Characteristics and Survival of Patients With Brain Stem Infarction

BY RAINER FOGELHOLM, M.D., AND KARI AHO, M.D.

Abstract: Characteristics and Survival of Patients With Brain Stem Infarction

A retrospective study of 141 patients with ischemic brain stem infarction admitted to the Department of Neurology, University of Helsinki, during 1966 to 1973 was performed. The patients were contacted by mail in January and February, 1974; in case of death, the death certificates were procured. The follow-up period was from 4 to 99 months (median 46.5 months), during which a total of 39 patients had died. A life table analysis gave a 50% probability of a seven-year survival after the stroke. Survival was similar for men and women, and age appeared to have little influence on the prognosis, with only a slightly higher case fatality in old age. Soft palate paralysis, disturbed sensorium, need of special treatment measures (feeding by gastric tube, intravenous infusions, etc.) during the acute phase, abnormalities in the ECG (T-wave negativity, S-T segment depression), fasting blood glucose 100 mg/100 ml or higher, and an abnormal EEG (slowing down of alpha rhythm alone or in association with paroxysmal and/or focal disturbances) were all associated with high case fatality. Preceding TIAs, blood pressure level, serum cholesterol and triglyceride values, and aortic arch angiogram findings, on the other hand, had no effect upon the prognosis. The effects of body build on prognosis remained obscure.

Additional Key Words
- Blood pressure
- Electrocardiogram
- Serum triglycerides
- Body build
- Aortic arch angiogram
- Electroencephalography
- TIA
- Blood glucose
- Cigarette smoking
- Serum cholesterol

Numerous syndromes following ischemic infarction in the territory of the vertebrobasilar arterial system have been well known since the last century. Although the proportion of brain stem infarctions of all brain infarctions has been estimated between 5% and 15%, very little attention has been paid to this clinical entity, its prognosis, and various factors associated with the prognosis. In the present study we have analyzed the survival of patients with brain stem infarction, and present factors that may help in assessing the prognosis of the patient.

Patients and Methods

The patient records in the Department of Neurology, University of Helsinki, for the years 1966 to 1973 were reviewed. A total of 142 patients with brain stem infarction were found. Etiological causes other than ischemic were excluded by all relevant methods, including neuroradiology, EEG, brain scan, CSF examination, etc. Also excluded were TIAs, by accepting only cases with symptoms and signs lasting for more than 24 hours. Patients with vertigo with or without auditory phenomena, although lasting for more than 24 hours, were not included in the present material unless they had other evidence of CNS involvement.

The majority of the patients had symptoms and signs of unilateral cranial nerve involvement associated with contralateral motor and/or sensory disturbances, and/or ipsilateral atactic disturbances of the extremities.

The following data were extracted from the case histories: (1) whether or not the stroke was preceded by TIAs, (2) the patient's subjective symptoms, (3) objective findings during the acute phase of the disease (80% of the patients were examined in our department during the first week after stroke, and 48% during the day of stroke), (4) the degree of dependence during the acute stage of the disease, (5) body build expressed as Quetelet's index (weight [kilogram] ÷ height [centimeter]^2 × 100), (6) blood pressure readings during the first day of stroke, and later the lowest value while in the hospital, (7) the electrocardiogram coded according to the Minnesota code by a well-trained nurse, (8) the serum cholesterol and triglyceride values, (9) the fasting blood glucose values and results of the oral glucose tolerance test, (10) the results of aortic arch angiograms, and (11) the results of electroencephalography. As a rule, the ECG, serum lipid and blood glucose estimations were performed during the first two to three days in the hospital.

Statistical assessment was carried out with either the chi-square or Student's t-test. In January and February, 1974, a questionnaire was mailed to the patients. The patients were asked about working capability and independence in activities of daily living before and after the stroke, about smoking and coffee habits, and about height and weight. An answer was obtained concerning 137 patients or, in cases of death or severe disability, from a near relative. Of the remaining, five were contacted by phone, and only one patient could not be traced and had to be discarded from the analysis.

The age and sex distribution of the material is shown in table I. The median follow-up period was 46.5 months (range 4 to 99 months) for the total patient material, being slightly longer for nonsurvivors than for survivors (51.5 versus 45.2 months).
BRAIN STEM INFARCTION

TABLE 1
Age and Sex Distribution

<table>
<thead>
<tr>
<th>Age</th>
<th>Sex</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th>Mean ± SD</th>
</tr>
</thead>
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<tr>
<td></td>
<td>Men</td>
<td>0</td>
<td>9</td>
<td>30</td>
<td>31</td>
<td>26</td>
<td>2</td>
<td>98</td>
</tr>
<tr>
<td></td>
<td>Women</td>
<td>1</td>
<td>1</td>
<td>13</td>
<td>21</td>
<td>7</td>
<td>0</td>
<td>43</td>
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<tr>
<td>Total</td>
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<td>1</td>
<td>10</td>
<td>43</td>
<td>52</td>
<td>33</td>
<td>2</td>
<td>141</td>
</tr>
</tbody>
</table>

Results

CASE FATALITY RATE
During the follow-up period a total of 39 patients had died. The causes of death are shown in table 2. The causes of death were obtained from the death certificates of all patients except one, whose death certificate could not be found.

A life table analysis of the data gives a 92% probability of surviving the first year, 81% the third year, 68% the fifth year, and 51% the seventh year after stroke (fig. 1). It should be noted that during the first four weeks of illness only seven patients (five men and two women) died. As is evident from table 2, the majority of deaths were due to cardiovascular causes, half of these due to cerebrovascular and half to cardiac causes.

The case fatality for men was slightly higher than for women (29% versus 23%) but the difference was not significant. When analyzed according to age no significant association could be found between age and high fatality rate, although among women a trend to higher case fatality with advancing age could be noticed (fig. 2). The mean age of the deceased was higher in both men (54.8 ± 9.3 versus 51.5 ± 9.0 years, NS) and women (56.9 ± 6.8 versus 50.4 ± 8.0 years, P < 0.05).

ASSOCIATION OF VARIOUS FACTORS WITH THE PROGNOSIS
TIAs preceding the brain stem infarction were encountered in 39 cases (27%), somewhat more commonly among men (31%) than women (21%). The prevalence of preceding TIAs was equal in both survival and nonsurvival groups.

The distribution of various subjective symptoms from the cranial nerves (visual field defects, diplopia, sensory and/or motor symptoms from the face, dysphagia, and speech disturbance) was similar in survivors and nonsurvivors. Of the subjective symptoms from the extremities (sensory, paretic, atactic), ataxia was reported significantly more often by the survivors (20% versus 12%), but it cannot be regarded as very reliable because of the nature of the complaint.

Of the various positive findings in cranial nerves II through XII, paresis of the soft palate was the only one in which the distribution between survivors and nonsurvivors was not equal. It was observed significantly more often (35% versus 54%) among the nonsurvivors (P < 0.05).

Neurological findings from the extremities (paresthesia, sensory impairment, ataxia) were similar in both survival groups. This was also true with respect to vomiting, disturbance in equilibrium, and nystagmus. Disturbed sensorium, most often in the form of somnolence, was encountered significantly more often among the nonsurvivors (9% versus 39%, P < 0.0005).

The need for special nursing measures during the acute stage of the illness seemed to be in close correlation with an adverse prognosis. About 60% of all patients, both survivors and nonsurvivors, were
bedridden during the acute phase. The necessity of intravenous fluid therapy, feeding by gastric tube, urinary catheterization, tracheostomy, and artificial ventilation was significantly more common among the nonsurvivors (P < 0.005). A closer analysis shows that the need for these measures was a strong predictor of early fatality. Seven of the 18 nonsurvivors who needed these special treatments died during the first four weeks of the illness, compared with none of the 21 nonsurvivors who did not need any special treatment ($X^2 = 9.9, P < 0.005$).

As a measure for body build, Quetelet's index was used in the calculations. Figures for height and weight were obtained for all but four men. The results showed that the nonsurviving men were leaner and the nonsurviving women more heavily built than the corresponding survivors (table 3).

Blood pressure readings during the first day of illness were available in 131 cases, 89 men and 42 women. The results are shown in table 4, indicating no significant difference between the survival groups. A closer analysis of the nonsurvivors did not disclose any difference in blood pressure values between early (≤ 4 weeks) and late deaths. During the hospital stay, the mean values of systolic blood pressure decreased by 31 to 37 mm Hg and no significant difference was found between the survival groups. The decrements in the mean diastolic pressures were 16 to 26 mm Hg and again no difference between the survival groups was seen (table 5).

An ECG was available for 136 of the patients. The Minnesota code takes into account the Q and QS items, axis items, high R-waves, S-T depression, T-wave items, A-V and ventricular conduction abnormalities, and arrhythmias. As a total, ECGs with some abnormality were more often encountered among the nonsurvivors. The figures were 75% and 59% for men and 67% and 45% for women, but the differences did not reach statistical significance.

An analysis of the following items was performed: Q and QS items, left axis deviation, high R-wave indicating left ventricular hypertrophy, S-T segment depression, and T-wave negativity and isoelectricity. The only items associated with an adverse prognosis were a negative or isoelectric T-wave in the leads projecting the left ventricle, and S-T segment depression. T-wave abnormalities were found in 57% of the nonsurviving men compared to 22% of the survivors (P < 0.001), and in 36% of the nonsurviving women compared to 13% in the survivors (P < 0.01). S-T segment depression also was encountered more frequently among the nonsurvivors. The difference in men (32% versus 25%) was not statistically significant, whereas in women there was a significant difference (56% versus 13%, P < 0.01). Conduction defects and arrhythmias were too infrequently encountered to allow statistical analysis.

Serum cholesterol values were available in 132 and triglyceride values in 114 of the cases. The means of cholesterol and triglyceride values according to survival are shown in table 6.

In men, the lipid values in the survival groups were quite similar. Nonsurvivor women, however, had significantly higher mean values of both cholesterol

<table>
<thead>
<tr>
<th>Sex</th>
<th>Survivors (Mean ± SD)</th>
<th>N</th>
<th>Nonsurvivors (Mean ± SD)</th>
<th>N</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men</td>
<td>0.268 0.033 69</td>
<td></td>
<td>0.251 0.040 25</td>
<td></td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>Women</td>
<td>0.262 0.047 33</td>
<td></td>
<td>0.276 0.066 10</td>
<td></td>
<td>NS</td>
</tr>
</tbody>
</table>

TABLE 3
Body Build Expressed as Quetelet's Index According to Survival
and triglycerides than the survivors. In this connection the small number of observations in the nonsurvival group must be noted. On the other hand, when two diabetic nonsurvivors with very high cholesterol (658 mg/100 ml and 337 mg/100 ml) and triglyceride (1,176 mg/100 ml and 618 mg/100 ml) values are deleted, the mean values come closer to the values of survivors, although still a bit higher (cholesterol 300 mg/100 ml, triglycerides 172 mg/100 ml).

An oral glucose tolerance test was performed on 62 men and 23 women and, in addition, a fasting blood glucose value was available for 29 men and 17 women. Those patients were classified as diabetics whose fasting value exceeded 100 mg/100 ml, one-hour value 180 mg/100 ml, and/or two-hour value 120 mg/100 ml. Fifty-nine (45%) of the patients were diabetics, but no clear association could be found between diabetes and survival. When, on the other hand, the calculations were performed on the fasting values only, values of 100 mg/100 ml or higher were more prevalent among the nonsurvivors. The figures for men were 26% and 11% (X² = 3.3, NS) and for women 40% and 0% (X² = 13.3, P < 0.001).

An aortic arch angiogram was performed only on about half of the patients (77/141), more often on the survivors (60%) than the nonsurvivors (41%). Thus it is obvious that the results obtained from these angiographical examinations must be taken with caution. The subclavian, common carotid, internal carotid, and vertebral arteries were analyzed to determine the presence of occlusion. Occlusion was found twice in an internal carotid artery and 35 times in a vertebral artery. In the vertebras the occlusion was on the left in 13 cases, on the right in 16 cases, and bilateral in three cases. When analyzed according to the fate of the patient, 45% of the survivors and nonsurvivors had occlusion of one or both vertebral arteries. Thus no difference could be found. A correlation between lateralization of the symptoms from the brain stem and an occluded vertebral artery was found. With a 70% to 80% probability, the symptoms emerged from the same side of the brain stem as the occluded vertebral artery. Because of the great number of nonexamined patients, especially among the nonsurvivors, a detailed scoring of the stenotic lesions was not attempted.

Electroencephalography was performed in 136 cases, the registration being made during the first week after stroke in 46 cases and at a later occasion in the others. Early registration was as frequent among the survivors as among the nonsurvivors. A normal alpha or low voltage fast registration was obtained significantly more often in the survival group (X² = 4.6, P < 0.05). Among the abnormalities encountered, the prevalence of a generalized slowing down of the alpha rhythm was higher among the nonsurvivors (X² = 6.2, P < 0.025), as were also generalized slowing associated with paroxysmal phenomena and/or focal disturbances (X² = 4.2, P < 0.05).

Data on smoking habits were obtained in 133 cases, 92 men and 41 women. Classifying those who had never smoked and the ex-smokers together as nonsmokers, 44% of the men and 61% of the women were nonsmokers. There was no difference between the survival groups according to smoking habits.

Data about coffee drinking habits were too incomplete to allow analysis.
TABLE 6
Serum Cholesterol and Triglyceride Values (mg/100 ml) According to Survival

<table>
<thead>
<tr>
<th>Sex</th>
<th>Cholesterol (Mean ± SD)</th>
<th>Triglyceride (Mean ± SD)</th>
<th>N</th>
<th>Nonsurvivors (Mean ± SD)</th>
<th>Triglyceride</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cholesterol</td>
<td>263.4 ± 50.9</td>
<td>67</td>
<td>263.3 ± 61.0</td>
<td>24</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>Triglyceride</td>
<td>164.8 ± 92.0</td>
<td>62</td>
<td>163.8 ± 63.9</td>
<td>20</td>
<td>NS</td>
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<tr>
<td>Women</td>
<td>Cholesterol</td>
<td>259.7 ± 61.0</td>
<td>31</td>
<td>339.4 ± 132.6</td>
<td>10</td>
<td>P &lt; 0.05</td>
</tr>
<tr>
<td></td>
<td>Triglyceride</td>
<td>135.1 ± 58.0</td>
<td>25</td>
<td>357.0 ± 340.9</td>
<td>9</td>
<td>P &lt; 0.05</td>
</tr>
</tbody>
</table>

Discussion
When one considers the results obtained in the present study, one must keep in mind that the material is selective. First, all patients with brain stem infarction admitted to our hospital were not treated in the Department of Neurology, but sometimes, especially the older patients, were treated in the Department of Medicine. Second, severely ill patients could be admitted directly to the intensive care unit and die there. Third, there may be a selection of patients admitted from other hospitals, the old and most severely ill being treated in the hospital of primary admission.

Nevertheless, the results of the present analysis give some useful information on the prognosis of brain stem infarction and on factors associated with the fate of the patients. Only a few of the patients were treated for short periods by anticoagulation, a therapy possibly altering the prognosis. Antihypertensive therapy was given to only 25 of the patients at the time of hospitalization.

The probability of survival seems to be somewhat better in the present series than in earlier studies on brain stem infarction and on factors associated with the fate of the patients. Only a few of the patients were treated for short periods by anticoagulation, a therapy possibly altering the prognosis. Antihypertensive therapy was given to only 25 of the patients at the time of hospitalization.

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The causes of death in the present material are similar to those in most of the earlier studies, although Marshall and Shaw found in their series with 90% hemispheral lesions that cerebrovascular causes accounted for twice as many deaths as cardiac causes.

The numerous factors analyzed with respect to prognosis showed no difference between the sexes, nor a clear-cut correlation between old age and high case fatality. This is in contradiction with the statements of many earlier observers, although actually the figures of Currier et al. give very little support to age as an important factor in determining the prognosis of brain stem infarction.

Among the many subjective symptoms analyzed, ataxia was the only one to have some prognostic value. Patients who did complain of ataxia fared better than the others. It might be that these patients were more alert and capable of describing their motor disturbances more exactly than only as nonspecific weakness. Of the objective findings in the neurological status, soft palate paralysis and disturbed sensorium were associated with an adverse prognosis. Patients who had to be fed by gastric tube or given intravenous infusions as a consequence of these conditions fared worse than the others. Grave signs also were urinary catheterization, tracheostomy, and the need for artificial ventilation.

That the nonsurvivor men were leaner than the survivors seems to us difficult to explain. The correlation analysis of the various factors showed that there was an inverse correlation between cigarette smoking and Quetelet's index (r = -0.198, P < 0.05). On the other hand, no association between smoking habits and survival was found.

The blood pressure values, whether registered at the very beginning of the illness or at a later date, were not in correlation with the patients' prognosis. This is in contradiction to most of the previous reports concerning cerebrovascular disease. Robinson et al., however, in their retrospective analysis of more
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than 800 ischemic stroke patients with a follow-up period of 9 to 19 years found no adverse effect of hypertension on the long-term prognosis. The fact that 18% of the patients in the present series received antihypertensive therapy may in some way mask the effects of high blood pressure, but other factors may be involved.

Abnormalities in the ECG were more common in the group of nonsurvivors, and a closer analysis of the items coded from the ECGs revealed that at least negative or isoelectric T-wave and S-T segment depression were associated with an adverse prognosis. There may be other signs in the ECG that point in the same direction but, e.g., conduction defects and arrhythmias were encountered too infrequently to allow analysis.

The value of the level of serum lipids as a predictor of the patient’s future must be taken as negligible. With respect to blood glucose, fasting values of 100 mg/100 ml or higher were more prevalent among the nonsurvivors.

Aortic arch angiogram was performed on only half of the patients but the high prevalence of vertebral artery thrombosis found in 45% of the angiograms should be noted. This figure is much higher than in studies that include all types of ischemic cerebrovascular disease, in which vertebral artery thrombosis is encountered in about 6% to 13%. The side of occlusion predicts the side of the brain stem from which the ischemic symptoms emerge. As a predictor of the patient’s prognosis, however, the angiogram seems to be of little value.

The EEG, when normal, points to a favorable prognosis. Abnormalities, especially a generalized slowing of the normal alpha rhythm alone or in association with paroxysmal phenomena and/or focal disturbances, seem to indicate a poor prognosis.

Acknowledgments

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4. Aho K: Unpublished data
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