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Studies on Cerebrovascular Stroke

I. Epidemiology of First-time Strokes in Persons under 70 Years of Age

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ABSTRACT

The present investigation was carried out to study the incidence of new cerebrovascular strokes (cerebral haemorrhage, cerebral infarction and cerebral embolism) in people under the age of 70. Such information has hitherto been lacking. The material comprises all cases from Uppsala county occurring between 1967 and 1971. The incidence was found to be 36/100 000 inhabitants. Of the total number of strokes, 25 % were recurrences. During the period of study the incidence showed a moderate but significant decrease. It is assumed that this decrease is due to an extended and improved treatment of hypertension. It was observed that there were 6 females below 40 years of age. All had been on oral contraceptives at the time of the stroke. There was a high incidence of diabetes and symptoms of cardiovascular impairment (hypertension, transient ischaemic attack (TIA), cardiosclerotic disease) in the series. A high incidence of myocardial infarction was found among the parents of the cases of cerebral haemorrhage. A high incidence of strokes was found among the parents of those having cerebral infarctions.

INTRODUCTION

In all modern communities, cerebrovascular diseases form a major health problem. In Sweden, cerebrovascular diseases (CVL) rank third as a cause of death (19). Not only do strokes cause a great number of deaths, the survivors are often severely crippled and call upon the resources of the community for long-term care and rehabilitation.

It may be assumed that better and more active treatment of predisposing factors such as hypertension and metabolic disorders like diabetes mellitus should be reflected in the decrease in the incidence of strokes. Thus, studies upon the incidence of strokes are of importance and interest not only to medical professionals but also to administrators and politicians concerned with public health problems.

Figures concerning the incidence of cerebrovascular diseases can be gained from the official life statistics. These have, however, the limitation, that only strokes resulting in death are registered, and no difference is made between recurrences and new strokes. In Sweden special studies of in-patient diagnosis in general (18) and strokes in particular (17) have been carried out in a particular hospital region. Both of these include recurrences.

Some information about the incidence of CVL can also be obtained from public health surveys. If extended long enough in time they may also to a certain degree reflect the change of the pattern of various diseases and the effect of preventive measures. The ideal method, of course, must be a prospective study of a defined population with registration of all new cases, e.g. following the Program of Treatment and Rehabilitation of Cerebrovascular Diseases, given by WHO in 1970 (21).

However, even a retrospective study, via hospital records, may give valuable information about the incidence of strokes. It will not be possible to detect minor strokes, but all strokes leading to hospitalization will be included. It would also be possible to obtain other information of interest concerning heredity, predisposing factors and previous treatments. One definite advantage is that the recurrent cases can be identified. Further the prognosis may be evaluated and, if the observation time is made long enough, changes in the outlook will also be registered.

The present investigation was performed with the aim of studying factors associated with the incidence and prognosis of first-time strokes. The study was limited to people under 70 years of age. Below this age the stroke in most patients means a sudden change from normal active life to some form of handicap, often severe, or death. In higher ages the

majority of the stroke patients have retired from active work and many are more or less handicapped by disease before the stroke. The present paper is a report of the incidence data.

MATERIAL AND METHODS

In accordance with the WHO recommendations, stroke has been defined as a sudden onset of focal neurological deficit due to a local disturbance in blood supply to the brain (21). Further, it has been required that the stroke shall lead to death or sequelae persisting more than 48 hours. Transitory ischaemic attacks (TIA) have not been included in the present material nor have subarachnoidal haemorrhages or stroke recurrences. The investigation was confined to patients under 70 years of age.

An attempt has been made to divide the material into the diagnoses cerebral haemorrhage, cerebral infarction, and cerebral emoblism.

The diagnosis of cerebral haemorrhage has been based upon autopsy, cerebral angiography and/or a clinical history strongly suggestive of haemorrhage. Additional information was in most cases obtained from a lumbar puncture. Cerebral emoblism was diagnosed from a suggestive clinical history and a reasonable source of emboli. The major part of the material was considered to be patients with cerebral infarction in the absence of a rapid onset or a heart disorder causing embolisation.

The investigation was designed to cover the five-year period 1967–71 and to include people living and registered in the county of Uppsala (C-county) which has about 200 000 inhabitants. In the area there were, at the time of the investigation, two hospitals with beds accepting acute admissions, one in the town of Enköping as well as the University Hospital of Uppsala. There were also two other hospitals, treating patients with acute disorders. Patients with acute strokes going to these hospitals first passed the emergency wards of the University Hospital.

With these criteria the record of the two hospitals mentioned were sought for the years under investigation. To ensure a complete coverage, all records with any form of cerebrovascular disease as major- or additional diagnosis were scrutinized by the author. A control was also made, that no acute admissions of patients with this type of disease had occurred at the other hospitals in the county. The hospitals for mental and chronic diseases were checked for patients suffering an acute stroke while under treatment there. The register of the department of pathology was scanned for patients admitted with stroke from other departments and not already registered in the medical department. Information was obtained from the Institute of Forensic Medicine (Statens Rättsläkarstation) about patients found dead after a stroke.

The information gathered from these sources was: Personal data, sex, age, marital status, education, social group (1), type of profession. Form of living: alone or not alone. Hereditary factors: whether the father or mother had had stroke or myocardial infarction. Previous medical history was registered with special reference to ischaemic heart disease or cardiac arrhythmia, intermittent claudication, hypertension and diabetes mellitus. The criteria for treatment of hypertension suggested earlier by Hood et al. was used (10, 11). Active, adequate treatment thus would mean a diastolic blood pressure (D.P.) level of ≤100 mmHg or, at least, full doses of two drugs. When possible, the information of treatment has been checked in the out-patient records or with private practitioners. In diabetes a fasting blood sugar level of ≤200 mg% and a urinary excretion of ≤20 g was required for acceptance of treatment as adequate.

Other previous or current diseases were also noted. Any previous manifestation of cerebral symptoms such as transitory ischaemic attacks (TIA) or vertigo and headache suggestive for hypertension was especially looked for.

The consumption of various medicines was also noted. An attempt was made to gather information concerning alcohol consumption and smoking habits. For younger females the use of oral contraceptives was registered. The clinical data on admission were collected and will be published in a subsequent report. The autopsy records of those who died during the hospital stay were checked and the anatomico-pathological diagnosis compared with the clinical one.

All the information gathered has been transferred to special record forms and from them to punch cards for subsequent computer analysis. The traditional chi-square test has been used on the statistical analysis.

Table I. *Total material, 347 patients, distributed according to age, sex and diagnosis*

	Age, years			
	≤49 *n*	50–59 *n*	60–69 *n*	Total *n*
Cerebral haemorrhage				
Men	8	18	28	54
Women	6	10	23	39
Cerebral infarction				
Men	9	27	70	106
Women	12	25	83	120
Cerebral embolism				
Men	2	0	10	12
Women	0	5	11	16
Total	37	85	225	347

RESULTS

471 records with the diagnosis of cerebral haemorrhage, infarction or embolus were found. 18 could be excluded as cases given wrong diagnosis code number, viz. 14 subarachnoidal haemorrhages and 4 subdural haematoma due to trauma. Four patients had initially been diagnosed as having suffered a CVL and discharged under that diagnosis, but later turned out to have cerebral tumour. In

Table II. *Distribution of patients according to diagnosis and year*

	1967	1968	1969	1970	1971	Total
Cerebral haemorrhage	35	21	10	17	10	93
Cerebral infarction	57	40	51	36	42	226
Cerebral embolism	6	3	5	8	6	28
Total	98	64	66	61	58	347

Table III. *Mean age and median for the whole material*

Years		
	Mean	Median
Cerebral haemorrhage	58.8	60
Cerebral infarction	60.8	63
Cerebral embolism	62.5	64
Total	60.4	63

none of these cases had cerebral angiography been performed. 102 cases had had a previous stroke with or without persistent sequelae.

Thus, there remained 347 cases, 172 men and 175 women, comprising 93 patients with cerebral haemorrhages, 226 with cerebral infarctions and 28 with cerebral embolus. Two cases of cerebral haemorrhage and one of cerebral infarction, found through the Institute of Forensic Medicine are included in these figures. The distribution according to sex, age and diagnosis is shown in Table I. The distribution in each separate year of the study is shown in Table II.

As the population at risk has varied during the observation period a recalculation per 100 000 inhabitants has been made for the first and the last year of the investigation (Fig. 1). The population figures used in the calculation have been taken from the official Swedish statistics (19). The total incidence of stroke in the age group below 70 years is 36/100 000. The mean age for the whole group was 59.9 years for men and 60.8 years for women. The means for the different groups are shown in Table III. The median ages are also shown.

The distribution within social groups corresponds closely with that of the general population of the country (12).

The available information about heredity for stroke and myocardial infarction is shown in Fig. 2. The information about heredity in a retrospective study must be incomplete in a certain number of cases. The number of patients lacking information is, however, rather small (6.6.%) probably due to the fact that most records are from a teaching hospital, where special attention is given to such details.

Table IV gives an analysis of the frequency of known hypertension and its treatment. In the total material, 52% of the patients where history was available had known hypertension. The expected figure is 28% (5). There is no significant difference in percentages of untreated and treated hypertension between the haemorrhage and infarction groups. Table IV also shows the frequency of previous cerebral symptoms in the form of TIA. There

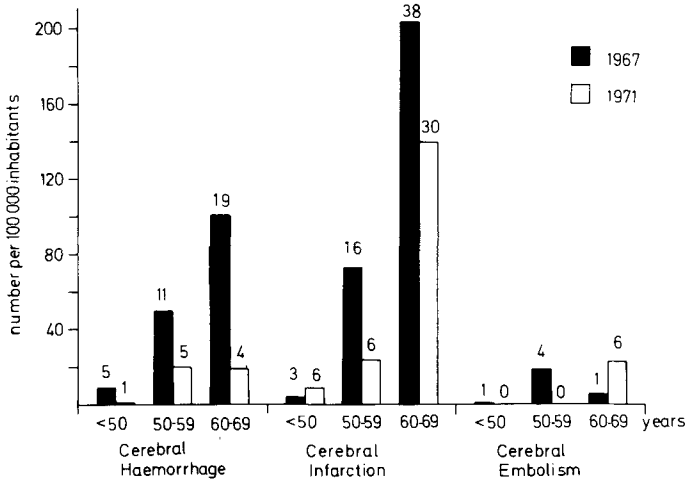

Fig. 1. Age-distribution of first attack of cerebrovascular lesion. Recalculated frequencies per 100 000 inhabitants. Figures above columns denote absolute numbers.

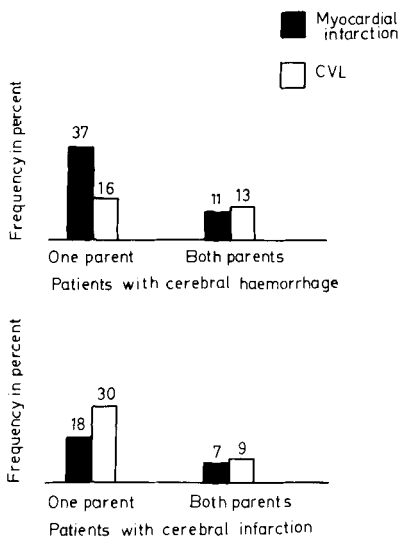

Fig. 2. Frequency of myocardial infarction and cerebrovascular lesion among the parents of stroke-victims.

is no difference in the frequency of TIA for the two groups. Registration of symptoms such as headache and vertigo were apparently made in an haphazard manner which did not permit a detailed retrospective evaluation.

The distribution of diabetes is shown in Table V. The table also includes the numbers of patients with a history suggesting arteriosclerotic heart disease. The frequency of previous cardiac infarction and angina pectoris was significantly higher among the patients with cerebral haemorrhage than among those with cerebral infarction ($p<0.05$). There was no significant difference in the distribution of heart failure or diabetes between the diagnostic groups. The overall prevalence of diabetes was 14%. There was a significant female predominance among the diabetics. There were three cases of intermittent claudication, all males and belonging to the cerebral infarction group. Nineteen cases of known renal insufficiency, (serum creatinine over 1.5 mg%) were found, 12 of these belonged to the haemorrhage group, the others to the infarctions. Renal transplantation had been performed in one case.

Thirteen patients had been given anticoagulant treatment immediately before the stroke. In 9 cases the indication was cardiac arrhythmia or recent myocardial infarction. The remaining 4 had had TIA. The distribution within the diagnostic groups was 4 patients with haemorrhage, 5 with cerebral infarction and 4 with embolus. All the haemorrhage cases were lethal and had been shown to have low prothrombin levels, two of them had known hypertension. In none of the cases with cerebral infarction or embolus had the anticoagulant treatment achieved therapeutic prothrombin level.

Six of the females had been taking 'the pill'. Two of them died. The duration of pill intake varied from 5 weeks to 2 years before the stroke. The information on smoking habits and alcohol consumption was too sparse to permit further analysis.

DISCUSSION

When studying the incidence, history and symptoms of a disease, the retrospective method offers advantages and disadvantages. On the positive side can be mentioned the possibility to make observations over longer periods within a reasonable time. Further, the diagnostic uncertainty, common in the acute or early stages of a disease, will be reduced or eliminated. The method may also offer technical and economic advantages. The main disadvantage is the difficulty in tracing all patients with the disease under study, and the difficulty in obtaining supplementary information. This is especially dis-

Table IV. *History of hypertension and TIA*

	Haemorrhage		TIA	Infarction		TIA
	n	%	*n*	*n*	%	*n*
History not obtainable	7	7		10	3	
No history of hypertension or known as normotensive	39	43	10	86	39	43
Known hypertension, not treated or treatment interrupted	16	17	12	39	15	30
Treatment inadequate	13	13	10	35	16	20
Good treatment	18	20	10	56	27	15
	93	100	42	226	100	108

Table V. *Frequency of diabetes and arteriosclerotic manifestations*

	Diabetes *n*	Myocardial infarction *n*	Angina pectoris *n*	Heart failure *n*
Cerebral haemorrhage				
Men	8	15	25	6
Women	10	5	4	4
Cerebral infarction				
Men	10	18	12	12
Women	20	5	7	10
Total	48	43	48	32

turbing when the original data are incomplete and/or the patient is dead.

The present series of acute first-time strokes must reasonably be assumed to be very complete. The symptoms of an acute stroke, even if minor, are highly alarming, and will lead the patient to hospital. In the county of Uppsala, hospital facilities are good, the ambulance service well developed and the population and practising doctors are used to having easy access to the hospitals. It is extremely unlikely that a patient with this type of disease should be cared for outside the hospital. This assumption is also supported by the fact that very few additional cases were found in the Institute of Forensic Medicine's register.

The difficulties concerning the collection of data on symptoms and previous history are apparent in the present material. In some instances the figures for frequency and incidence must be regarded as minimum figures. In others the information has been too scarce to permit any discussion or analysis whatsoever.

The differentiation of the material into the separate diagnostic groups cannot always be made on a clear-cut basis. Signs and symptoms do not always permit the differentiation between haemorrhage and infarction. Errors must occur especially in mild cases. While most of the patients with clinically diagnosed haemorrhages have been autopsied, this is not the case with those suffering cerebral infarction. The large group of survivors classified as cerebral infarctions may contain some cases of small haemorrhages which have been wrongly diagnosed. Still the proportion between the diagnostic groups in the present material is in good agreement with other findings in recent series of Kannel (13) and Kurtzke (15).

An earlier investigation carried out in the Uppsala hospital region showed an overall incidence of 169/100 000 for cerebral haemorrhages, infarctions and emboli together (17). This figure is somewhat higher than a more recent one from Göteborg, where Tibblin & Harmsen calculated a figure of 150/100 000 (8). They found an incidence of 52/100 000 for all CVL below the age of 65. Considering that their material contains recurrences, TIA, and subarachnoid haemorrhages, their incidence figure agrees very closely with our incidence figure of 36/100 000 for new strokes occurring before 70 years of age.

In the present material 1 % of the cases, originally diagnosed as strokes, turned out to be intracerebral tumours. In none of these cases had cerebral angiography been performed. Dalsgaard-Nielsen (4) found a higher figure in 1955. More active diagnostic measures may have contributed to the improvement.

The overall incidence for the sexes is equal. There is no significant sex difference in any of the age groups. It may be of interest to observe that all 6 female patients below 40 with cerebral infarction had taken oral contraceptives in the period immediately prior to the stroke. The probable connection between CVL and contraceptives has previously been pointed out, e.g. by Ask-Upmark (3) and Tausk (20).

The heredity data (Fig. 2) have been compared with corresponding information from a health control of 50-year-old men in Uppsala (9). The incidence of CVL or myocardial infarctions in one of the parents of these men was found to be 25 % and 22.5 % respectively, in the latter study. The corresponding figures in this study, for both parents having the diseases were 2 % for both CVL and myocardial infarction. As seen in Fig. 2 the familial occurrence of myocardial infarction in the cerebral

haemorrhage group is considerably higher, the incidence amongst parents being about 50%. On the other hand, in the cerebral infarction group there is a considerable over-representation of strokes among the parents. The differences are statistically significant ($p<0.05$). The findings may suggest the existence of hereditary patterns in the occurrence of strokes, which has been postulated by Larsson (16).

As shown in Fig. 1 there is a downward trend in the incidence of haemorrhages and infarctions when the first year of the investigation is compared with the last. Because of the difficulties, discussed above, in differentiating infallibly between infarction and haemorrhage the statistical analysis has been performed for both groups together. The difference is significant ($p<0.05$) for both the age groups 50–59 and 60–69 years. There is a small increase in the number of cerebral infarctions under 50 years of age. This is entirely due to the 6 females with CVL who took oral contraceptives.

The cause of the decrease can be argued. As stressed by Kannel (14) the most powerful factor operating in the development of stroke is hypertension. Earlier Swedish investigations by Aurell & Hood (2) and Hood et al. (10) have shown that a downward trend in the incidence of stroke exists for the first decade in which active anti-hypertensive treatment was available in Sweden. As shown by Hood et al. (11) there has been a considerable improvement in the prognosis for severe hypertension actively treated. An indication of a more active approach to hypertensive disease is found in the fact, that during the years of the present investigation, the number of patients examined and treated for hypertension increased by 50% at the Department of Medicine in Uppsala.

In the whole material, the frequency of known hypertension is 50% in cases with haemorrhage and 60% in the group with cerebral infarction. In both groups about 60% of the hypertensives were untreated or inadequately treated, viz. Table IV. The frequency of untreated and inadequately treated cases is reduced by about 20% when the first and the last years of the study are compared. This may be considered as further indication of improved therapy, resulting in a reduced incidence of stroke. Still the number of cases with untreated hypertension is high and so are the figures for inadequate or interrupted treatment. These figures support the impression reported by Ericsson (5) from a similar population. The same tendency has been pointed out by Hood (10) in another part of the country.

The prevalence of diabetes is about the same as observed in similar Swedish materials (6, 10). The percentage does not differ for the different years of observation, nor the type of treatment. The figures observed are considerably higher than those expected in a population with corresponding age distribution (7). It is unlikely that the observed reduction of strokes has been influenced by the diabetic disease.

The incidence of embolism does not show this apparent decreasing trend (Fig. 1). In more recent years, however, the cases have been found exclusively in the highest age group and none had valvular disease. It may be concluded, that the patient with valvular heart disease (with or without arrhythmia) is now given sufficient anticoagulant treatment and the main source of embolism is arteriosclerotic disease.

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