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Studies on Cerebrovascular Stroke

III. Long-term Prognosis and Clinical Findings in a Follow-up Study of a Stroke Material

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ABSTRACT

The present paper reports the third part of an investigation of first-time cerebrovascular strokes occurring in people under the age of 70. The long-term prognosis for 214 patients discharged alive from hospital after the acute phase of the stroke is presented. The clinical and laboratory findings for 114 patients alive at the time of a follow-up examination 32 months after the stroke are discussed. The long-term prognosis could be predicted best by a score, calculated from the neurological findings on admission after the acute stroke. Recurrence of stroke was associated with a very high mortality. Forty-five per cent of the patients who survived the first month had died by the time of follow-up. About 15% were able to return to normal life or go back to work. There was a trend among patients originally severely handicapped to improve their performance ability. Factors influencing the chances for rehabilitation are discussed. Among the survivors there was a strikingly high percentage of patients with overt diabetes or decreased glucose tolerance, of patients with arteriosclerotic heart disease and patients with elevated serum triglyceride levels. These findings are discussed.

INTRODUCTION

In two previous papers the epidemiology and short-term prognosis of first-time cerebrovascular strokes in a Swedish county have been discussed (13, 15). In an attempt to predict the immediate mortality a form of score system based on the neurological deficit on admission, turned out to be a useful and very reliable tool. The aim of the present paper is to present the subsequent fate of the patients who were discharged alive and to discuss the influence of various factors on long-term prognosis and rehabilitation.

MATERIAL AND METHODS

The criteria for the selection of patients have been discussed in detail earlier as has the differentiation into the various diagnostic groups (13). The material thus consists of 214 patients under 70 years of age with first-time stroke, discharged alive from the hospital after the acute phase of the disease with the diagnoses cerebral haemorrhage, cerebral infarction or cerebral emoblism occurring during the years 1967–71. The follow-up investigation started on September 1, 1969, and ended on December 31, 1973.

The patients have been traced by means of the hospital records and the Public Office Register in the county. Through the Public Office, information about deaths among patients under observation has been obtained continuously. When a patient was dead, hospital records, autopsy records and death certificates were checked. A total observation time of up to 84 months was obtained for those who entered the study in 1967.

The patients who survived were invited to a three-day examination at the university hospital. The follow-up examinations were intended to be performed 32 months after discharge from hospital following the stroke. This interval was chosen to allow the investigation of survivors of strokes suffered in 1967 to commence at the study's start in 1969. With this interval it could also be assumed that the surviving patients were in a steady state with respect to vocational re-adaptation and the activities of daily living (ADL). The follow-up examination interval was reduced in 8 patients to 24 months when the investigation ended in December 1973. In 6 patients the interval was 34 months. Thus the range was 24–34 months for the total 114 patients.

The follow-up examination started with a detailed medical history concentrating on the time after the discharge from hospital and including treatment in institutions or at home, rehabilitation measures and other forms of support from the community. Any other disease of importance was noted. The records from institutions were checked and further information were gathered from treating physicians, social workers and relatives. Additional information was obtained from the Local Social Insurance Office about the various social insurance benefits received by the patients.

The clinical examination included a detailed neurological status. The degree of handicap was assessed and classified in the following three grades according to Fällström (16):

1. *Moderate physical handicap:* Moderate reduction of

Table I. *Distribution according to diagnosis, age and sex for the whole material (214 patients) on discharge from hospital*

	Age, years			
	≤49 *n*	50–59 *n*	60–69 *n*	Total *n*
Cerebral haemorrhage				
Men	2	1	4	7
Women	2	2	1	5
Cerebral infarction				
Men	8	18	54	80
Women	10	23	67	100
Cerebral embolism				
Men	2	0	8	10
Women	0	4	8	12
Total	24	48	142	214

ability to move about, or moderately reduced function in one arm.

2. *Considerable physical handicap:* Moderate reduction in ability to move about and moderately reduced function in one arm, or capacity to move only with braces or crutches, or greatly reduced function in one arm with the other unaffected, or moderately reduced function in both arms.

3. *Severe handicap:* Dependent on wheel-chair, or severely reduced function in one arm and moderately or severely reduced function in the other, or combination of leg and arm handicap judged to be more severe than moderate, or reduction in ability to move about and moderately reduced function in one arm. Bed-ridden patients are also included in this group.

The blood pressure was registered after 15 min rest twice daily with a mercury sphygmomanometer. Mental abnormalities were noted, and if necessary, an examination by a psychiatrist was performed.

The laboratory analyses included determination of haematocrit, counting of red and white blood cells, erythrocyte sedimentation rate (ESR), electrolytes, uric acid, cholesterol and triglycerides. The serum cholesterol and the triglycerides were assayed in an Isopropanol extract of serum by using a Technicon dual-channel system (N-24 A and N-70). Samples were drawn on 2 consecutive days and the mean values calculated. An intravenous glucose tolerance test (IVGTT) was also performed with a glucose dose of 0.5 g per kg body weight administered as a 50% solution. Blood samples for determination of glucose in plasma were taken at 10 min intervals over one hour. The glucose tolerance was expressed as a k-value calculated from the formula:

$$K=\frac{e\log 2\times 100}{T/2}$$

where the $T_{1/2}$ is the time in minutes required for the concentration to be reduced by half its value.

An X-ray of the chest with determination of the heart-volume in sitting position was performed. Standard 12-channel ECG was registered.

All patients could be traced. Two had settled abroad and one refused to participate in the follow-up. These patients are registered as alive and are included in the life tables (Fig. 5).

STATISTICS

A life table was constructed according to the principles described by Bradford-Hill (19) and Cutler (6) to survey mortality in this consecutive study. The life table for a corresponding model population was obtained from figures in the official Swedish statistics (32). The calculations were performed by computer (program BMD 01S). For testing the correlations between simple single percentages the ordinary chi-square test has been used.

For further analysis of various factors of predictive importance upon the mortality, the AID (Automatic Interaction Detector Computer Program) has been used. The AID-technique has been used earlier in this investigation (15) and is described in detail by Morgan & Sonqvist (31) and Sköldenberg (30).

RESULTS

The sex and age distribution in the whole material and in the diagnostic groups are shown in Table I. The various degrees of handicap on discharge are presented in Table II. The disposal of patients after discharge from hospital is shown in Fig. 1, where even the further transferrals between institutions and home or vice versa have been registered. It is seen from the figure, that it was possible to discharge almost half of the patients with cerebral infarction from institutions back to their homes.

Fig. 2 shows the mortality up to the time of follow-up examination, i.e. after 32 months. At this time the mortality is 45% (97/214). About 75% of the deceased (74/97) died of sequelae of the initial stroke or in a recurrent stroke. It is worth noting that all the deaths within the emoblism group (5 cases) were caused by a recurrence. Among the other deaths, 20 were due to cardiovascular disease, myocardial infarction or heart failure. The remaining three deaths were due to: gastric

Table II. *Handicap on discharge from the hospital*

	Cerebral haemorrhage	Cerebral infarction	Cerebral embolism
No handicap	0	1	0
Moderate handicap	1	42	9
Considerable handicap	10	8	94
Severe handicap	3	43	3
Total	12	180	22

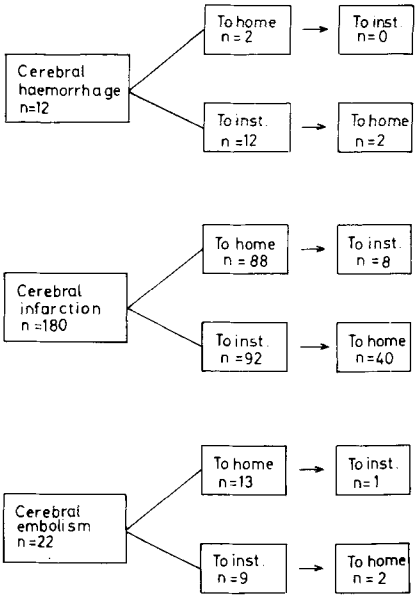

Fig. 1. Patient disposal at discharge from the hospital and subsequent fate.

carcinoma, prostatic carcinoma and one of trauma.

In Table III some factors are analysed with respect to the mortality before follow-up. It will be seen, that there is a slight increase in mortality in the patients over 60 years of age. The difference is not significant, however, when the normally increased mortality in the corresponding population is taken into consideration. The calculation was performed by a modified chi-square test. There is no significant difference between the sexes, nor between diabetics and non-diabetics, or between patients with and without hypertension.

The value of a score-system, based on the neurological symptoms on admission, as a predictor for the acute outcome has been discussed earlier (15). For comparison, the acute and late mortality in the total initial material (344 patients) divided into score-groups is shown in Fig. 3. It is obvious that

Table III. *Age, sex, hypertension and diabetes in relation to mortality up to follow-up. Number of deaths in parentheses*

	Age, years		
	≤49	50–59	60–69
Men	12 (6)	19 (4)	66 (30)
Women	12 (2)	29 (12)	76 (43)
Total	24 (8)	48 (16)	142 (73)

Patients with diabetes on discharge	30 (14)	Patients with hypertension during the observation time	87 (40)
Patients without diabetes on discharge	184 (83)	Patients without hypertension during the observation time	127 (57)

the score-system is also of predictive value for the late prognosis. This is further shown by the AID analysis, when the score-system is weighted together with other independent variables and recurrences, resulting in the predictor tree in Fig. 4.

The mortality figures are presented in Fig. 5 in the form of a life table, which has been calculated from the score groups. The additional deaths after follow-up are also included. No further analysis of the cause of deaths has been made. The life table shows that the time for follow-up was adequate to enable assessment of mortality.

A further presentation of the 114 patients in the follow-up is made in Table IV, there the distribution according to diagnosis, sex and age is shown. Some important parts of the socio-medical status of the patients is found in Table V. It should be mentioned that the age for receiving old-age pension in Sweden can vary, depending on profession. The majority, however, receive full pension at the age of 67. Fifteen persons, who already received a pension before the stroke, are included in the group of old-age pensioners.

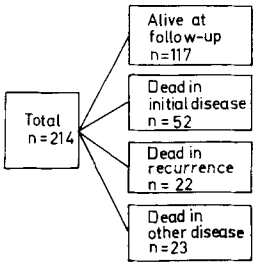

Fig. 2. Mortality up to follow-up examination.

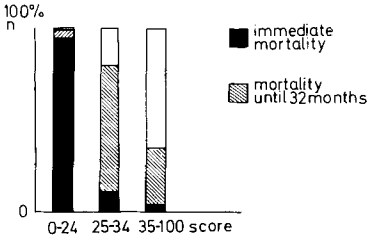

Fig. 3. The immediate and late mortality correlated to the score calculated at the acute admission.

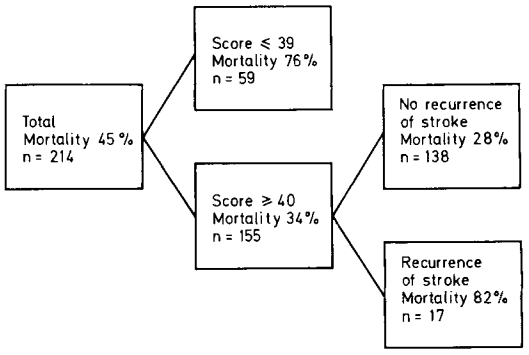

Fig. 4. Predictor-tree. Group: Patients discharged alive from the hospital after the stroke. Dependent variable: Dead or alive at the follow-up examination. Independent variables: Age, sex, profession (classified according to Fällström (16)), social-group, living alone, score on admission, handicap on discharge, hypertension, cardiac disease, ECG, recurrence of stroke, metabolic disorder, psychiatric abnormalities. The split between the score groups is significant, as is the further split on recurrence.

As the handicap on discharge from the hospital was registered, it is possible to study the changes in level of disablement up to the time of follow-up. In Table VI the diagram shows these changes as well as the numbers of patients dead or lost. It should be stressed, that the state of disease is definitely not static. Among the survivors a tendency towards a higher level of performance dominates. The favourable effect on the whole group is, however, counterbalanced by the high mortality among those with a considerable handicap.

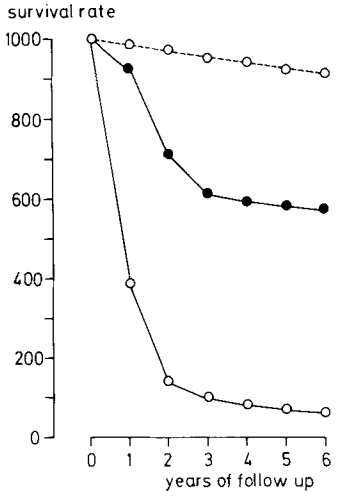

Fig. 5. Life-table. Survival rates for patients with score 15–34 (○—○) and 35–100 (●—●) compared with a model population of the same age structure (○---○).

Table IV. *Distribution of the patients at follow-up according to diagnosis, sex and age*

	Age, years		
	≤49	50–59	60–69
Cerebral haemorrhage			
Men	1	1	1
Women	1	1	0
Cerebral infarction			
Men	6	11	26
Women	7	15	30
Cerebral embolism			
Men	1	0	5
Women	0	3	5
Total	16	31	67

The patient's ability to return to the previous occupation, be it in employment or normal activities as a housewife or retired person is, however, only to a limited extent reflected in the degree of handicap. Thus Table V has been constructed to show the correlation between the degree of handicap and some important socio-medical factors. The table shows that even persons with moderate to severe handicap have been able to return to normal occupation. A closer analysis shows that in all these cases no intellectual impairment, aphasia or mental symptoms such as emotional instability, irrascibility, emotional incontinence or memory impairment were present. On the other hand, there are a large number of psychiatric symptoms and aphasia amongst those with moderate handicap who have not returned to work. This group also includes 2 patients who had epileptic attacks after the stroke.

The patients presented in Table VI, who started with a moderate or considerable handicap, and who shifted to a higher level of ability, were significantly younger than the rest of the group. Further, psychiatric symptoms and aphasia were much less common among these patients. Three patients changed to the severely handicapped group after leg-amputation because of diabetic gangrene. Formal rehabilitation has been carried out in 114 cases, of which 40 could return to work or complete independence in ADL. Definite conclusions about the correlations between the rehabilitation measures and the effect can, however, not be drawn.

The distribution of diastolic blood pressure (DP) is shown in Table VII.

The ECG findings are shown in Fig. 6. According to the principles described earlier, the ECGs have

Table V. *Correlation between some socio-medical factors and handicap at follow-up*

Socio-medical variable	No handicap	Moderate handicap	Considerable handicap	Severe handicap	Total *n*
Working	22	10	2	0	34
Sickness benefit because of the stroke	1	1	0	0	2
Temporary disablement pension	0	4	1	0	5
Disablement pension	0	13	17	8	38
Old-age pension	9	19	6	1	35
Total	32	47	26	9	114

been divided into two groups: *Normal* or *Pathological* (15). The findings are compared with figures from a health survey in the same county for the same time period. The percentage of pathological ECG's is considerably higher in the stroke group. When judging the result it should be noted, that the mean ages for the pathological groups are about the same. The control group from the health survey represents a somewhat lower mean age.

The heart-volumes are shown in Table VIII. The upper normal limits have been set to 550 and 500 ml/m² BSA for men and women respectively. As seen, about 2/3 of the patients have heart volumes above these limits.

Table VI. *Shifts of the degree of handicap from the discharge after the acute stroke up to follow-up*

Handicap on discharge	*n*	Handicap at follow-up *n*	
No	1	1	No
Moderate	52	24	No
		15	Moderate
		2	Considerable
		0	Severe
		10	Dead
		1	Lost
Considerable	112	7	No
		32	Moderate
		20	Considerable
		2	Severe
		49	Dead
		2	Lost
Severe	49	4	Considerable
		7	Severe
		38	Dead

Table VII. *Distribution of diastolic blood-pressure (DP) at follow-up*

DP, mmHg	No. of patients	%
≤99	76	67
100–119	25	22
≥120	13	11

The routine laboratory tests for blood values did not show any special pattern. No elevated calcium levels were registered. In a few cases elevated levels of uric acid were observed, but the patients were all taking diuretics, which could explain this finding. The distribution of the *k*-values of the intravenous glucose tolerance tests are shown in Table IX. The limits for diabetic, borderline and normal are *k*-values of ≤0.90, 0.91–1.10 and ≥1.11 respectively according to Wahlberg 1966 (33). In the table, 17 patients with clinically overt diabetes have been excluded. For comparison a normal reference material (Wahlberg) is used.

The levels of cholesterol and triglycerides are presented with the mean level and the 85th percentile in Table X. The upper 'normal' limit ($M+2$ S.D.) in this laboratory is 310 mg% for cholesterol and 1.80 mmol/l for triglycerides. In the calculations 2 patients taking clofibrate because of known hyperlipidaemia have been excluded.

DISCUSSION

The long-term mortality among those discharged alive is higher than in many other observed materi-

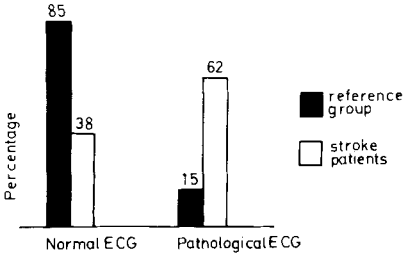

Fig. 6. Distribution of ECG-findings at follow-up, compared with a normal population.

Table VIII. *Distribution according to heart volume and sex (3 patients missing)*

Heart volume ml/m² BSA . . .	≤549	550–649	≥650	Total
Men	16	26	12	54
Heart volume ml/m² BSA . . .	≤499	500–599	≥600	Total
Women	16	25	16	57

als. The median survival time in the present material is 3.1 years, or almost identical with the time up to follow-up examination. Other authors such as Adams & Merret (1) found a median survival of 6.6 years for almost the same age groups, and Hutchison & Acheson (21) observed an even longer time. However, these authors also include transitory ischaemic attacks (TIA). Most of the differences between the results obtained probably depend on incongruity of the materials. Eisenberg (7) noted that 2/3 of the patients died within one year, when all ages were included. The correlation between prognosis and the age in the present material agrees with the findings of Marshall & Shaw (27) and Felger (12).

Earlier works by Marshall & Shaw (27) and Wyle (34), pointed out, that hypertension previous to the stroke indicated a worse prognosis. This could not be verified by Adams (2) or Merret & Adams (28). The present investigation does not show any relation between previous hypertension and the late outcome of the stroke. This could be explained by the fact that the control of blood pressure is usually better after the stroke, when the patient as a rule is under continuous supervision. The value of antihypertensive treatment after an established stroke has recently been stressed by Beevers et al.

Table XI. *Distribution of k-values on intravenous glucose tolerance test (17 patients with overt diabetes have been excluded)*

	k-value					
	≤0.90		0.91–1.10		≥1.11	
	n	%	*n*	%	*n*	%
Number of patients	21	22	14	14	62	64
Percentage in control material		4		10		86

Table X. *Serum lipids at follow-up*

	Mean (mg%)	85th percentile (mg%)
Cholesterol		
Men	253 S.D. 47	282
Women	255 S.D. 51	288
	Mean (mmol/l)	85th percentile (mmol/l)
Triglycerides		
Men	2.27 S.D. 0.62	2.86
Women	2.40 S.D. 0.85	3.18

(3). Earlier, Hood pointed out that there is no risk of precipitating a stroke with antihypertensive treatment (20). The small number of recurrent strokes in the present material does not permit statistical analysis, but it should be noted that about 25% were cerebral emboli occurring in patients with atrial fibrillation. None of the cases was on anticoagulant treatment.

As shown by the AID analysis, the initial neurological deficit, reflecting the brain damage (15) is also of predictive value for the long-term prognosis. Recurrence indicates a complication with very high mortality.

The clinical features of the surviving patients followed-up support further that the stroke victim often has several manifestations of other types of vascular impairment. There is a preponderance of heart-volumes above the upper normal limit, which in absence of myocarditis, valvular disease, shunts or other anatomical abnormalities indicates the presence of arteriosclerotic heart disease. This is also supported by the over-representation of pathological ECGs. In an earlier paper, the prognostic importance of the ECG was pointed out (15). In the AID analysis for the long-term survival the ECG could not be shown to be an important predictor for the mortality, which can be explained by the high immediate mortality among patients with pathological ECG. This is in accordance with the observation by Marquardsen (26), that the initial ECG does not influence the outcome after 3 years.

The high percentage of overt diabetes among the stroke victims has been discussed earlier, and is about the same as found in other studies, Meyer

(29), Hood (20) and Kurland (25). Further analysis of carbohydrate metabolism has shown a clear over-representation of decreased glucose tolerance among the survivors. The correlation between impaired glucose tolerance and ischaemic heart disease has earlier been widely discussed, but hitherto less attention has been attributed to their correlation to strokes. Another evidence for the importance of disturbed glucose metabolism is the fact, that leg amputation because of diabetic gangrene was necessary in three cases.

The serum lipid findings have to be interpreted with care because of lack of adequate reference material. Hedstrand (18) in a health survey of 1 000 males aged 50 during the same time period and in the same laboratory found an 85th percentile of 275 mg% for cholesterol and 2.70 mmol/l for triglycerides respectively. As the mean age for the present material is 61.1 for men the figures are reasonably comparable. The number of male patients with levels above these limits in the present investigation is 17% for cholesterol and 26% for triglycerides. The difference for triglycerides is significant ($p<0.05$). Carlson et al. found in the Stockholm prospective study serum cholesterol levels in men to be constant for the age 45–65, but serum triglyceride levels tend to decline after the age of 55 (4). For women, the corresponding figures are 16.8% and 31.5% respectively. The difference for triglycerides is significant ($p<0.01$). However, it must be stressed, that the figures are not directly comparable, as females are known to have higher serum lipid levels in these age groups compared with men (4). To summarize, there is evidence that in both males and females the triglyceride levels are higher than should be expected.

The opinion about the importance of the various serum lipids in the development of cerebrovascular disease is not uniform. Kannel (22), pointed out, that an elevated cholesterol level before the age of 50 years may indicate an increased risk of a later stroke. Later, Kannel (23) also stated that even if there exists an association, it will be attenuated with advancing age. Feldman (11) found cholesterol levels generally elevated, often in association with those of triglycerides. Cummings (5) did not find any differences in cholesterol and triglyceride levels from a control group of patients who survived a stroke more than 2 years. On the other hand, Katzuki (24) reported significantly higher levels of triglycerides but not cholesterol in stroke victims. Our observations seem to agree with those of Katzuki's. It must be borne in mind, however, that various factors that cannot be critically evaluated in the present material, e.g. different degree of immobilization and dietary habits, may influence the triglyceride levels. The distribution of the serum lipid levels in the original stroke population is unknown, the representativity of the late survival group cannot be decided. Of course there is no reason to assume that the survivors should form a special bad selection, from the serum lipid point of view. Still it would not be justified to attempt detailed conclusions as to the nature of the connection between elevated serum triglycerides and the cerebrovascular laesions.

Conclusions on the effect of rehabilitation must be drawn with care. It is obvious, that a small group could return to work or complete independence in ADL. These patients represent a group with favourable factors, such as relative youth, few psychiatric symptoms and absence of aphasia. Under such circumstances even patients with considerable physical handicap have been able to return to work. On the other hand, even a minimal physical handicap in combination with mental disturbances and/or aphasia leads to disablement pension. It is further noted that a small group with the favourable factors mentioned above shifted from the level of considerable handicap to minimal or no handicap at all without formal rehabilitation. If comprehensive rehabilitation training is started, it may denote a selection in itself, as the patient may be judged to have a reasonable chance of recovery. On the other hand, not starting rehabilitation may indicate that the prognosis is too bad or that the patient may have the ability to train himself. The results of rehabilitation are also influenced by other factors, such as previous occupation, home conditions, attitude from relatives and, not least, the policy of the physicians concerned. This has further been demonstrated in Sweden by Ekvall (8) and Fällström (16) and in Norway by Gogstad (17). It is also worth noting that Feldman et al. (10), in an unselected group of stroke patients found the same degree of recovery amongst patients who had received comprehensive formal rehabilitation compared with the controls who had only received "normal functional medical care". On the other hand, minimal changes for the individual patient can be of great importance facilitating the ADL-activities and reducing the need for help in various forms.

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