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The Prognosis for Patients with Cerebrovascular Stroke and Transient Ischemic Attacks

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ABSTRACT

The prognosis for 281 patients with cerebrovascular stroke and 44 patients with TIA is presented. These patients were registered during a prospective epidemiological survey of cerebrovascular diseases in the community of Söderhamn. There was an average population of about 32.000 during the study period. More than 30 % of the stroke patients died during the first 3 months. After 4 years the mortality was about 70 % in stroke and 40 % in TIA patients. The prognosis was tested towards symptoms and signs. Eleven signs were significantly correlated to adverse outcome in the stroke group, e.g. Babinski's sign present, complete extremity paresis, lowered level of consciousness, fever, tachycardia, anemia and elevated systolic blood pressure. During follow-up at intervals of 1, 2 and 3 years about 60 % of the stroke survivors were at home, 20 % in old age homes, and 20 % in hospitals.

Key words: Stroke, TIA, prognosis, follow-up.

Abbreviations: TIA = transient ischemic attacks, RIND = reversible ischemic neurological deficit, BP = blood pressure, CSF = cerebrospinal fluid.

INTRODUCTION

Cerebrovascular stroke is a medical urgency as the lesion may be lethal by affecting the vital centers of the brain stem (6, 8, 18, 20, 22). Also, complications due to immobilization or concomitant diseases contribute to immediate as well as late mortality (14, 19). Early prognostication is necessary for the selection of patients needing intensive care. In spite of improved laboratory techniques, we are dependent upon the recognition of alarming symptoms and signs. Combination of such variables may also be used as prognostic scores (4, 9).

Knowledge about the long-term prognosis is of certain importance for rational utilization of rehabilitation facilities. The placement of patients

will also be facilitated, if the outcome could be accurately predicted. Finally, the proportion of disordered people during subsequent years may be calculated, if the average survival time is known and the incidence of new cases is determined (12).

In this paper we present, on the basis of a prospective epidemiological study, the mortality rates, the signs and symptoms with adverse influence on the prognosis and also the further placement of patients with stroke and TIA.

PATIENTS AND METHODS

All new cases of stroke and TIA were registered in the community of Söderhamn during the period May 1, 1975 and April 30, 1978. The study population was on an average 32.000. The method for tracing and registration has been described in detail elsewhere (25). All age-classes, except children, were included. Interviews were conducted and physical examinations were performed by the members of the medical staff at the Söderhamn Hospital as soon as the patients became known (Table 1). A special form was constructed for the purpose of this study, including a neurological status schedule. In 90.7 % the initial examination took place at our hospital. Two (0.6 %) of the patients were registered after sudden death due to autopsy-verified cerebrovascular disease, while 8,7 % were examined at home or in other hospitals. Controls were made at intervals from the debute of about 3 months and 1, 2 and 3 years.

Table 1. Time from onset of symptoms until examination in 281 patients with stroke and 44 patients with TIA.

Time in hours	Stroke %	TIA %
< 1	7.1	15.9
1 - 2	12.1	2.3
2 - 3	9.3	15.9
3 - 6	14.9	29.4
6 - 12	12.8	15.9
12 - 24	9.3	6.8
24 - 48	6.8	0
> 48	27.7	13.6

Long-term anticoagulant treatment was given to 74 patients, of which 34 had cerebral embolism from the heart, 15 had RIND and 25 had TIA. Three TIA patients underwent neck vessel surgery and 3 patients with subarachnoid hemorrhage were operated for ruptured aneurysms.

DEFINITIONS

The definitions of stroke and TIA were in accordance with the recommendations of WHO.

Stroke was defined as "rapidly developed clinical signs of focal (and/or global) disturbance of cerebral function, lasting longer than 24 hours or leading to death with no apparent cause other than vascular". The term "global" mainly applies to the case of subarachnoid hemorrhage.

TIA was defined as "rapidly developed clinical signs of focal cerebral dysfunction of presumed vascular origin not lasting more than 24 hours".

The term recurrent stroke was used for a new stroke taking place more than 3 weeks after an initial stroke.

Cerebral infarction, whatever the cause, was diagnosed if CSF examination, radiological (computed tomography or angiography) or isotope examinations were done without signs of intracranial bleeding. A subgroup was constituted by those with reversible ischemic neurological deficit of longer duration than 24 hours (RIND).

Intracerebral hemorrhage was diagnosed if any of the above mentioned examinations revealed intracranial bleeding and the patient displayed focal neurological deficits. Sub- or epidural hemorrhages were not included.

In the case of subarachnoid hemorrhage the CSF was macroscopically hemorrhagic, while the patient lacked gross neurological deficits of focal type.

The CSF was considered to contain significant amounts of blood, if the red cell count exceeded $10 \times 10^6/l$ and the protein concentration was equal to or more than 0.9 g/l. A xanthochromic specimen, after centrifugation had been rapidly performed, was diagnostic of intracranial bleeding. Also, a slight pleocytosis in CSF, when tapped after more than 24 hours, was thought to represent a hemorrhagic lesion.

The ECGs were classified according to the Minnesota code (3). The following numbers were classified as definite ECG-changes: 1.1.1 - 1.2.8, 2.1 - 2.5, 3.1 - 3.3, 4.1 - 4.4, 5.1 - 5.4, 6.1 - 6.5, 7.1 - 7.6, 8.0 - 8.6, 8.9 and 9.2. Appearence of a pathological Q-wave and/or appearence or disappearence of a localized ST-elevation followed by a T-wave inversion in 2 or more of the 12 leads and 2 S-ASAT values above the upper limit of the reference range with a maximum about 24 hours after onset of symptoms, in combination with a S-ALAT maximum after about 36 hours and lower than the S-ASAT maximum were diagnostics of acute myocardial infarction.

Hypertension was defined according to WHO as BP equalling or exceeding 160 mm Hg systolic or 95 mm Hg diastolic. A single value was not sufficient for diagnosis. In case we lacked written information, a history of continuous treatment with antihypertensive agents was considered sufficient for diagnosis.

Mean BP comprises the mean value of 5 measurements performed on at least 3 different days.

Mean body temperature is the mean of the morning and afternoon values during the first week.

Deaths which were due to increased intracranial pressure or complications of recumbent positioning, e.g. bronchopneumonia, pulmonary embolism, and feeding difficulties, i.e. aspiration, are referred to as stroke-related.

STATISTICS

Life tables were calculated for different subgroups of patients using the Biomedical Computer Programs P-series. The method used is the acturial life table, which groups data by time intervals (7). The range of survival time, in the present case 4 years, is automatically divided into 10 equally spaced intervals. The number of patients exposed to the risk of dying during the interval (r_i) is expressed in the formula $r_i = n_i - \frac{1}{2}c_i$, where n_i = number of patients entering the interval and c_i = number of patients censored during the interval. The censoring was a consequence of the design of the study, as patients were continously registered for 3 years. All follow-ups were stopped on the same date. No patients were lost to follow-up for reasons other than death or censoring. When calculating life tables it was assumed, on the other hand, that all patients were followed from the same date but for different lengths of time (the date for censoring or death). The survival curves were automatically tested for equality with use of the Mantel-Cox and Breslow statistics. The latter, giving greater weight to early observations, will be referred to in this paper.

If data for a certain variable was missing in less than 5 % of the patients, it was assumed that the unknown distribution was the same as the known. If more than 5 % were lacking information, the actual factor was analysed only if knowledge about it was independent of the cooperation of the patient. Then, the possibility of a systematic relationship between missing data and mortality was tested by cross-tabulation. The variables that fulfilled these criteria of independence are displayed in Table 2 and 3. Those influencing the survival curves (Table 2) were cross-tabulated and the chi-square test was performed to determine whether a systematic relationship existed between them.

RESULTS

The mortality after stroke was most pronounced during the first three months, when 34 % of the patients died (Fig. 1a). The first week alone contributed to 13 % (Fig. 1b). There was no significant difference between the sexes during the four-year period. Of the 160 deaths in the stroke

Table 2. Proportion of stroke patients having signs correlated to increased 3-month mortality.

	n	%	P-value
Babinski's sign present	118	42	< 0.001
Lowered level of consciousness	85	30	< 0.001
Complete extremity paresis	81	29	< 0.001
Respiratory abnormality	43	15	< 0.001
Mean body temp. above 38°C	42	15	< 0.001
Eye deviation	37	13	< 0.001
Anemia	26	9	< 0.05
Unequal pupil size	17	6	< 0.05
Heart frequency above 120/min	8	3	< 0.05
Mean body temp. below 36°C	6	2	< 0.001
Mean systolic BP above 200 mm	4	1	= 0.017

Table 3. Variables that did not discriminate with respect to 3-month mortality rate in stroke patients.

	n	%
History of ischemic heart disease	95	34
hypertension	135	48
diabetes	42	15
Definite ECG changes	219	78
Localized neck vessel bruits	20	7
Convulsions	14	5
Acute myocardial infarction	10	4
Elevated EVF	9	3
Diastolic BP		
BPs on admission		
Body temperature on admission		
Serum Na, K and Ca		

group, at least 73 % were stroke-related. The 34 %, who died within 3 months, had an average survival time of 1.5 months while the other 66 % had an average survival time of 46 months, making the mean survival time for the whole group 30.87 months or about 2 years and 7 months.

The survival curves for different diagnostic subgroups of stroke and for TIA patients were not equal (Fig. 2, $p < 0.0001$). Patients with intracerebral hemorrhage, cerebral infarction and unspecified stroke displayed the greatest mortality. The patients with RIND revealed a comparatively low mortality rate during the first period. After that, the slope of the curve was the same as the one for patients with intracerebral hemorrhage, cerebral infarction and unspecified stroke. In patients with subarachnoid hemorrhage all deaths ($n = 5$) occurred during the first four months.

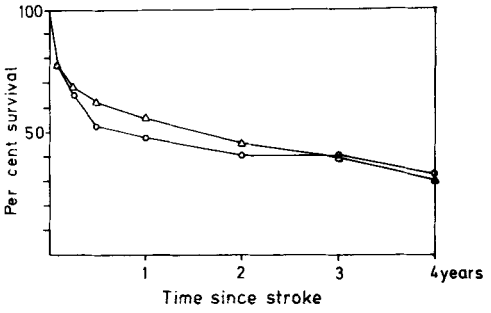

Fig. 1 a.

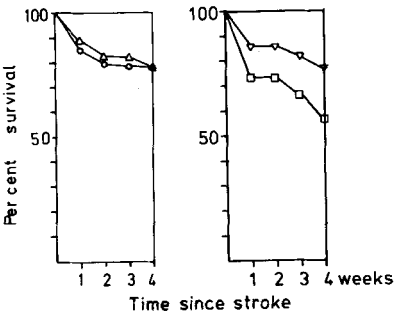

Fig. 1 b. Fig. 1 c.

Fig. 1a and b. Survival after first stroke in 154 men (Δ) and 127 women (o). c. Survival after stroke recurrence with respect to major (□) and minor (▽) symptoms in 57 patients.

The TIA patients showed increasing mortality rates for the successive periods. During the follow-up, four TIA patients out of 10 died in connection with stroke.

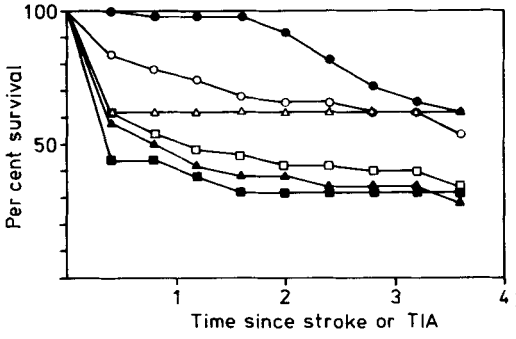

Fig. 2. Survival for patients with different kinds of stroke and for TIA patients. Cerebral infarction (□) n = 99 (35.2 %), intracerebral hemorrhage (■) n = 52 (18.5 %), subarachnoid hemorrhage (Δ) n = 13 (4.6 %), RIND (o) n = 56 (19.9 %), stroke unspecified (▲) n = 61 (21.7 %) and TIA (●) n = 44. Intervals = 4 years x 1/10.

In Table 2 the variables which adversely influenced the three-month survival time are listed. Of these, there was significant correlation between complete extremity paresis and Babinski's sign, and between complete paresis and fever ($p < 0.01$, respectively). Chest X-ray revealed bronchopneumonia in 21 (50 %) of the patients with fever. No correlation was found between fever and type of diagnosis. The survival curves, with respect to level of consciousness, degree of extremity paresis and fever are displayed in Figures 3 - 5.

The variables that did not discriminate with regard to three-month mortality are shown in Table 3. Definite ECG changes were present in 78 % of the stroke and 75 % of the TIA patients (missing data in 5 %). Twenty-five per cent had chronic atrial flutter/fibrillation, while 1 patient had paroxysmal

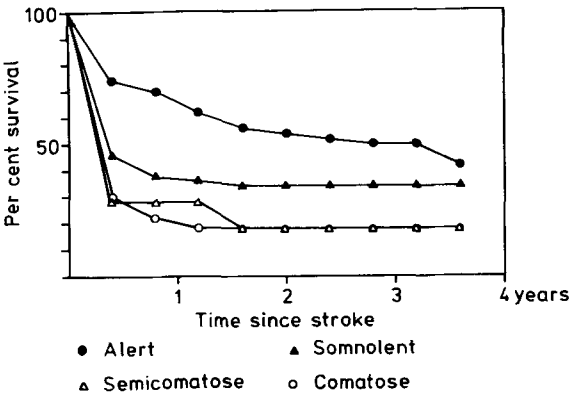

Fig. 3. Survival after stroke with respect to level of consciousness. Altert n = 192 (68.3 %), somnolent n = 47 (16.7 %), semicomatose n = 27 (9.6 %), comatose n = 11 (3.9 %) and missing data n = 4 (1.4 %). Intervals = 4 years x 1/10.

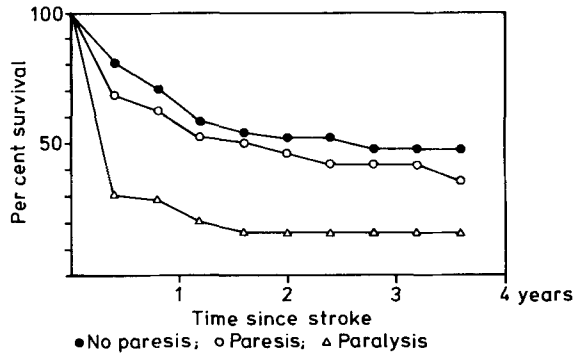

Fig. 4. Survival after stroke with respect to motor strenght in the right arm. No paresis n = 156, paresis n = 80, complete paresis n = 36 and missing data n = 9. Intervals = 4 years x 1/10.

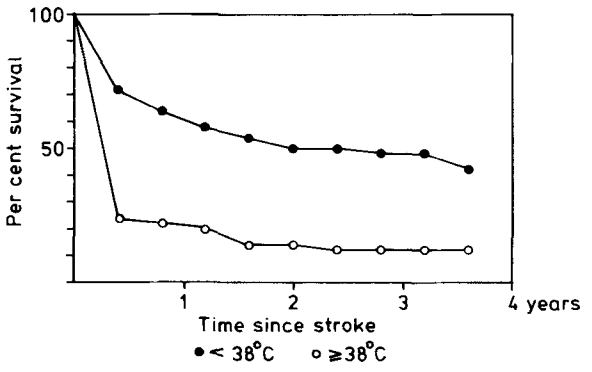

Fig. 5. Survival after stroke with respect to mean body temperature. Temperature less than 38°C n = 196, temperature equal to or more than 38°C n = 42 and missing data n = 43. Intervals = 4 years x 1/10.

atrial fibrillation. Four per cent of the stroke patients fulfilled the criteria for acute myocardial infarction, but none was diagnosed in the TIA group. The frequency of ischemic heart disease, hypertension and diabetes was about the same in the TIA as in the stroke group.

As regards age, the three-month mortality was not influenced, while the proportion of elderly females (80 years or more), and elderly males, (70 years or more), significantly decreased during the first two years in the stroke group ($p < 0.01$ and $p < 0.05$, respectively).

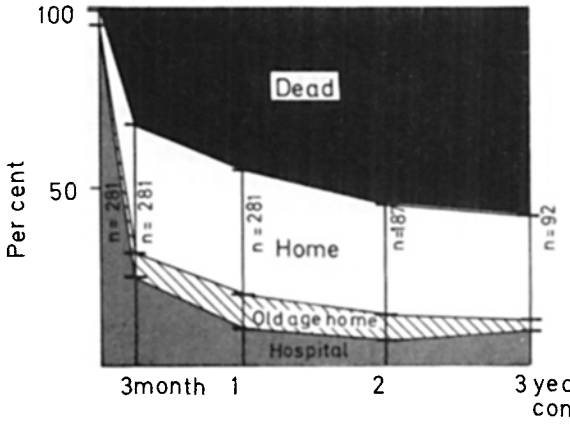

Fig. 6. Distribution of stroke patients by time.

The immediate mortality after each stroke recurrence was about the same as after the initial insult (Figs. 1b and c).

The placement of the patients is displayed in Figures 6 - 7. The majority of the stroke survivors, about 60 %, were at home at the 1-, 2- and 3-year controls, while about 20 % were treated in hospitals or living in old age homes. Initially almost all TIA survivors lived at home, while the percentage in hospital was about 20 % at the 2- and 3-year controls.

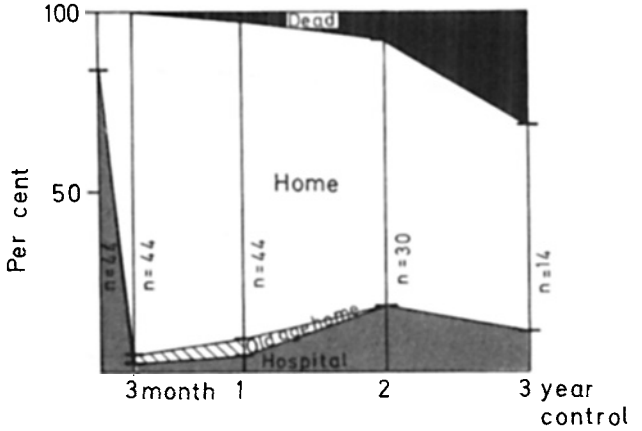

Fig. 7. Distribution of TIA patients by time.

DISCUSSION

This study was designed as a complete census of patients with stroke and TIA in Söderhamn. It may also be possible to generalize conclusions regarding epidemiology to the whole of Sweden, as the distribution of variables like age and sex are similar to those in the whole country (25). On the other hand, information of the outcome for these patients must be used with care, when discussing the natural course of cerebrovascular stroke and TIA, as many were treated with anticoagulants and some were operated. Previous analyses of the influence by anticoagulant treatment in these patients did not, however,

confirm any positive effect on the survival (26). The mentioned problems are common in all modern studies, which include a representative patient population.

The most critical period for the stroke patients in this study was the first three months. This pattern was most pronounced in the patients with subarachnoid hemorrhage and least marked in those with RIND. Regarding patients with intracerebral hemorrhage, cerebral infarction and unspecified stroke the survival curve profiles were similar in contrast to other studies, where the prognosis for patients with intracerebral hemorrhage was worst (1, 13, 24). This may partly be due to our diagnostic criteria, as our infarction group was divided into patients with long- and short-lasting (RIND) symptoms. The diagnosis of intracerebral hemorrhage in the mentioned studies was also based on laboratory examinations, but the relative differences must be interpreted carefully as the quality of the examinations vary, as well as the intensity with which they were performed. The proportion being classified as intracerebral hemorrhage was 18.5 % in the present study as compared to 10 - 16 % in other Nordic countries (1, 24). Regrettably, the diagnostic accuracy will remain a problem particularly in epidemiological studies, and also in an unselected hospital population due to limited capacity for computed tomography of the head and spinal fluid analyses (21). Thus, the recognition of clinical signs, which indicate increased risk for the patient, is most important.

Eleven of the variables, investigated early in the course of the disease (Table 1), were correlated to an adverse outcome. The appearance of such symptoms may thus be taken as an ominous sign. Surprisingly, only complete paresis and Babinski's sign and complete paresis and fever were significantly correlated, though most signs must be measures of a latent variable, i.e. the lesion. This is possibly due to missing data and gives a false picture of the p-values (Table 2), that would be obtained if variables were combined. However, the goal of these analyses was to point out some signs of importance for the prognosis, rather than localizing the site of the lesion in each case. Probably the relationship between paralysis and fever is due to a greater risk for infections in these patients. The adverse influence of fever on the prognosis has been described previously (14). In animal experiments, the brain edema increases with elevation of the body temperature, which is explained by a greater metabolic demand (16). It is well known that multiple signs of brain stem dysfunction are associated with adverse outcome (19).

The observed prevalence of diabetes, 15 %, was about the same as in previous reports (2, 17). The diagnosis of myocardial infarction is complicated by the appearance of enzymes indicative of myocardial affection in serum of stroke patients without conclusive ECG changes (23). Elevation or depression

of the ST-segment, peaked, flat or negative T-wave and different kinds of arrhythmias have been reported in stroke patients (5, 11, 15), but the cause is still obscure. The frequency of patients with chronic atrial flutter/fibrillation is high, about 25 %, in the present as well as another study of aged stroke patients (5). Cerebral embolism of cardiac origin in patients with rheumatic or ischemic heart disease has been thought to justify anticoagulant treatment (10), but the frequency of complications to treatment was considerable in the present material (26).

In the TIA group, the successively increasing mortality rate reflects the high prevalence of cardiovascular diseases as well (26).

Clinical scores, combining certain variables, may be useful when one wants to compare the outcome of subgroups of patients during follow-up (4). The present study indicates that such scores should include neurological signs, but also information regarding respiration, blood pressure and body temperature for the prediction of short-term outcome for life expectancy.

The placement of the stroke and TIA patients during this relatively long follow-up is influenced by many factors. Knowledge of the need for institutional care in a population is important for planning, regardless of the cause. The present figures demonstrate, that about 20 % of stroke survivors need hospital care. No comparable figures for the long-term prognosis in the Nordic countries have been published. On the basis of an English population study Weddel (27) concluded, that the number of disabled at 3 months was a small part of those initially disabled by stroke.

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