Discussion

The pathogenesis of the hypertensive intracerebral hematoma supposes rupture of a microaneurysm of a cerebral arteriole due to angioneurosis. Oneda found that microaneurysms develop after fibrinoid degeneration of the arterial wall. As to the frequency and distribution of microaneurysms, it seems related to cerebral hemodynamics, although cerebral blood flow is frequently determined in these patients. It seems reasonable to expect that the prognosis of patients with cerebral infarction in relation to brain circulation — A 7-Year Follow Up Study

MASATOSHI FUJISHIMA, M.D., KATSUYA NISHIMARU, M.D., AND TERUO OMAE, M.D.

SUMMARY Seventy-seven patients with cerebral infarction have been re-examined every year and followed for 7 years. Thirty-one patients had normal cranial blood flow (BF) and the remaining 46 had subnormal cranial BF, determined by the intravenous RISA method at the time of the original attack.

During a 7-year follow up, 7 patients (22.6%) of the normal cranial BF group died; 3 of stroke and the remaining 4 from other causes, while 24 patients (52.2%) of the subnormal cranial BF group died; 13 of stroke and the remaining 11 of various diseases. The cumulative survival rate was consistently lower in the subnormal cranial BF group than the normal one. This difference reached statistical significance at 5 and 7 years of follow up. However, stroke recurrence did not differ significantly between the 2 groups. This suggests that a decreased cranial BF is an indicator of a poor long-term prognosis.

Long-Term Prognosis for Cerebral Infarction in Relation to Brain Circulation — A 7-Year Follow Up Study

Masatoshi Fujishima, M.D., Katsuya Nishimaru, M.D., and Teruo Omae, M.D.

REFERENCES


From Second Department of Internal Medicine, Faculty of Medicine, Kyushu University, and Third Department of Internal Medicine, Faculty of Medicine, Fukuoka University, Fukuoka City, Japan.
Reprint requests to Dr. Fujishima, 2nd Dept, Internal Medicine, Faculty of Medicine, Kyushu University, Maidashi 3-1-1, Higashi-Ku, Fukuoka City 812, Japan.
The following criteria were used in the assessment of severity of neurologic deficits and associated diseases:

1. Severity of stroke — Evaluated according to a rating scale which is based primarily on motor function.①
   0 = no neurologic deficit, 1 = hemiparesis, 2 = hemiplegia.
2. Hypertension — Based on the blood pressure level and the grade of hypertensive vascular changes, a previous history of hypertension, in-hospital blood pressure level equal to or greater than 160/95 mm Hg, hypertensive retinopathy and ventricular hypertrophy on ECG. The details of this scoring have been reported previously.②

Results

According to their cranial BF values, the patients were classified into two major groups; one having normal cranial BF (1500 ± 390 ml/min: mean ± 2 SD) and the other having subnormal cranial BF (less than 1110 ml/min). Table 1 gives a clinical summary of the 77 patients on entry into this study. The average age and the number of the patients who had grade 2 severity neurologic deficits was greater in the subnormal cranial BF group. Hypertension, laterality of involvement of the brain or the interval from the onset to cranial BF study did not differ between two groups.

During the follow up period, 27 patients had 41 recurrent cerebrovascular episodes; two were transient ischemic attacks, two were subarachnoid hemorrhage and the remaining 37 cerebral infarction. Sixteen patients died from stroke (15 of recurrent attack and 1 of original stroke) and another 15 patients died of various diseases other than stroke (3 of stomach cancer, 3 of pneumonia, 2 of myocardial infarct, 2 of peritonitis and 1 of each of the following diseases: lung cancer, colon cancer, uremia, carbon monoxide intoxication and a traffic accident.)

Table 2 summarizes the number of recurrences and deaths during the 7-year follow up by cranial BF level and age. Of

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**Table 1 Clinical Summary of 77 Patients with Cerebral Infarction at Entry into Study**

<table>
<thead>
<tr>
<th>CBF</th>
<th>Cases (M:F)</th>
<th>Age (yrs)</th>
<th>Hypertension</th>
<th>Severity of neurologic deficits (grade)</th>
<th>Latency of involvement of brain</th>
<th>Interval from onset to CBF study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>31 (23:8)</td>
<td>53.7±1.9</td>
<td>-</td>
<td>15 16</td>
<td>24 7</td>
<td>13 18</td>
</tr>
<tr>
<td>Subnormal</td>
<td>46 (36:10)</td>
<td>59.8±1.5</td>
<td>+</td>
<td>12 34</td>
<td>27 19</td>
<td>20 26</td>
</tr>
</tbody>
</table>

*Values are mean ± SEM. See text for further explanations.

CBF = Cranial blood flow.

Cranial BV = \( Vp \times \frac{Ch}{Cp} \times \frac{Cp}{Ch} \) (ml)  (1)

where \( Vp \) is the volume of saline with an adequate amount of RISA contained in a plastic model of the human skull (phantom); \( Ch \) is the count rate of radioactivity from the patient’s head determined 5 min after intravenous RISA injection; \( Cp \) is the count rate of radioactivity in the phantom head held in the same position as the patient’s head; \( Ch \) is the count rate of radioactivity of the patient’s blood, and \( Cp \) is the count rate of the saline with RISA in the phantom.

Cranial BF is calculated by the following equation:

Cranial BF = \( \frac{\text{Cranial BV}}{TT} \times 60 \) (ml/min)  (2)

The details of this technique and the methodological validity have been reported elsewhere.③
TABLE 3  

<table>
<thead>
<tr>
<th>CBF Level</th>
<th>Cases</th>
<th>Death (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>normal</td>
<td>31</td>
<td>3 (9.7)</td>
</tr>
<tr>
<td>slight</td>
<td>20</td>
<td>4 (20.0)</td>
</tr>
<tr>
<td>moderate</td>
<td>17</td>
<td>5 (29.4)</td>
</tr>
<tr>
<td>severe</td>
<td>9</td>
<td>4 (44.4)</td>
</tr>
</tbody>
</table>

slight: mean - 2SD > CBF > mean - 3SD, 
moderate: mean - 3SD > CBF > mean - 4SD, 
severe: mean - 4SD > CBF.

28 patients aged 60 years or over who had a decreased cranial BF, 10 patients (35.7%) died of stroke and 9 (32.1%) from other causes, their combined death rate (67.8%) was significantly higher than for those below 40 with normal cranial BF, (0.5%), but not significant when compared with normal cranial BF patients aged 60 years or over because of the small number of patients. 

Table 3 shows that death rate for stroke is consistently increased when related to the degree of decrease in cranial BF. The death rate was 44.4% in these patients who had a severe reduction of cranial BF and 9.7% in those with normal cranial BF. 

Figure 1 shows the survival rate in the 2 groups during the follow up period. The cumulative survival rate was consistently lower in the subnormal cranial BF group than for the normal cranial BF group. This difference reached significance at 5- and 7-year intervals from onset. 

In 46 survivors, the severity of stroke at the end of 7-year follow up is summarized in table 4. Four patients (17%) in the normal cranial BF group and only 1 (5%) of the abnormal cranial BF group had a complete recovery.

Discussion

The validity of the intravenous isotope technique in cranial blood flow studies has been discussed by many investigators. The hemispheric dilution curve obtained from one collimated detector is composed of radioactivity passing through the cerebral hemisphere and tissues supplied by the external carotid artery. Less than 10% of the dilution curve is generated by radioactivity from external carotid flow. The cranial BF value for normal subjects measured by our intravenous RISA method is somewhat greater than that by 131I antipyrine technique developed by Reinmuth et al. Nilsson et al. demonstrated a good correlation between the intravenous and the 133Xe clearance method. The former method tends to over-estimate cerebral blood flow because of the contribution from the external carotid artery. This error, however, is constant over the whole range from normal blood flow values to zero blood flow. Therefore, a decrease in cranial blood flow implies largely a decrease in cerebral blood flow. 

According to Marquardsen’s retrospective study of a large number of patients with acute cerebrovascular diseases, the factors affecting long-term prognosis are: a past history of heart failure, coronary artery disease, hypertension, signs of diffuse cerebral damage including dementia and urinary or bowel incontinence, an abnormal ECG, poor recovery of motor function, failure to regain independence. In his series the principal causes of death among stroke survivors were recurrent stroke, myocardial infarction, heart failure and/or bronchopneumonia, pulmonary infarction and uremia. 

During a 7-year observation in the present study, 35.1% of all 77 patients experienced a recurrent stroke, and 40.3% died; 20.8% from stroke and the remaining 19.5% from other causes. According to other investigators, cumulative fatality rates of survivors for stroke are variable and range from 44 to 58% for 5 years. In Pincock’s 8-year follow up study, 11.9% of 101 survivors with an average age of 63.5 years died from stroke, and in Robinson’s series, 25.0% of 737 patients. From our results, the rate for stroke death during a 7-year period was related to the cranial BF level, 9.7% of those with normal cranial BF and 28.3% of those with subnormal cranial BF died from stroke. Death from stroke was more frequent in those with severe reduction of cranial BF.

Two important factors influencing survival occur in the subnormal cranial BF group. First, the average age of this group was slightly greater than the other. There was 30% difference in survival rate between the patients with an average age of 53.7 years who had normal cranial BF and those of 59.8 years who had subnormal cranial BF. This difference could not be explained by age-difference alone. Secondly, a greater number of patients with grade 2 severity of neurologic deficit were found in the subnormal cranial BF

![Figure 1. Cumulative survival rate of patients with cerebral infarction who had normal cranial BF and who had subnormal cranial BF. At 5 and 7 years after onset, the difference is statistically significant.](image-url)
group. Robinson et al. found that the severity of the original stroke is correlated with mortality among survivors. He found a significant difference in mortality at 3 years of observation between the stroke survivors with grade 1 neurological signs and symptoms or no residual disability as compared to those with more severe residual disability. This difference did not reach 15% at 3 years of follow up and became smaller at 7 years. The influence of severity of neurologic deficit on the survival rate in our series is minimal, less than 15%.

Two other important factors influencing long-term mortality — the level of blood pressure and the presence of heart disease — appear independent of the direct consequences of the stroke itself. Marshall and Kaeser et al. have shown that long-term mortality among stroke survivors whose diastolic blood pressure exceeds 110 mm Hg is significantly greater than among those whose pressure is below this level. In the present study, half of the patients with normal cranial BF and two-thirds of those with subnormal cranial BF had hypertension, the difference in the mortality rate between the 2 groups could not be explained by the presence of hypertension alone. Heart disease is another important factor influencing long-term survival. However, in this study there were only 2 deaths from myocardial infarction, 6.5% of all deaths or 13.3% of deaths from various causes other than stroke. This rate was lower than for several other studies.

The stroke survivors whose cranial BF is decreased tend to have a higher mortality for stroke or from other causes than those whose cranial BF remains normal. Cranial BF measurements are valuable not only in assessing the pathophysiological state of cerebral infarction but also in predicting the prognosis of stroke patients.

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