Cerebral blood flow (CBF) has prognostic significance in chronic stroke,1-3 reflecting the extension or severity of vascular lesions of the brain.4-6 Mean levels of CBF remain virtually unchanged in many cases despite improvement of clinical symptoms7-8 and electroencephalographic findings.8,9 Among patients with chronic stroke, cerebral circulatory reserves may be reduced in some cases because of diffuse vascular changes. By monitoring CBF, the early detection of CBF declines should predict deterioration of symptoms or recurrence of stroke.

Hypertension is the most important of all stroke risk factors. Although it remains controversial whether or not a consistent J-shaped relation exists between blood pressure levels and morbidity or mortality from stroke, in the elderly stroke mortality tends to increase when systolic blood pressure is lowered to below 120 mm Hg or 137 mm Hg.11 These critical levels of blood pressure have usually been based on analysis of initial or past levels of blood pressures, and the data of present or prospective levels of blood pressure or changes in blood pressure from initial levels were not described. In clinical practice, levels of blood pressure often vary from initial levels during chronic antihypertensive therapy or even in the untreated condition.

The purpose of the present study was to determine factors that influence changes in CBF among patients with chronic stroke. Possible effects of changes in blood pressure, age, sex, and hematocrit on CBF were evaluated.

Subjects and Methods

From October 1981 through December 1987, 1417 patients with stroke were admitted to the Stroke Care Unit in Fukuoka Higashi National Hospital. Regional CBF was measured in a total of 541 patients, of whom 55 patients (35 men and 20 women; mean±SD age, 62±11 years; range, 36 to 86 years) underwent serial CBF measurements and were admitted to the present study. Thirty-nine patients suffered from brain infarction and 16 from brain hemorrhage. Patients with brain infarction were divided into two groups by computed tomographic (CT) findings: 22 patients with subcortical infarction (including lacunae) and 17 with cortical infarction. Inclusion criteria were the following: (1) patients with chronic unilateral supratentorial infarction or hemorrhage, detected by the initial brain CT in the
hemisphere ipsilateral to the expected lesion, (2) in which the first CBF was measured 17±62 weeks (median, 6 weeks) after onset of stroke (95% within 16 weeks), and (3) who received a second CBF measurement between 18 and 54 months (mean, 28±10 months) after the first measurement of CBF. In 10 nonstroke cases, matched for age (61±9 years), sex, and blood pressure levels, values of CBF were measured at the intervals of 27±6 months (range, 19 to 44 months). Hypertension was defined as systolic blood pressure greater than or equal to 160 mm Hg and/or diastolic blood pressure greater than or equal to 95 mm Hg.

Regional CBF was measured by the $^{133}$Xe inhalation technique as described previously. Briefly, 11 collimated scintillation detectors were bilaterally attached on the surface of the head. Gas mixture of $^{133}$Xe (3 mCi/L) was administered for 1 minute, and the clearance curves were recorded for 10 minutes. Blood flow to the gray matter (Fg) was calculated by two-compartmental analysis. The values from each detector on one side were averaged to provide ipsilateral mean hemispheric CBF. Levels of blood pressure, end-tidal PCO$_2$, hematocrit, and hemoglobin were all monitored. All CBF values were corrected to arterial PCO$_2$ of 36.5 mm Hg, according to Maximilian et al.

All data are expressed as mean±SD. Values of CBF and physiological parameters among the four groups were analyzed by analysis of variance (ANOVA) and Scheffé's test. Changes in these variables between the first and second measurements were examined by two-tailed paired t tests. Patients with or without antihypertensive treatment were compared among the four groups by χ$^2$ tests. Correlations between CBF, age, or blood pressure levels and between changes in CBF and blood pressure were evaluated by a simple regression analysis. Changes in CBF were included when they were 15% or more because the reproducibility error of CBF determinations using the $^{133}$Xe inhalation method carries an error of 10% to 15%. Blood pressure changes in patients with brain infarction with decreased, unchanged, and increased CBF were analyzed by ANOVA and Scheffé’s test. Differences were considered significant when the probability value was less than .05.

**Results**

The characteristics of the 55 stroke patients and 10 control subjects are displayed in Table 1. Hypertension was observed in 89% of stroke patients and 70% of control subjects. The percentage of patients who received antihypertensive drug therapy at the first measurement was 14% for those with subcortical infarction and 12% for those with cortical infarction; in comparison, 56% of patients with brain hemorrhage were treated (P<.01). The level of blood pressure, however, did not differ among the four groups. During the follow-up period, no deterioration of clinical outcome or recurrence of stroke was observed. Average values for blood pressure did not change from the first measurement in control subjects and in stroke patients except for the group with cortical infarction, in which diastolic and mean arterial blood pressures significantly decreased by 7 mm Hg and 6 mm Hg, respectively, while average CBF was not reduced (Table 1).

At the time of the first measurement, the average CBF within the ipsilateral hemisphere was 57±11 mL/100 g per minute for subcortical infarction, 46±15 mL/100 g per minute for cortical infarction, and 47±11 mL/100 g per minute for brain hemorrhage (Table 1), which was significantly lower than that within the contralateral hemisphere for each group (P<.01). CBF in patients with cortical infarction or brain hemorrhage was also 14 to 18 mL/100 g per minute lower than that among control subjects (P<.05, Table 1). By cross-sectional analysis, the age-related reductions in CBF were observed in both hemispheres in the control hemisphere.
The similar correlation was also significant in 17 patients with cortical infarction. If the patient whose CBF in the ipsilateral hemisphere decreased by 21 mL/100 g per minute is excluded, the relation between change in mean arterial blood pressure and change in CBF in the ipsilateral hemisphere was still significant (P=.0315); however, the relations between change in mean arterial blood pressure and change in CBF in the contralateral hemisphere or between the change in systolic blood pressure and change in CBF were not significant. In patients with brain hemorrhage or control subjects, there were no correlations between changes in blood pressure and CBF observed in either of the two hemispheres. In control subjects, CBF within the right hemisphere decreased with the increase of hematocrit (P=.025), but the correlation was not significant when one patient whose CBF decreased by 23 mL/100 g per minute was excluded.

In 10 patients whose CBF decreased more than 15% compared with initial levels, systolic, diastolic, and mean arterial blood pressure decreased significantly by 24, 12, and 16 mm Hg (mean values), respectively (P<0.05,
TABLE 2. Changes in Physiological Parameters in 39 Patients With Chronic Cerebral Infarction With Increased, Unchanged, or Decreased Cerebral Blood Flow

<table>
<thead>
<tr>
<th></th>
<th>Decreased CBF (&gt;15% Decrease) (n=10)</th>
<th>Unchanged CBF (n=19)</th>
<th>Increased CBF (&gt;15% Increase) (n=10)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Meas 1</td>
<td>Meas 2</td>
<td>Meas 1</td>
</tr>
<tr>
<td>Age, y</td>
<td>63±9</td>
<td>65±9</td>
<td>65±10</td>
</tr>
<tr>
<td>Subcortical/cortical infarction</td>
<td>5:5</td>
<td>27±9</td>
<td>28±10</td>
</tr>
<tr>
<td>Cerebral blood flow, (mL/100 g)/min</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ipsilateral hemisphere</td>
<td>53±14</td>
<td>39±14**†#</td>
<td>56±11</td>
</tr>
<tr>
<td>Contralateral hemisphere</td>
<td>56±11</td>
<td>41±12†</td>
<td>58±10</td>
</tr>
<tr>
<td>Systolic BP, mm Hg</td>
<td>155±26</td>
<td>131±25†</td>
<td>148±20</td>
</tr>
<tr>
<td>Diastolic BP, mm Hg</td>
<td>87±7</td>
<td>75±9</td>
<td>86±12</td>
</tr>
<tr>
<td>Mean arterial BP, mm Hg</td>
<td>110±12</td>
<td>94±11‖</td>
<td>106±13</td>
</tr>
<tr>
<td>Change in systolic BP, mm Hg (range)</td>
<td>-25±32 (-90 to 8)*†</td>
<td>0±19 (-28 to 40)</td>
<td>3±22 (-32 to 26)</td>
</tr>
<tr>
<td>Change in mean BP, mm Hg (range)</td>
<td>-15±17 (-44 to 5)*†</td>
<td>1±14 (-20 to 40)</td>
<td>3±15 (-20 to 19)</td>
</tr>
<tr>
<td>Change in systolic BP, mm Hg (range)</td>
<td>-16±14 (-49 to 1)*†</td>
<td>-2±12 (-19 to 32)</td>
<td>-1±11 (-16 to 15)</td>
</tr>
<tr>
<td>Change in mean BP, mm Hg (range)</td>
<td>-14±10 (-36 to 1)*†</td>
<td>-1±14 (-16 to 44)</td>
<td>-1±10 (-14 to 15)</td>
</tr>
<tr>
<td>Hemoglobin, g/dL</td>
<td>14.3±1.8</td>
<td>14.5±2.2</td>
<td>13.7±1.3</td>
</tr>
<tr>
<td>Hematocrit, %</td>
<td>42±5</td>
<td>43±6</td>
<td>40±3</td>
</tr>
<tr>
<td>Hypertension</td>
<td>9 (90%)</td>
<td>16 (84%)</td>
<td>3 (16%)</td>
</tr>
<tr>
<td>Antihypertensive treatment</td>
<td>1 (10%)</td>
<td>7 (70%)</td>
<td>3 (16%)</td>
</tr>
</tbody>
</table>

Values are mean±SD. CBF indicates cerebral blood flow; Meas, measurement; and BP, blood pressure.
*P<.05 vs unchanged CBF group by analysis of variance (ANOVA) and Scheffe’s test.
†P<.05 vs increased CBF group by ANOVA and Scheffe’s test.
‡P<.05 vs unchanged CBF by ANOVA and Scheffe’s test.
§P<.005 vs measurement 1 by two-tailed paired t test.
**P<.005 vs contralateral hemisphere in stroke patients by two-tailed paired t test.

P<.005, and P<.005, respectively; Table 2). In 19 patients with unchanged CBF or 10 with increased CBF of more than 15%, the levels of blood pressure did not change (Table 2, Fig 3). Changes in systolic and mean arterial blood pressure in patients with decreased CBF were −25±32 mm Hg (range, −90 to 8 mm Hg) and −16±14 mm Hg (range, −49 to 1 mm Hg), respectively (Table 2, Fig 3), which were significantly greater than those of other two subgroups: 0±19 mm Hg (range, −28 to 40 mm Hg) and −2±12 mm Hg (range, −19 to 32 mm Hg) in patients with unchanged CBF, or 3±22 mm Hg (range, −32 to 26 mm Hg) and −1±11 mm Hg (range, −16 to 15 mm Hg) in patients with increased CBF. In patients with unchanged or increased CBF, levels of systolic blood pressure were all maintained above 110 mm Hg at the second measurement, and changes in systolic and mean arterial blood pressure did not fall below −20% and −16%, respectively (Table 2).

Discussion

Main results of our study were the following: (1) changes in CBF correlated well with changes in systolic and mean arterial blood pressures in 39 patients with chronic cerebral infarction; (2) of these, in 10 patients whose CBF decreased more than 15%, systolic and mean arterial blood pressure significantly decreased by 25 mm Hg and 16 mm Hg (mean values), respectively; and (3) in 29 patients with unchanged or increased CBF, levels of systolic and mean arterial blood pressure did not significantly change, and decreases in systolic and mean arterial blood pressure did not exceed 32 mm Hg (20% decrease) and 19 mm Hg (16% decrease), respectively. All levels of systolic blood pressure were maintained above 110 mm Hg.

Stroke affects mainly the elderly, and 67% of our stroke patients and 80% of our control subjects were older than age 60 years at the time of the second measurement. In the control subjects and patients with subcortical infarction, age-related reductions in CBF were observed at the time of the first study, which was compatible with previous reports.15,16 In patients with

FIG 3. Bar graph shows changes in systolic and mean arterial blood pressure in 10 patients with chronic cerebral infarction with decreased cerebral blood flow (CBF), 19 patients with unchanged CBF, and 10 patients with increased CBF.
subcortical infarctions, the annual rate of CBF reduction (0.6 mL/100 g per minute per year) was approximately a third of that measured in control subjects, but CBF decreased at an earlier age of onset. Decline in CBF was not related to the duration of the follow-up period, probably because the duration of follow-up (mean, 27 months) was not long enough.6,17 In elderly hypertensive patients, lower limits of cerebral autoreg-ulation shift to levels higher than those among young hypertensive patients.18 Although our patients were not examined in the acute stages, elderly patients, whose baseline cerebral perfusion has already decreased close to the thresholds of their cerebral autoregulatory reserve, are at a higher risk of cerebral hyperperfusion even when systemic arterial blood pressure declines gradually.

The vast majority of our patients had long-standing hypertension. In hypertensive stroke patients, it has been reported that CBF decreases to a greater extent than among those without hypertension.24 Long-standing hypertension in itself shifts the lower limits of the autoregulatory threshold upward; even after effective and long-standing antihypertensive treatment, readaptation of cerebral autoregulation is not always com-
pleted, so that the lower limits of autoregulatory thresholds are still higher than in normotensive subjects.20 Although the aforementioned study dealt with an acutely induced hypotension, during long-term therapy some hypertensive patients have been reported to show CBF decreases below critical levels and to develop brain ischemic infarction brought about by reductions of blood pressure.21,22 Hypertensive patients with multi-
infarct dementia experienced deterioration of neurological symptoms when systolic blood pressure was lowered below 135 mm Hg.23 These patients may be considered to be on the threshold of their cerebral autoregulatory reserve; they therefore require a higher level of blood pressure to maintain sufficient cerebral perfusion. From our data, among patients with unchanged or increased CBF, systolic blood pressures of 110 mm Hg or greater and decreases in systolic and mean arterial blood pressure of 32 mm Hg or more (20% decrease) and 19 mm Hg or more (16% decrease), respectively, might suggest the critical ranges of blood pressure reduction. However, we have preliminarily assessed relations be-
tween changes in CBF and blood pressure, and addi-
tional further longitudinal observations of changes in CBF, blood pressure, and neurological prognosis will be required.

In patients with chronic cerebral hemorrhage, there were no correlations between changes in blood pressure and CBF. The younger age of these patients compared with those with cerebral infarctions and milder arterio-
sclerotic changes may, in part, explain these autoregulatory differences between patients with cerebral infarc-
tion and those with cerebral hemorrhage. In control subjects, CBF was maintained constant despite the changes in blood pressure, confirming that vascular functions for autoregulatory adaptation in nonstroke patients, as expected, are well preserved compared with those in stroke patients.

In our patients, CBF data at the first measurement were obtained at more than 1 month after the stroke to avoid the management difficulties frequently encountered during the acute stage and the interference of brain edema or intracranial hypertension. In most of our patients, brain edema is felt to resolve within the first 4 weeks after cerebral hemorrhage by the findings of follow-up CT scans and stabilized neurological defi-
cit, and there may be little effect of perihemotoma edema on CBF data at the time of first measurement.

Blood viscosity is mainly dependent on hematocrit and serum fibrinogen values,25 and among our control subjects hematocrit appears to the another possible factor that predicts changes in CBF. Among our pa-
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