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.

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.

stroke who have a decreased cerebral or cranial blood flow might be worse than for those who have a normal blood flow. It is not known whether recurrence, and long-term mortality are different in these two groups of patients.

Methods

Of 260 patients admitted to our clinic for evaluation of cerebrovascular diseases between 1962 and 1967, 153 had had cerebral infarction. Of these 153 patients, 77 were selected for study. They had had a stroke within the

THERE HAS BEEN no report of a prospective study on the long-term prognosis of patients with cerebral infarction 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
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.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.

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 original stroke) and another 15 patients died of various diseases other than stroke. Table 2 summarizes the number of recurrences and deaths during the 7-year follow up by cranial BF level and age. Of

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Clinical Summary of 77 Patients with Cerebral Infarction at Entry into Study</th>
</tr>
</thead>
<tbody>
<tr>
<td>CBF</td>
<td>Cases (M:F)</td>
</tr>
<tr>
<td>Normal</td>
<td>31 (23:8)</td>
</tr>
<tr>
<td>Subnormal</td>
<td>46 (36:10)</td>
</tr>
</tbody>
</table>

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

CBF = Cranial blood flow.

Cranial BF was calculated by the following equation:

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

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

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Recurrence of Stroke and Death from Various Causes Related to CBF Level and Age at Entry</th>
</tr>
</thead>
<tbody>
<tr>
<td>CBF</td>
<td>Age (yrs)</td>
</tr>
<tr>
<td>normal</td>
<td>&lt;60</td>
</tr>
<tr>
<td></td>
<td>≥60</td>
</tr>
<tr>
<td></td>
<td>Total</td>
</tr>
<tr>
<td>subnormal</td>
<td>&lt;60</td>
</tr>
<tr>
<td></td>
<td>≥60</td>
</tr>
<tr>
<td></td>
<td>Total</td>
</tr>
<tr>
<td>Total</td>
<td>77</td>
</tr>
</tbody>
</table>
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.1-12 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 curves is generated by radioactivity from external carotid flow.8 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.8 Nilsson et al.4 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.9 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,7 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, the 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
definitely infrequent as compared with those in the group. Robinson* 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 Kaeser10 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.8, 9, 14 The lower mortality from heart disease in our series seems due to ethnic origin; in the Japanese population the incidence of coronary heart disease and cardiac deaths are definitely infrequent as compared with those in Caucasians.10

Prosenz et al.16 have reported a significant difference in cerebral blood flow values between one group of patients with stable or increasing neurological deficits and one with transient or improving neurological deficits during an average follow up of 16.9 months. They concluded that regional cerebral blood flow measurements permit the prediction of the future clinical course of the individual patients. Yamaoka et al.17 have also described a higher incidence of recurrent infarction in patients whose cerebral blood flow did not return to normal after the original attack. 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.

References

Long-term prognosis for cerebral infarction in relation to brain circulation--a 7-year follow-up study.
M Fujishima, K Nishimaru and T Omae

*Stroke*. 1977;8:680-683
doi: 10.1161/01.STR.8.6.680

*Stroke* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1977 American Heart Association, Inc. All rights reserved.
Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/8/6/680

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in *Stroke* can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to *Stroke* is online at:
http://stroke.ahajournals.org//subscriptions/