Acknowledgment

The authors wish to recognize and thank Ms. Gisela Davis and Mrs. Vicky Drake for their contribution to this project. Their technical abilities and assistance were necessary and valuable parts of the work.

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Prognosis of Occlusive Cerebrovascular Diseases in Normotensive and Hypertensive Subjects

MASATOSHI FUJISHIMA, M.D., TERUO OMAE, M.D., YO TAKEYA, M.D., MORIYUKI TAKESHITA, M.D., JUN OGATA, M.D., AND KAZUO UEDA, M.D.

SUMMARY Comparison of the clinical features, especially prognosis, in cerebral infarction was made between nine normotensive subjects and 16 hypertensive patients with an 80% stenosis or occlusion of the intracranial or extracranial arteries. Our own criteria for evaluating hypertension were employed on the basis of the following items: a past history of hypertension, blood pressure levels on admission and during hospitalization, degree of retinopathy, and ECG changes. In 17 of 25 cases, brain circulation was measured by the intravenous RISA technique.

Abnormalities of the EEG and reduction of cranial blood flow were greater, and an early prognosis for neurological deficits in the first two months after the onset of stroke was poorer in the hypertensive group than in the normotensive group. These results are contradictory to the observations of others.

Introduction

OUR PREVIOUS EXPERIMENTAL STUDIES1-3 have shown that bilateral carotid artery occlusion caused an extremely higher mortality and a greater increase in anaerobic glycolytic metabolites such as lactate and lactate/pyruvate ratio of the brain in spontaneously hypertensive rats than in normotensive Wistar rats, and that the ischemic lesions were diffuse and severe in the former and small and circumscribed in the latter. These observations suggest that hypertension per se, but not the vascular changes secondary to the persistent high blood pressure (BP), seems to cause the derangements of cerebral circulation, resulting in severe and diffuse cerebral infarction.

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Contrary to these experimental studies, the degree of recovery in cerebral infarction is less poor in patients with hypertension of diastolic blood pressure above 110 mm Hg than in those below that level. Strokes in hypertensives present a picture of a small deeply situated lesion, whereas strokes in normotensives show large cortical and subcortical lesions. Furthermore, patients with hypertension have a lower mortality in the first two months after stroke than those with normal blood pressure.

These contradictory observations of the influence of hypertension on the pathophysiology of cerebral infarction developed in humans and induced in animals are unexplained. The purpose of the present study was to clarify the effect of hypertension on prognosis in patients with cerebral infarction. For this reason, we selected normotensive subjects and hypertensive patients with cerebral infarction, who had an 80% stenosis or occlusion of the intracranial or extracranial arteries on angiography to obtain a similar model to our previous experimental studies.

Methods

Twenty-five of 153 patients with cerebral infarction admitted to our Clinic during a period of seven years were selected for the present study. All 25 patients had an 80% stenosis or occlusion of the intracranial or extracranial arteries on angiography.

The patients were divided into two groups (normotensive and hypertensive) in accordance with arbitrary point values assigned for the evaluation of hypertension as follows.

1. Past history of hypertension: complex of > 160 mm Hg systolic or ≥ 95 mm Hg diastolic = 3 points, either ≥ 160 mm Hg systolic or ≥ 95 mm Hg diastolic = 2 points, hypertension present but BP level not recorded = 1 point, and history not present or not described = 0 point.

2. BP level on admission and during hospitalization: persistent or frequent rise in BP to both > 160 mm Hg systolic and ≥ 95 mm Hg diastolic = 3 points, either > 160 mm Hg systolic or ≥ 95 mm Hg diastolic = 2 points, normal BP without treatment = 0 point.

3. Retinopathy graded by the Keith-Wagener-Keidai classification: Grades IIb, III or IV = 3 points, Grade I = 2 points, and Grade O = 0 point.

4. ECG findings: high voltage of QRS complex with ST-T changes = 3 points, high voltage of QRS complex only = 2 points, ST-segment depression and/or T wave changes = 1 point, and normal pattern or dysrhythmias = 0 point.

BP level at the time of onset of stroke was excluded from the evaluation of hypertension because of the frequent development of a transient or fluctuating rise in BP at the time of onset or an early stage of stroke, especially brain stem lesions.

Total points of each item divided by the number of items available represent a mean scoring point for hypertension. The patients with more than 1.0 point were defined as being hypertensive, and those with 1.0 point or less as being normotensive.

There were nine normotensives and 16 hypertensives as shown in table 1.

In seven of nine normotensives and 10 of 16 hypertensives, brain circulation was determined by the intravenous RISA method. Two hundred microcuries of I\textsuperscript{131} RISA were injected rapidly into the antecubital vein, and the hemispheric RISA dilution curves were obtained by NaI scintillation detectors collimated separately to each hemisphere. Cranial blood flow, mean cranial transit time, cranial vascular resistance and arm-to-brain circulation time were obtained. The methodological and technical details have been reported elsewhere.

Results

Age and sex distributions of the patients in both normotensive and hypertensive groups are given in table 2. There was no remarkable difference in the age and sex distributions between the two groups. There were three cases complicated with diabetes mellitus in the hypertensive group compared with only one case in the normotensive group.

The location of cerebral lesions, diagnosed by a carefully taken history and complete neurological examinations, is cited in table 3. In each group, left hemispheric lesions were observed more frequently than right-sided lesions or brain stem lesions.

EEG was performed in all 25 patients. The results, given in table 4, show that the moderately to severely abnormal EEG with asymmetry occurred more commonly in the hypertensive group (56%) than in the normotensive one (33%).

Cerebral angiography of at least three neck vessels was performed in all patients, and the sites of an 80% stenosis or occlusion of either the intracranial or extracranial arteries are shown in table 5. Occlusion of the middle cerebral artery was revealed in six of nine (67%) normotensives, being greater than in seven of 16 (44%) hypertensives, although in-

<table>
<thead>
<tr>
<th>Site of Cerebral Lesions</th>
<th>Normotensives</th>
<th>Hypertensives</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left hemisphere</td>
<td>6 (67)*</td>
<td>9 (56)</td>
</tr>
<tr>
<td>Right hemisphere</td>
<td>2 (22)</td>
<td>6 (38)</td>
</tr>
<tr>
<td>Brain stem</td>
<td>1 (11)</td>
<td>1 (6)</td>
</tr>
<tr>
<td>Total</td>
<td>9 (100)</td>
<td>16 (100)</td>
</tr>
</tbody>
</table>

*Numbers in parentheses are percent.
ter nal carotid occlusion was less frequent in the former than in the latter.

Cerebrospinal fluid pressure was normal in all 16 hypertensives except one whose pressure was 360 mm H₂O, whereas only one of nine normotensives had a high CSF pressure of 320 mm H₂O. There was no significant difference in mean values for CSF pressure or protein content between the two groups as shown in table 6.

According to the clinical course within two months following the onset, an early prognosis (the severity scale of clinical status) was classified into four grades as follows: a complete or nearly complete recovery with minor residuals as Grade 1 (recovered), the most symptoms subsiding but with residual deficit as Grade 2 (ameliorated), no apparent improvement or deterioration of the symptoms as Grade 3 (not recovered or worsened), and deaths as Grade 4. The patients of Grades 1 and 2 were generally considered together and expressed as "improved," and those of Grades 3 and 4 as "nonimproved." In this study, none of the cases of Grade 4 was included.

Relationship between an early prognosis and a blood pressure level in patients with cerebral infarction is given in table 7. In the normotensive group, eight of nine (89%) patients showed a slight to complete recovery from symptoms as against only 5 of 16 (31%) patients in the hypertensive group, whereas 11 (69%) of the latter group and only one (11%) of the former had no improvement or deterioration of neurological deficits. These differences were significant at the 2.5% level (Chi-square tests with Yates modification). Figure 1 depicts the relationship of mean scoring points for hypertension and grading for prognosis in normotensives and hypertensives with cerebral infarction. Grade I: recovered, Grade II: ameliorated, and Grade III: unchanged or worsened. Open and closed circles indicate normotensive and hypertensive patients, respectively.

Table 5 summarizes in table 8. Cranial blood flow in hypertensive stroke patients was significantly decreased to 74% of normotensive stroke patients, 77% of non-stroke hypertensive subjects and 63% of normotensive controls. Cranial vascular resistance in hypertensive stroke patients was significantly greater than that in normotensive stroke patients. Both mean transit time and arm-to-brain circulation time were more prolonged in hypertensive stroke patients than in normotensives, but the difference did not reach statistical significance.

Discussion

Our previous experimental studies have shown that 72% of spontaneously hypertensive rats died within 24 hours following bilateral carotid occlusion as opposed to only 16% of normotensive rats, and that both cerebral anaerobic glycolytic metabolites as lactate and pyruvate and cerebral lactate/pyruvate ratio reflecting the cytoplasmatic redox state were increased to eight times normal at one hour, 12 times at five to six hours, and nine times at 24 hours following bilateral occlusion of the carotid artery in hypertensive rats but not in normotensive rats. Water content of the supratentorial portion in these hypertensive rats was also significantly increased at five hours after carotid occlusion. These experimental studies strongly suggest that hypertensive rats with occlusion of the carotid arteries might have

### Table 4 Electroencephalogram

<table>
<thead>
<tr>
<th>Results</th>
<th>Normotensives</th>
<th>Hypertensives</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>2(22)*</td>
<td>4(25)</td>
</tr>
<tr>
<td>Slightly abnormal</td>
<td>4(45)</td>
<td>3(19)</td>
</tr>
<tr>
<td>Moderately abnormal</td>
<td>1(11)</td>
<td>4(25)</td>
</tr>
<tr>
<td>Severely abnormal</td>
<td>2(22)</td>
<td>5(31)</td>
</tr>
<tr>
<td>Total</td>
<td>9(100)</td>
<td>16(100)</td>
</tr>
</tbody>
</table>

*Numbers in parentheses are percent.

### Table 5 Cerebral Angiogram

<table>
<thead>
<tr>
<th>Site of occlusion</th>
<th>Normotensives</th>
<th>Hypertensives</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICA</td>
<td>1(11)*</td>
<td>4(25)</td>
</tr>
<tr>
<td>MCA</td>
<td>6(67)</td>
<td>7(44)</td>
</tr>
<tr>
<td>Vertebral or subclavian</td>
<td>1(11)</td>
<td>3(19)</td>
</tr>
<tr>
<td>artery</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Basilar artery</td>
<td>1(11)</td>
<td>1(6)</td>
</tr>
<tr>
<td>Posterior cerebral artery</td>
<td>0</td>
<td>1(6)</td>
</tr>
<tr>
<td>Total</td>
<td>9(100)</td>
<td>16(100)</td>
</tr>
</tbody>
</table>

ICA = internal carotid artery; MCA = middle cerebral artery.

*Numbers in parentheses are percent.

### Table 6 CSF Pressure and Protein Content

<table>
<thead>
<tr>
<th></th>
<th>Normotensives</th>
<th>Hypertensives</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial pressure</td>
<td>127 ± 26 (9)</td>
<td>153 ± 17 (15)</td>
</tr>
<tr>
<td>Protein (mg/dl)</td>
<td>47 ± 6 (8)</td>
<td>62 ± 8 (14)</td>
</tr>
</tbody>
</table>

Values are mean ± SEM, ( ) = number of cases.
severe and fatal ischemic changes of the brain. We also have observed that a diffuse and large infarct was located in the hemispheric cortex and the basal ganglia in hypertensive rats, despite a small and circumscribed lesion in normotensive rats.

In humans, however, Prineas and Marshall\(^4\) have reported that strokes in normotensive subjects, age 55 years or less, had been accompanied more frequently by an abnormal EEG, whereas strokes in hypertensives had less severe abnormalities. Although the severity of stroke in terms of the immediate disability was the same in the two groups, the degree of recovery was very different. In the normotensive group, 21% of 67 survivors showed little or no recovery as against only 6% of the survivors in the hypertensive group. The authors\(^7\) concluded that the frequency of a marked abnormality or asymmetry of the EEG, the high incidence of dysphasia, and little recovery in normotensive stroke patients indicate the presence of a large lesion of cortical or subcortical distribution. On the other hand, the findings in hypertensive stroke patients suggest small, deeply situated lesions. Hughes et al.\(^1\) have studied hypertensive patients with dementia, preceded or accompanied by stroke, who had multiple small ischemic softenings in the basal ganglia in the territory of the perforating arteries.

Harrison and Marshall\(^5\) noted that carotid occlusion in cerebral infarction was more common in normotensives (25%) than in hypertensives (9%), being of significant difference. Cerebral infarction in normotensives was more often due to a cortical infarct from the carotid occlusion or thromboembolism, whereas in hypertensives a significant number of strokes were due to the more deeply situated lesions, perhaps related to the special small-vessel changes in penetrating arteries in the putamen and the internal capsule.

Rønnow-Jessen\(^6\) found that the mortality in cerebral infarction was 23.3% in 90 hypertensives and 22.3% in 122 normotensives, and the recovery rates were 44.4% and 48.2%, respectively, indicating the prognosis of the two groups to be the same. Similarly, in the patients with abnormal cerebral angiograms, there was no difference of mortality and restitution between the hypertensive and non-hypertensive groups. Merrett and Adams\(^8\) also reported that mortality in the survivors of strokes was not influenced by the presence of hypertension, being contradictory to the observations of Prineas and Marshall,\(^4\) who found an adverse effect of hypertension on mortality after cerebral infarction. In long-term prognosis, the presence of a diastolic BP of 110 mm Hg or more or of ECG abnormalities such as left ventricular hypertrophy or ischemic changes did significantly reduce the survival rate, i.e., the two-year life expectancy decreasing from 96% to 75%.\(^9\)

In the present study, however, hypertensive patients showed more severe abnormalities on the EEG, a greater reduction of cranial blood flow, and a poorer early prognosis than did normotensive patients, indicating that in hypertensives a fairly large ischemic lesion could be located in the hemispheric cortex or subcortex rather than the deeply sited portion. The difference between our findings and those of others\(^4,\)\(^5\) may be attributable to the materials or the inconsistencies in definition of hypertension. We selected cases with cerebral infarction having a concomitant occlusion of the cerebral arteries, and employed our own criteria for the evaluation of hypertension.

Concerning the definition of hypertension, Low-Beer and Phear\(^10\) reported that blood pressure at the time of onset of stroke does not differ significantly from the habitual blood pressure of the patients, and that the blood pressure recording on admission does not differ markedly from the subsequent reading except when complicating factors such as hemorrhage, dehydration, heart failure, myocardial infarction and hypotensive therapy were present. Actually, blood pressure tended to be high at the time of onset, falling gradually over the next certain period of time in those who survived, and then increasing. Adams\(^1\) reported that within 24 hours of onset the blood pressure was 179.0/106.5 mm Hg in ten men and 200.8/110.4 mm Hg in 21 women; then the BP fell to 127.5/83.0 mm Hg and 149.6/87.0 mm Hg, respectively, six to eight weeks later. Therefore, blood pressure at the time of onset or on admission seems unlikely to be representative of the habitual blood pressure.

In most observations, patients with diastolic blood pressures of 110 mm Hg or above at the time of onset or admission are referred to as the hypertensive group and those with pressures below 110 mm Hg as the non-hypertensive or normotensive group. However, the division of patients according to the diastolic blood pressure level at 110 mm Hg seems inadequate because, in the non-hypertensive group, a considerable number of patients with a mild-to-moderate

---

**Table 7 Early Prognosis**

<table>
<thead>
<tr>
<th>Prognosis</th>
<th>Normotensives</th>
<th>Hypertensives</th>
</tr>
</thead>
<tbody>
<tr>
<td>Improved</td>
<td>8 (89)*</td>
<td>5 (31)</td>
</tr>
<tr>
<td>Nonimproved</td>
<td>1 (11)</td>
<td>11 (69)</td>
</tr>
<tr>
<td>Total</td>
<td>9 (100)</td>
<td>16 (100)</td>
</tr>
</tbody>
</table>

*See text for classification of early prognosis. Numbers in parentheses are percent.

---

**Table 8 Brain Circulation in Normotensive and Hypertensive Patients With or Without Cerebral Infarction**

<table>
<thead>
<tr>
<th></th>
<th>Normotensives</th>
<th>Hypertensives</th>
<th>Probability</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Stroke patients</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cranial blood flow (ml/min)</td>
<td>1.276 ± 118</td>
<td>950 ± 92</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Cranial vascular resistance (mm Hg/ml/min)</td>
<td>8.56 ± 0.93</td>
<td>12.08 ± 1.15</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Mean transit time (sec)</td>
<td>9.2 ± 0.8</td>
<td>11.2 ± 0.6</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Arm-to-brain circulation time (sec)</td>
<td>17.3 ± 2.6</td>
<td>18.5 ± 1.0</td>
<td>&gt;0.50</td>
</tr>
<tr>
<td><strong>Non-stroke patients</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cranial blood flow (ml/min)</td>
<td>1,501 ± 62</td>
<td>1,239 ± 53</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Cranial vascular resistance (mm Hg/ml/min)</td>
<td>6.13 ± 0.28</td>
<td>11.53 ± 0.62</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean transit time (sec)</td>
<td>9.1 ± 0.4</td>
<td>9.8 ± 0.4</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Arm-to-brain circulation time (sec)</td>
<td>13.1 ± 0.7</td>
<td>16.0 ± 1.0</td>
<td>&gt;0.20</td>
</tr>
</tbody>
</table>

Values are mean ± SEM.
diastolic hypertension or severe systolic hypertension are included. For these reasons, we used our own criteria for evaluating whether or not the patients were hypertensive on the basis of blood pressure and the hypertensive vascular changes as follows: the blood pressure levels before stroke, at the time of admission and during hospitalization; the severity of retinopathy, and ECG abnormalities. Therefore, there are no reports strikingly comparable with our study concerning recovery of the neurological deficits after cerebral infarction in hypertensive and normotensive groups.

The present results are compatible with our previous experimental studies indicating that hypertensive patients or rats with cerebral infarction which develops spontaneously or is experimentally induced and with occlusion of the intracranial or extracranial arteries, tend to have a poorer prognosis than do normotensive patients or rats.

References


Scanning Electron Microscopic Appraisal of a New Micro T-Tube

F. KARL GREGORIUS, M.D., AND ROBERT W. RAND, M.D.

SUMMARY A new micro T-tube, 0.6 mm in outer diameter, has been constructed. Use of this tube has allowed 1-mm common carotid artery (CCA) bypass for periods of time up to 22 minutes. After bypass, scanning electron microscopic observation of sutured CCA endothelium showed widespread destruction, scattered attached platelets and other formed blood elements, as well as microthrombi both at suture lines and in areas in contact with T-tubes. Despite microthrombi, 41 of 42 CCAs were patent after anastomosis. Silicone cuffs and 8-0 ties secured T-tubes inside vessels with no apparent difference in underlying endothelial destruction.

Methods

We used silicone tubing with diameters of 0.64 mm (outer) and 0.3 mm (inner) in the T-tube construction* shown in figure 1, suturing it end-on into 0.6 mm holes in separate sections of tubing with 10-0 suture, sealing it with silicone cement, and securing it to blunt 25-gauge needles with single 10-0 ties. We anesthetized 22 Sprague Dawley rats weighing 250 to 450 gm with Nembutal, 6 to 7 mg/100 gm. Both the left and right CCA, measuring 0.9 to 1.5 mm in diameter, were exposed, and tracheostomies were performed as previously described.

The CCA were clamped, severed, and irrigated with diluted heparin solution (10 U per cubic centimeter of saline). Silicone cuffs cut from tubing with diameters of 0.64

*Silastic medical-grade tubing manufactured by Dow Corning Corporation, Midland, Michigan.
†Silastic medical adhesive, Silicone type A, manufactured by Dow Corning Corporation, Midland, Michigan.

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Stroke. 1976;7:472-476
doi: 10.1161/01.STR.7.5.472

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