LONG-TERM EFFECTS OF STROKE

by

Matti Viitanen

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LONG-TERMS EFFECTS OF STROKE

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Umeå 1987
LONG-TERM EFFECTS OF STROKE

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ABSTRACT

Stroke, which has an increasing incidence with age, causes an irreversible brain damage which may lead to impairment, disability and decreased life satisfaction or death.

Risk factors for death, recurrent stroke and myocardial infarction, were analyzed in 409 stroke patients treated at the Stroke Unit, Department of Medicine, Umeå University Hospital, between Jan. 1, 1978 and Dec. 31, 1982. The causes of death were related with the time of survival. In fully co-operative (n=62) 4-6 year stroke survivors, the occurrence of motor and perceptual impairments, of self-care (ADL) disability and of self-reported decreased life satisfaction due to stroke was determined.

The probability of survival was 77% three months after stroke, 69% after one year, and 37% after five years. Multivariate statistical analysis indicated that impairment of consciousness was the most important risk factor for death followed by age, previous cardiac failure, diabetes mellitus, intracerebral hemorrhage and male sex. During the first week, cerebrovascular disease (90%) was the most dominant primary cause of death, from the second to the fourth week pulmonary embolism (30%), bronchopneumonia during the second and third months and cardiac disease (37%) later than three months after stroke. The risk of recurrence was 14% during the first year after stroke and the accumulated risk of stroke recurrence after 5 years was 37% after stroke. The estimated probability of myocardial infarction was 7% at one year and 19% at 5 years. High age and a history of cardiac failure increased the risk of recurrent stroke. The risk of myocardial infarction was associated with high age, angina pectoris and diabetes mellitus. The highest risk of epilepsy was found between 6 and 12 months after stroke.

Motor impairment prevailed in 36% of the long-term survivors, perceptual impairments in up to 57% and decreased ADL-capacity in 32%. As regards ecological perception, perceptual function variables were distinctly grouped into low and high level perception which together with motor function explained 71% of the variance of self-care ADL. While levels of global and of domain specific variables of life satisfaction appeared stable in clinically healthy reference populations aged 60 and 80 years, the stroke had produced a decrease in one or more aspects of life satisfaction for 61% of the long-term survivors. Although significantly associated with motor impairments and ADL disability, these changes could not only be attributed to physical problems.

Key words: stroke, cerebrovascular disease, prognosis, recurrent stroke, myocardial infarction, epilepsy, life satisfaction, motor function, self-care ability, perception, causes of death.
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Matti Viitanen

Umeå 1987
To Siri
and my Parents
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<tr>
<td>ADL</td>
<td>activities of daily living</td>
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<tr>
<td>ASA</td>
<td>acetylsalicylic acid</td>
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<td>CVD</td>
<td>cerebrovascular disease</td>
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<td>ICIDH</td>
<td>International classification of impairments, disabilities, and handicaps</td>
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<td>SAH</td>
<td>subarachnoidal hemorrhage</td>
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<td>TIA</td>
<td>transient ischemic attack</td>
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ABSTRACT

Stroke, which has an increasing incidence with age, causes an irreversible brain damage which may lead to impairment, disability and decreased life satisfaction or death.

Risk factors for death, recurrent stroke and myocardial infarction, were analyzed in 409 stroke patients treated at the Stroke Unit, Department of Medicine, Umeå University Hospital, between Jan. 1, 1978 and Dec. 31, 1982. The causes of death were related with the time of survival. In fully co-operable (n=62) 4-6 year stroke survivors, the occurrence of motor and perceptual impairments, of self-care (ADL) disability and of self-reported decreased life satisfaction due to stroke was determined.

The probability of survival was 77% three months after stroke, 69% after one year, and 37% after five years. Multivariate statistical analysis indicated that impairment of consciousness was the most important risk factor for death followed by age, previous cardiac failure, diabetes mellitus, intracerebral hemorrhage and male sex. During the first week, cerebrovascular disease (90%) was the most dominant primary cause of death, from the second to the fourth week pulmonary embolism (30%), bronchopneumonia during the second and third month and cardiac disease (37%) later than three months after stroke. The risk of recurrence was 14% during the first year after stroke and the accumulated risk of stroke recurrence after 5 years was 37%. The estimated probability of myocardial infarction was 7% at one year and 19% at 5 years after stroke. High age and a history of cardiac failure increased the risk of recurrent stroke. The risk of myocardial infarction was associated with high age, angina pectoris and diabetes mellitus. The highest risk of epilepsy was found between 6 and 12 months after stroke.

Motor impairment prevailed in 36% of the long-term survivors, perceptual impairments in up to 57% and decreased ADL-capacity in 32%. As regards ecological perception, perceptual function variables were distinctly grouped into low and high level perception which together with motor function explained 71% of the variance of self-care ADL. While levels of global and of domain specific variables of life satisfaction appeared stable in clinically healthy reference populations aged 60 and 80 years, the stroke had produced a decrease in one or more aspects of life satisfaction for 61% of the long-term survivors. Although significantly associated with motor impairments and ADL disability, these changes could not only be attributed to physical problems.

Key words: stroke, cerebrovascular disease, prognosis, recurrent stroke, myocardial infarction, epilepsy, life satisfaction, motor function, self-care ability, perception, causes of death.
ORIGINAL PAPERS


IV. Bernspång B, Viitanen M, Eriksson S. IMPAIRMENTS OF PERCEPTUAL AND MOTOR FUNCTIONS. THEIR INFLUENCE ON SELF-CARE ABILITY 4-6 YEARS AFTER STROKE. Submitted.

INTRODUCTION

A. HISTORY

In Nej Jing, the oldest preserved Chinese book of medicine (475-221 BC) the risk of apoplexy was said to be greatest in the summer when the pulse was as a stroke of a hammer and when the pulse was still stronger the disease struck all at once\(^1\).

At about the same time apoplexy was described in the Hippocratic writings (400 BC)\(^2\). The heating of the blood vessels of the head was thought to cause the flow of black bile into the head or to attract phlegm, and aphasia was first connected with right side hemiplegia.

Aretaios\(^3\) (50 or 150 AD) described the brain lesion as being on the opposite side of the trunk of the paralysis and also mentioned the possibility of urinary retention or incontinence. He observed that the disease usually affected the elderly who often died. The most important treatment in more severe apoplexy was phlebotomy and the degree of phlebotomy should be calculated exactly so as not to kill the patient. Phlebotomy could be repeated.

Soranus of Ephesus (A.D. 98-138) reported that "hemiplegic paralysis" was common in old age, occurred seldom in youth and occurred most frequently in the winter.

Gabriel Fallopius (1561) described the arterial circle of vessels at the base of the human brain. In his illustration, however, there were no the posterior communicating arteries. Casserio showed the complete union of the posterior communicating arteries as early as the year 1616, but only on one side. Willis (1664) described the circle of Willis and the intracerebral blood vessels and also reported the clinical importance of the circle. He also observed that damage in the region of the capsula interna could cause hemiplegia. Johan Jacob Wepfer of Schaffhausen (1658) illustrated the siphon of the carotid arteries and described the course of the middle cerebral artery. In a Treatise on Apoplexy (1658), Wepfer described cerebral hemorrhage as a cause of apoplexia and patients who recovered from hemiplegia within 24 hours. He recognized that an obstruction between the cerebral arteries and jugular veins could produce an apoplexy. He also described the signs of those at risk to develop apoplexy: namely the obese whose face were livid and those whose pulse were constantly irregular. Hypertensive individuals or subjects with
cardiac risk were said to run a greater risk of stroke. Francois Bayle (1677) related cerebral sclerosis with apoplexy.

In the 18th century, van Swieten (1754) suggested that cerebral embolism may cause apoplexy. William Heberden (1802) described transient cerebral vascular insufficiency, which could precede paralysis. Serres (1822) described a patient with cerebellar apoplexy and Parker (1845) reported pontine apoplexy. Abercrombie (1828) tried to classify apoplexy into three classes: primary apoplexy was described as intracerebral hemorrhage or massive cerebral infarction, the second class was those with a sudden pain in the head (most cases can be recognized as subarachnoid hemorrhage) and the third class consisted of patients with sudden hemiplegia/paresis without stupor, which may include patients with cerebral vascular insufficiency. As late as the mid-19th century cerebral vascular occlusion was described as a cause of cerebral softening and brain infarction. Henry Duret (1873) demonstrated the areas of distribution for the anterior, middle and posterior cerebral arteries and the penetrating branches to the basal ganglia and brain stem. Gowers (1875) described a patient with mitral stenosis who suffered from blindness and contralateral hemiplegia. At autopsy, emboli were found in the middle cerebral artery and in the central retinal artery. The origin of the emboli was found in the auricular appendages.

Chiari (1906) pointed out that the main source of emboli in the elderly was in the carotid bifurcation. (for reviews see4,5)

B. INCIDENCE OF CEREBROVASCULAR DISEASE

1. Global aspects

a. First stroke

In the National Survey of Stroke study in USA, 1971-1976, Kuller and co-workers6 observed an annual incidence rate of initial stroke of 1.4/1000 population. In South Alabama, USA, 1980, the (hospitalization) incidence of first stroke was 1.4/1000 population and the diagnostic distribution of the events was 85% cerebral infarctions, intracerebral hemorrhages 8%, subarachnoidal hemorrhage 6% and unspecified type 1%7.

In a multicenter study, coordinated by the WHO8, stroke was registered between 1971 and 1974 in 17 centres. The highest incidence was in Akita,
Japan, 3.2/1000 of the whole population and 32.6/1000 population 75 years and older. Four of these 17 centres were in Northern Europe. In Copenhagen, the incidence rate was 2.6/1000 of the whole population and in the population 75 years and older 15.3/1000, in Espoo, Finland 1.5 and 28.1, respectively, and in North Karelia, 2.0 and 18.2. In Sivenius's study in Kuopio, Finland\(^9\), the incidence of stroke was 2.4 for the whole population and for 75 years and older 23.5.

b. **Recurrent stroke**

In the WHO epidemiological multicenter study\(^8\), recurrent stroke was found in 14% of the patients under 65 years and in 18% over that age. There was no difference between the sexes nor between the European centres. In an epidemiological study in Alabama\(^7\), 13% of all strokes were recurrent and, 26% in the National Survey of Stroke study\(^10\) and in Oxfordshire, Great Britain\(^11\), 24% were recurrent.

In a group of hospitalized stroke patients, in Stockholm\(^12\), a history of previous stroke was reported in 19% and in Söderhamn\(^13\), in 17%, and in Umeå, 30% had had a previous stroke\(^14\).

In follow-up studies, in Framingham, USA, Sacco and co-workers\(^15\) reported a 42% five-year cumulative recurrence rate in men and a 24% rate in women, and in Beijing, China Chen and Ling\(^16\) found a cumulative recurrence rate in cerebral thrombosis after one year of 13%, after two years 19% and after three years 33%, and in cerebral hemorrhage 5%, 10% and 10% respectively. Sivenius and co-workers\(^9\) (1985) had a recurrence rate of 6% during the first year after stroke in Kuopio, Finland, and Ahlsiö and co-workers\(^17\) found recurency in 23% after two years in Stockholm.

2. **Swedish data**

A Swedish study of the incidence of hospital admissions caused by stroke in Uppsala (1964), gave a rate of 2.3 admissions /1000 population\(^18\). Ten years later in the same catchment area 0.4/1000 inhabitants under the age of 70 were admitted to hospital due to first stroke\(^19\). In Gothenburg, patients 15-65 years of age were registered from 1971 to 1974 and the crude annual incidence was 0.5 per 1000 population in men and 0.3 in women and in both sexes 0.4\(^8\). The overall incidence of stroke in Söderhamn, 1975-1978, was 2.9/1000 and the
The mean age for both sexes was 73 years; men 71 years and women 75 years, and the incidence of stroke increased by 55% per 5-year interval of age. In an epidemiological study in Lund, in 1983 and 1984, the crude and age adjusted incidence of first stroke was 1.7/1000 population and for all strokes 2.0. The incidence for the age groups 65-74 years was 6.0, 75-84 years 13.6, and over 85 years 18.9 per 1000 population. In northern Sweden stroke incidence was 3.9/1000 in age group 55-64 years and 9.8/1000 in the population aged 65-74 years.

3. Changes in incidence

In the population of Rochester, Minnesota, Matsumoto and co-workers observed a decreased average annual incidence rate between the groups studied from 1945 through 1954 and from 1955 through 1969, and Garraway and co-workers found a decreasing incidence of cerebral infarctions between the populations studied from 1945 to 49 and from 1970 to 74. This decrease occurred, in both sexes and in the higher age groups.

In Hisayama, Japan, a trend towards a decreasing incidence of stroke was observed by Ueda and co-workers. The 5-year incidence of intracerebral hemorrhage in men decreased and the same trend was observed also in cerebral infarctions in both sexes.

Kotila compared the incidence of stroke in Espoo and Kauniainen, Finland, between 1972-73 and 1978-80 and found a declining trend in the age-adjusted incidence of stroke. The largest, statistically significant decline was observed in the incidence of cerebral hemorrhage in men and subarachnoid hemorrhage in women. The incidence of cerebral infarction was unchanged.

In a study in Stockholm, based on data obtained from the Swedish Cause of Death Register and the Inpatient Care Register, Alfredsson and co-workers found a decreasing trend in the age-adjusted incidence of first stroke in women. In men, the incidence of all strokes increased roughly by 1.8% annually and this increase was observed both in first and in recurrent strokes. In Gothenburg, stroke incidence decreased in women aged 15-65 years between 1971 and 1981 but in men it remained unchanged.
C. RISK FACTORS FOR CEREBROVASCULAR DISEASE

1. General aspects

The incidence of stroke is strongly related with age and the rate more than doubles per decade after 55 years\(^7,8,9,22\). For example, in Copenhagen\(^8\) in the age groups 55-64, 65-74 and over 75, the incidences were 2.7, 5.7 and 15.3 per 1000 population respectively.

*Male sex* is overrepresented especially in atherothrombotic brain infarctions\(^21,28\).

*Race* has proved to be as a risk factor. Blacks had higher age-specific incidence rates than whites in South-Alabama\(^7\) and Maoris than non-Maoris in New Zealand\(^29\). In studies from Japan, Japanese\(^8,30\) had a higher incidence than Europeans but the stroke incidence rate of Hawaiian Japanese men appeared to be similar to that of occidentals\(^31\).

*Familial factors* are reported to be a risk factor by Diaz and co-workers\(^32\), and the living relatives of the stroke or the TIA patient had multiple stroke risk factors (as for example hypertension, heart disease) and may therefore run a greater risk of stroke than the relatives of the patients' spouses.

*Diabetes mellitus* is a risk factor for atherothrombotic brain infarction and the risk is higher in women than men\(^33\). The risk is strongly correlated with hypertension, but according to Abbot and co-workers\(^34\), diabetes mellitus is an independent risk factor for thromboembolic stroke. Weinberger and co-workers\(^35\) observed in their study of 102 consecutive patients with peripheral artery disease that patients with diabetes mellitus had higher risk of stroke and were more prone to irreversible destruction of ischemic brain tissue than non-diabetics, regardless of the nature of the circulatory disturbance.

The Framingham data\(^36\) showed that stroke risk is strongly related to the elevation of blood pressure. *Hypertension* was the dominant predisposing factor for stroke. It was highly related both to atherothrombotic brain infarction and intracerebral hemorrhage\(^36,37\). Patients with hypertension were prone to develop cardiac impairments, such as cardiac enlargement, which can be seen on X-ray and atrial fibrillation and ECG abnormalities. These changes are far more frequently observed in patients with CVD\(^38\).

The risk of developing stroke from all diagnoses is threefold in patients with coronary heart disease. *Congestive cardiac failure* increases the general risk for atherothrombotic brain infarction, in which there is a 9-fold increase
In Tilburg, the Netherlands myocardial infarction and cardiac arrhythmias were found to be significant risk factors for stroke, and the relative risk was greater among young persons in the study. Atrial fibrillation is correlated especially with embolic brain infarctions.

Previous transient ischemic attack (TIA) had a significant excess risk of stroke compared with controls in Rochester, Minnesota and the Netherlands. Muuronen and Kaste found a 4.8% risk of brain infarction in patients with TIA during the follow-up time. The risk of stroke is shown to increase among TIA patients, if other stroke risk factors were also present.

Bonita and co-workers observed a 3-fold increase of the risk of stroke for smokers compared with non-smokers and this association remained significant after adjusting for hypertension. Herman and co-workers reported that smoking was not associated with stroke.

Hillbom and Kaste reported, in a consecutive series of 100 15-55-year-old patients with ischemic brain infarction, that for 40% ethanol intoxication preceded the symptoms and out of them twenty patients were still intoxicated at the time of admission. The frequency of ethanol intoxication preceding stroke was 4-7 times higher in males and 6-15 times higher in women than that of an age and sex related Finnish population. The ethanol-induced risk of stroke was highest in middle-aged women and young men. Occasional and heavy drinking increased the risk of stroke. In contrast, in the Honolulu Heart Program there was no significant correlation between alcohol consumption and thromboembolic cerebral infarction. Compared with non-drinkers, the risk of hemorrhagic strokes was doubled in light drinkers (1-406 g/month) and almost trippled in heavy drinkers (>1160 g/month) and was independent of hypertensive status or other risk factors. No association between alcohol and stroke has been found in some other studies for a review see.

Obesity has been shown to be a risk factor in many studies (for a review see) which may be related to hypertension and diabetes mellitus.

Elevated blood cholesterol and lipids were risk factors in younger patients in The Framingham studie and in middle-aged men in Finland. Low physical activity during leisure time was reported by Herman and co-workers as a significant risk factor and in a multivariate regression analysis it was shown that persons with regular non-strenuous activity had a greater relative risk compared with individuals with regular strenuous activity. It is also reported that low physical activity at work was associated with an
increased risk of stroke\textsuperscript{53}.

Dyken and co-workers\textsuperscript{49} considered geographic location, season, climate, socioeconomic factors, and oral contraceptive use to be less well-documented risk factors.

2. \textit{Risk factors for recurrent stroke}

There have been few studies concerning recurrent stroke and the number of patients included has been rather small. Consequently, the information of risk factors for recurrent stroke are limited. It also is preferable to use a multivariate analysis for large materials in order to estimate the independent importance of other risk factors. The decreasing incidence also may make the pattern of risk factors change with time.

Hypertension, the most important risk factor for stroke, increases the risk of recurrence. Diastolic blood pressure was shown to be a risk of subsequent stroke in patients with one or more TIAs\textsuperscript{54}, and antihypertensive therapy reduced the incidence of fatal and non-fatal stroke recurrence\textsuperscript{55,56,57}.

Marquardsen\textsuperscript{58} showed in his study an increased risk of recurrence in younger survivors, patients with previous stroke and patients with motor deficits. In 1983 Sacco and co-workers\textsuperscript{15} reported from the Framingham study that recurrent stroke was common after atherothrombotic brain infarction and it was usually of the same type as the previous stroke. It did not depend on age, but on the presence of cardiac comorbidity prior to initial stroke and hypertension. The influence of these factors was greater in men, who had a five-year cumulative recurrence rate of 42\%, than in women, who had only a 24\% recurrence rate.

Previous stroke multiplies the risk of recurrent stroke compared with that of the first stroke\textsuperscript{59} and is shown to be a risk factor for cerebral infarctions and all strokes\textsuperscript{53}.

3. \textit{Prevention of stroke}

Miettinen and co-workers\textsuperscript{60} reported from a Finnish multifactorial primary prevention trial in which vascular diseases, hyperlipidemias, hypertension, smoking, obesity and abnormal glucose tolerance were treated in a high risk test group, a considerably improved risk factor status and a reduced incidence of stroke in middle-aged men. A similar intervention trial
was performed in the USA but did not diminish stroke mortality more than in the control group which may be an effect of the fact that the risk factors of the control group diminished.

The positive effect of hypertension treatment on stroke mortality and morbidity is well-documented. The decrease in mortality varied from 34 to 93% and the morbidity (fatal and non-fatal stroke) decreased by 34-74%. In the North Karelian study, mortality from stroke decreased in men between the periods from 1971 to 1972, 1977 to 1978 and 1980 to 1981 and in women between the first two periods and, thereafter, it increased, which may depend on relaxed hypertension control. In the reference area, the trend of decreasing mortality was observed between cohorts. Hypertension treatment in patients over 60 reduced the rate of fatal stroke by 30% compared with the rate of the control group. The rate of all strokes was reduced by 58% compared with the rate of the control group.

There is no solid scientific background yet for the reasons why prophylactic acute and long-term treatment with anticoagulants is given to patients with TIA and atrial fibrillation. Acetylsalicylic acid treatment of TIA patients may have some effect on carotis-TIA patients and on patients with several TIA.

D. PREVALENCE OF CEREBROVASCULAR DISEASE

The overall prevalence rate of cerebrovascular disease in England and Wales, in a study carried out between 1955 and 1956, was found to be 4.9/1000 population (men 4.5 and women 5.2). In Rochester, Minnesota, 1970, the prevalence was 6.1/1000 population and in the age group 65-74 years 4% had had a stroke and for 75-year-olds and older this figure was 8%. In the National Survey of Stroke study in the USA, the prevalence was estimated to be 7.9/1000 population for all ages.

Petlund (1970) found, in the county of Aust-Agder in Norway, that the point prevalence rate for stroke was 4.4/1000 population (4.0 men and 4.8 women). In a Finnish population study, 1973-1976, the age-adjusted prevalence of stroke was 10.3/1000 in men and 5.8/1000 in women. The highest prevalence was found in men old 65-74 years (38.6/1000) and in women over 75 years of age (32.4/1000). In Copenhagen, Denmark, 1976, the prevalence was 6.5/1000 in men and 3.9/1000 in women.
1. General aspects

A normative model of the consequences of stroke is given in the International Classification of Impairments, Disabilities, and Handicaps (ICIDH): 80:

ETIOLOGY → PATHOLOGY → MANIFESTATION/DISEASE → IMPAIRMENT → DISABILITY → HANDICAP

According to the ICIDH the person who evaluates the impairments, disabilities and handicaps classifies them all normatively. The definitions are:

IMPAIRMENT is a loss or abnormality of psychological, physiological or anatomical structure or function. Impairments reflect disturbances on the organ level.

DISABILITY is a restriction or lack (resulting from impairment) of the ability to perform an activity in the manner or within the range considered normal for a human being. Disabilities reflect disturbances on a personal level.

HANDICAP is a disadvantage for a given individual, resulting from impairment or disability. The six dimensions of handicaps represent the socialization of impairments or disabilities.
Fugl-Meyer and Fugl-Meyer have described a model where the end point is not normative.

According to them, common impairments after brain damage are:

**Mobility:**
- motor function
- joint function/pain

**Sensing:**
- exteroception
- proprioception
- perception

**Cerebral integration:**
- cognition
- communication (aphasia)
- motor praxis (apraxia)

**Intrapsychological** (such as depression, stigmatization)

Several authors have attempted to analyze the predictive value of different impairments in the early stage for the final functional outcome after stroke (for review see 82). There is a positive correlation between the degree of impairment on admission and on discharge. High age implies here a negative correlation. Whereas many factors may play important roles as early predictors of the late outcome after stroke, there appears, however, to be no valid mathematical model for the reasonably powerful early prognostication of functional recovery. Early rehabilititative measures, such as physio- and occupational therapy, may, though, shorten the length of stay in the acute wards and improve the functional recovery.

In this dissertation the functions/impairments focused on were motor control, perception, cognition and depression. Ability/disability was measured in terms of daily self-care proficiency while life satisfaction was recorded by means of self-reports.

### 2. Impairments

#### a. Mobility

Classically, the major sign of stroke is hemiparesis/plegia. Petlund reported a prevalence of hemiplegia/hemiparesis in 39% of stroke survivors in Norway, and Sørensen and co-workers in 44% in Denmark.

In the long-term follow-up by Marquardsen, 63.6% of the men and
67.7% of the women had residual hemiplegia one year after stroke, after 5 years 57.4% and 63.5% and after ten years 61.5% and 56.4%. Kotila and co-workers found hemiparesis in the acute stage in 73% of the patients, after three months in 50% and after one year in 37% of the one-year survivors.

b. Perception

Perception is most frequently studied in terms of neglect and hemi-inattention. The anatomical correlation of this symptom is localized much more frequently to the inferior parietal lobe of the right hemisphere than to the frontal lesions. Neglect occurs also with lesions confined to subcortical grey structures, such as the basal ganglia and the thalamus and, sometimes, with cortical frontal lobe damage.

Patients with left-sided hemiplegia showed less spontaneous improvement and less social adjustment than patients with a right-sided motor impairment. Moreover, Denes and co-workers reported a lower degree of improved self-care ability and in motor function and more frequent and severe unilateral spatial neglect in left than in right-sided hemiplegic patients. Kinsella and Ford found that four out of seven (57%) patients had remaining hemi-inattention 18 months after stroke and these seven patients were more dependent on total ADL than patients without this symptom in the acute phase. Hier and co-workers reported that 9 weeks was the median duration for the recovery of left hemisphere neglect. In a study of 72 patients with minor stroke or TIA, a worse performance was found in Rey's figure-copying test in patients with the former than the latter or in controls. This indicate that perceptual impairment is not correlated to hemiplegia and that it is important to investigate all stroke patients.

c. Cerebral integration

In Petlund's study 25% of the patients with hemiplegia/paresis had cognitive impairment. In Copenhagen, Denmark, there was a prevalence of impaired memory in 56% of the stroke patients.

Cognitive impairment has been found to prevail in 22% of men and 31% of women one year after stroke, after five years 34%/36% and after ten years 15%/36% . Cognitive impairment in stroke patients, measured with Mini-Mental State test, has been shown to be influenced negatively by depression,
lesion volume and age. Frontal lobe ischemia was correlated with disorientation as to time and space, and left mid-temporal ischemia was correlated with memory disturbances and dyscalculia. Kotila and coworkers, using a battery of neuropsychological tests, found cognitive impairments in 39% of one-year stroke survivors under 65 years of age.

d. Intrapsychological impairments

Poor psychosocial adjustment with depression, anxiety and fear of relapse has been observed after a stroke as has also irritability and inability to control anger. Robinson and Price reported a depression prevalence of 22% 3-4 years after stroke and of 27% after 5-6 years. In comparison, about 15% of the elderly who lived at home were found to suffer from depression. Brain damage in the left frontal lobe was closely associated with depression up to one year after stroke. The depression correlated significantly with self-care disability up to two years, peaking at six months. Depression may interact with disability and impair recovery.

Denial is a common defence against the psychologically critical impact of a stroke. Whereas denial in the acute phase may be psychosocially adaptive, persistent denial or minimization of impairments can be detrimental to the long-term social adaption after stroke. In the long run, however, focussed illness behavior with regressive dependency appears to be the most common intrapsychological problem among stroke patients, and, in addition, feelings of being stigmatized are common. Some 50% of hemiplegic patients admitted to the Department of Rehabilitation Medicine, Umeå, reported symptoms of stigmatization throughout their first year after stroke.

3. Disabilities

The ability to manage the simple tasks of daily self-care is a major concern for the stroke patient. Other important aspects of ability/disability are occupation, leisure and sexuality. Hence, disabilities must be seen in relation to the goals the patient had before and can set up after stroke. Ability to manage self-care is, however, a basic survival goal, and the capacity to do so has been widely measured in studies of the outcome of stroke treatment (for a comprehensive review see)
The point prevalence of self-care disabled men after stroke in Aust-Agder county in Norway, 1965, was 2.4/1000 population and for women 3.7/1000 and for the whole population 2.7/1000\(^{77}\).

Kotila and co-workers\(^ {86}\) found that 68% of the one-year stroke survivors were ADL-independent. Garraway and co-workers\(^ {106}\) made a comparison between a stroke rehabilitation unit and medical units in a follow-up of a controlled trial of stroke patients who were independent pre-stroke, not unconscious on admission and who could not walk without aid or had hemiplegia. When discharged from hospital, 58% of the patients from the stroke unit and 37% from the medical units were independent. After one year the corresponding figures were 55 and 57%.

In the Espoo-Kauniainen study\(^ {86}\), 69% of patients who survived one year had returned home within 3 months and 78% within 12 months. In Söderhamn\(^ {13}\) about 10% of stroke patients were hospitalized after one year, and in Umeå the corresponding figure was 16% (patients treated at general medical wards)\(^ {84}\). The positive effect of stroke units on outcome has been shown in many studies\(^ {107,108,109}\) and in Umeå only 7% of patients with cerebrovascular disease need nursing-home care after one year\(^ {84}\).

Petlund\(^ {77}\) found disability caused by stroke alone in 42% of stroke survivors, and caused by stroke together with other disabling disease in an additional 21%. Aho and co-workers\(^ {8}\) reported that, after one year, 62% were independent as regards self-care while 9% were totally dependent on other people. Ahlström and co-workers\(^ {17}\) found that about 75% were ADL-independent two years after stroke. Andrews and co-workers\(^ {110}\) showed that there was no difference in self-care ability between younger and elderly stroke patients during the first year after stroke, but the latter were more often institutionalized than the younger with similar functional level of recovery. Severe ADL disability was found in 28% of patients over 65 years old one year after stroke.

"Time is what I have" is a remark often made by long-term stroke survivors. In agreement with other authors, Fugl-Meyer and co-workers\(^ {111}\) reported that the majority of subjects who suffered a first stroke in their vocationally active years never returned to work. In Northern Sweden almost 90% of younger patients with hemiparesis/-plegia do not take up to their premorbid leisure activities again to the full\(^ {112}\); while Trudel and co-workers\(^ {113}\) showed a loss of leisure activities in 37.5% of carotid endarterectomy survivors. Labi and co-workers\(^ {114}\) reported a decrease in
socialization outside their homes for 51% of physically restored long-term stroke survivors, and within their homes for 36%, and a decreased social activity involving hobbies/interests for 46% of the women and 29% of the men.

4. Life satisfaction

Some objective indicators of a good quality of life are health, sufficient funds, absence of psychological distress, and availability of a supportive family and friends\textsuperscript{115}.

Measurements of quality of life have become increasingly popular during the last quarter of a century. Many different approaches and theoretical models have been proposed (for general overviews see\textsuperscript{116,117}). The latter authors\textsuperscript{117} equated quality of life with life satisfaction. They also categorize quality of life/life satisfaction into one general "global" and several domain specific areas. There are only a few studies of life satisfaction among the post-stroke population. Sjögren\textsuperscript{103} found that younger first stroke subjects with hemiplegia/paresis to a great extent reported decreases in domain specific satisfaction regarding leisure (approximately 80%) and sexual life (67% in males and 42% in females). The decreases closely paralleled decreased activity in these areas. Ahlsiö and co-workers\textsuperscript{17}, found that, in a consecutive sample of stroke patients, global life satisfaction had decreased for 77% of patients.

D. MORTALITY AND PROGNOSIS AFTER CEREBROVASCULAR DISEASE

1. General aspects

In the National Survey of Stroke Study\textsuperscript{118} in the USA, the mortality rate was 48% after one year and 70% after five years. The mortality rate among patients aged 65-74 years was similar (41% after one year and 66% after 5 years) to that of all patients but the age group 75-84 years (54% after one year and 78% after 5 years) had an approximately 25% higher mortality rate and patients over 85 years (72% after one year and 93% after 5 years) about 50% higher mortality after one year and after five years. In Söderhamn\textsuperscript{13}, 34% of patients had died during the first three months after stroke and about 70%
after four years. Mortality from stroke in Stockholm\textsuperscript{26} was, for men 60-69 years 9 /1000 population and, for women of the same age, 5.2/1000. In the age groups 70-79 and 80 years and older, the mortality rate for men was 22 and 54/1000 and for women 20 and 43/1000.

2. Changes

Stroke mortality has declined by 76% over thirty years in Rochester, Minnesota, and the primary cause, according to Whisnant\textsuperscript{119}, is that the incidence of stroke has decreased. A decline is reported from other parts of the USA\textsuperscript{120,121}, Australia\textsuperscript{122}, Taiwan\textsuperscript{123} and Europe\textsuperscript{124,125}.

In Norway, mortality statistics have shown a steady decline in stroke mortality\textsuperscript{126}, except for patients with intracerebral infarction and over 70 years old. In Stockholm, the mortality from stroke decreased annually by 2.3% in men and 3.5% in women from 1974 to 1981\textsuperscript{26}.

3. Risk factors for death

Many studies\textsuperscript{8,13,58,124,127,128,129} have reported that the most important prognostic factor for death is impairment of consciousness has been in the acute phase. Other clinical symptoms, related to the neurologic damage and reported as prognostic indicators, are degree of hemiplegia\textsuperscript{127,128}, pupillary abnormalities, paralysis of conjugate ocular movement, bilateral extensor plantar response and respiratory abnormalities\textsuperscript{58}.

Long-term prognosis is also affected by age\textsuperscript{58,122,127,128,129,130}, earlier hypertension\textsuperscript{58,130,131}, cardiac failure\textsuperscript{131}, atrial fibrillation and myocardial infarction\textsuperscript{130} and male sex\textsuperscript{131}. Diabetes mellitus\textsuperscript{130,182} and peripheral vascular disease\textsuperscript{130} have been reported as negative prognostic factors for late survival. On the other hand, Abu-Zeid and co-workers\textsuperscript{127}, Kotila\textsuperscript{124} and Howard and co-workers\textsuperscript{129} could not show any significant effect of diabetes mellitus, hypertension, hypertensive cardiac disease, myocardial infarction and atrial fibrillation on survival.

4. Causes of death

Paper II reports the causes of death from different studies. In the acute phase, cerebrovascular disease is the main cause of death (31-59%). In
follow-up studies, cerebrovascular disease was found as the cause of death in
23-48% and cardiac diseases in 18-39% of the cases. Bronchopneumonia
varied as the cause of death from 9-34%. Pulmonary embolism was found at
autopsy and varied from 0-18% as cause of death.

Ueda and co-workers\textsuperscript{24} found in their epidemiological study, in which the
autopsy rate was 88%, that the underlying cause of death in patients with the
initial clinical diagnoses of cerebral infarctions was 54% cerebral infarction,
5% cerebral hemorrhage and 41% other causes. In cerebral hemorrhages the
cause of death was 88% cerebral disease per se. Autopsy-verified causes of
death in the study above\textsuperscript{132} were cerebrovascular disease 23%, malignancy
25%, respiratory tract infection 17%, myocardial infarction 4% and other
causes 31%.

\textbf{E. MORBIDITY AFTER CEREBROVASCULAR DISEASE}

\textit{1. Myocardial infarction}

Increased heart-type creatine phospho-kinase isoenzyme (CK-MB) values
have been reported in acute stroke\textsuperscript{133,134}. Norris and co-workers\textsuperscript{135}
demonstrated increased CK-MB iso-enzyme in 11% of acute stroke patients
and these patients also showed more evidence of acute myocardial ischemia on
their ECG. Arrhythmias often occur in acute stroke\textsuperscript{136,137}. From autopsy
studies, focal myocardial damage is reported more often in patients with
intracranial lesions. This leads to rapid increase in intracranial pressure
which, it is postulated, increases the levels of plasma catecholamines\textsuperscript{138}. von
Arbin and co-workers\textsuperscript{139} found enzyme curves suggestive of acute
myocardial infarction in 6% of patients with acute cerebral infarction but
only in 1% of hospitalized controls. Signs of myocardial infarctions of
various ages were found in 79% at autopsy. Of these, 11% happened just prior
to stroke, 15% were concomitant with the stroke and 7% occurred
immediately post-stroke. In 16% of patients without clinically suspect
myocardial infarction, myocardial infarction was found at autopsy. Coronary
artery disease was frequently found in patients with TIA or minor stroke\textsuperscript{140}.

In studies of the natural history of stroke from the 1960's, the risk of
myocardial infarction was 1.8-3.0% annually\textsuperscript{141,142}. Marquardsen\textsuperscript{58}
reported 37 myocardial infarctions in 362 discharged patients (10.2%).
Leonberg and Elliot\textsuperscript{143} in a preventative study of 88 survivors after the first
cerebral infarction found, in a mean follow-up period of five years, five fatal and two non-fatal myocardial infarctions (8%). In the Swedish Cooperative Study of ASA\textsuperscript{144}, 44 of 505 selected patients (8.7%) with cerebral infarction suffered a myocardial infarction during a two-year follow-up. Other therapeutic trials reported a rate of 1.5-3% annually\textsuperscript{145,146}.

2. Epilepsy

Shinton and co-workers\textsuperscript{147} showed that stroke patients had a prior epilepsy prevalence of 45/1000 compared with 6/1000 in that of matched controls.

In an autopsy study, Richardson and Dodge\textsuperscript{148} found epilepsy in 5.8% of patients with cerebral hemorrhage and in 1.3% of the controls. Convulsive seizures occurred in 28% of patients with cortical lesions. In Marquardsen's study \textsuperscript{58}, 23 out of 404 patients had epileptic seizures, none of them had a pre-stroke history of epilepsy. Typical Jacksonian seizures were not noted and the focal convulsion occurred on the affected side in 9/23 patients and grand mal seizures were found in 12 patients. Pirttimäki and co-workers\textsuperscript{149} reported a 9% incidence of epilepsy in stroke patients. Electroencephalographic examination showed that 14 out of 29 (48%) patients had no signs of irritative activity. Autopsies showed one or more cerebral infarctions in the cortex in 11 patients, only one subcortical infarction was found. In a prospective study, 73 patients under 75 years of age with ischemic stroke were followed up by Rosenkvist and Skyhøj Olsen\textsuperscript{150} 2-4 years after the stroke and they found an epilepsy rate of 11%.

G. AIMS OF THE PRESENT STUDY

The aims of the present study were to:
- estimate the long-term survival of CVD patients and to weigh risk factors that could have effects on survival!
- describe the causes of death after stroke
- estimate the risks of recurrent stroke, myocardial infarction and epilepsy during the long-term follow-up and to weigh the risk factors which have an influence on recurrent stroke and myocardial infarction
- describe the occurrence of motor and perceptual impairment on self-care ability in communicable 4-6 year stroke survivors and to analyze the effects of motor impairment and self-care disability on life satisfaction
PATIENTS and METHODS

Methods and procedures are described in detail in each article (I-V) and are summarized here.

1. Background population (I-V)

Umeå University Hospital has a catchment area of 9409 km² with a population of 116 000 (49.6% men). Seventy percent live in the city of Umeå and have a lower average age than the inhabitants in the surrounding rural area.

Acute stroke patients from the catchment area are admitted to the Department of Medicine (250-325 patients/year). Patients with subarachnoid hemorrhage are admitted to the Department of Neurosurgery and have been excluded from this presentation.

Patients with intracerebral hemorrhage, non-embolic cerebral infarction, embolic cerebral infarction and TIA were included in the present thesis as "stroke" patients.

2. The Non-Intensive Stroke Unit at the Department of Medicine, University Hospital, Umeå, Sweden

Patients from the catchment area of Umeå University Hospital, regardless of age, who, with no preceeding trauma to the head, present focal neurological dysfunction of a duration not exceeding one week or patients with TIA during the last week, are admitted to the Stroke Unit if there is a bed available.

The stroke unit is a 6-bed, non-intensive care and research unit for patients who meet the admission criteria, and has been described in detail in previous publications\textsuperscript{151,152,153}. The patients have been shown to be representative of all those patients admitted to hospital for acute stroke within this district\textsuperscript{84}.

3. Patients

1. In articles I, II and III, all patients with a well-defined CVD-diagnosis who were treated in the Stroke Unit at the Department of Medicine, between Jan. 1st 1978 and Dec. 31st 1982, a total of 409 patients with specific stroke diagnosis, were included out of the 428 patients with acute cerebrovascular...
disease. The 19 patients excluded did not fulfill the diagnostic criteria (see definition below). In studies I and II, patients were followed up to June 30, 1984 or to death, and, in study III, 3.5-7 years after stroke or to death. All patients were accounted for.

2. In articles IV and V, all 120 4-6 year survivors from the patients who had been treated at the Stroke Unit between Jan. 1st 1978 and Sept. 30th 1981 were initially included. After the exclusion of unwilling or non-communicable subjects, 75 and 62 remained to be investigated in IV and V (patients with TIA excluded), respectively. Sixty subjects (26 subjects aged 78-81 years and 34 subjects 60-61 years) who had not been hospitalized during the last 7 years and were clinically healthy were taken as the reference group for life satisfaction variables.

4. Definitions

a. Definition for previous disease (I-III)

Previous stroke - acute CVD in medical history and treated in hospital.
Previous TIA - acute focal neurological deficits of vascular origin lasting less than 24 hours in the medical history.
Hypertension - a history of high blood pressure, treated with antihypertensive agents.
Cardiac failure - typical symptoms of this disease treated with digitalis or diuretics.
Atrial fibrillation - a history of irregular cardiac rhythm, verified by electrocardiogram.
Angina pectoris - exertion-correlated substernal or left-sided chest pain, disappearing within ten minutes upon rest or upon taking nitroglycerin.
Myocardial infarction - a hospital report of myocardial infarction.
Diabetes mellitus - diagnosed by a physician or newly detected during hospital stay for stroke (not based on elevated glucose levels in the early phase).

b. Criteria for clinical diagnoses in the Stroke Unit (I-V)

Intracerebral hemorrhage - signs of an intracerebral hemorrhage on
computerized tomography (CT scan), a hemorrhagic pattern in spinal fluid analysis or hemorrhage found at autopsy.

Non-embolic cerebral infarction - focal neurological deficits persisting more than 24 hours with no signs of a hemorrhage on CT scan or on analysis of spinal fluid analysis or verified infarction; no potential source of emboli at autopsy.

Embolic cerebral infarction - diagnostic criteria as for non-embolic infarction but with a potential source of embolus (atrial fibrillation or a recent acute myocardial infarction with mural thrombosis found at autopsy, rheumatic valvular disorder, endocarditis, mitral valve prolapse and/or previous history of systemic embolisation) and sudden onset of symptoms.

Transient ischemic attack (TIA) - focal neurological deficits of presumed vascular origin and of less than 24 hours' duration.

c. Clinical and autopsy criteria for causes of death (II)

CVD - Clinical picture of CVD with decreasing consciousness. Autopsy findings confirming CVD with large hemispheric involvement, brain stem infarction or hemorrhage, and signs of brain edema with uncal herniation.

Cardiac disease - Clinical evidence of cardiac failure, myocardial infarction and severe pulmonary edema. Autopsy findings of pulmonary edema supported by evidence of underlying significant heart disease.

Bronchopneumonia - Clinical picture of pneumonia with fever and autopsy findings of confluent bronchopneumonia involving at least the major part of one lobe.

Pulmonary embolism - Clinical picture of pulmonary embolism confirmed by arterial blood gas determination, chest X-ray, pulmonary scintigraphy or pulmonary-artery angiography. Saddle pulmonary embolus or bilateral multiple pulmonary emboli at autopsy.

Other causes - Other diseases that lead to death and cases where neither clinical picture, nor laboratory, radiological or autopsy findings gave an apparent cause of death.

d. Criteria for events after stroke (III)

Recurrent stroke - When the WHO definition of stroke was fulfilled and occurred more than one week after the index event.
Myocardial infarction - Defined by WHO criteria\textsuperscript{155}.

Epilepsy - When paroxysmal and transitory seizures developed suddenly, ceased spontaneously and showed a tendency to recur, this led to drug treatment\textsuperscript{156}.

5. Methods

Motor function was assessed in articles IV-V using a stroke specific test, developed by Fugl-Meyer and co-workers\textsuperscript{157}, based on the motor development concepts described by Twitchell\textsuperscript{158}. The test is valid and has been found to be valid and reliable\textsuperscript{159,160}. Perceptual function was evaluated in paper IV using a tool which is a modification of that developed at the Loewenstein Rehabilitation Hospital, Raanana, Israel\textsuperscript{161}. Cognition as an aspect of cerebral integration was assessed using the test developed by Folstein and co-workers\textsuperscript{162} (Mini Mental State). Occurrence of depression was screened using the method described by Montgomery and Åsberg\textsuperscript{163}. Self-care ability (self-care ADL) was measured using a stroke specific method\textsuperscript{164}, by which twenty items within the sphere of hygiene, dressing and feeding were assessed. Life satisfaction was gauged through structural interviews using the subjects' self-reported global (one item) and domain specific (6 items) satisfaction prior to the stroke (retrospect) and at the time of the investigation. Thus changes could be computed.

6. Statistical methods

The Mantel-Haenszel life table technique\textsuperscript{165} was used to estimate the proportion of survivors and instances of recurrent stroke, myocardial infarction and epilepsy (I-III). Relative risks between subgroups of patients were calculated using the log rank test(I). Multivariate analysis was performed with BMDP's program for regression on life table curves with Cox's proportional hazard model\textsuperscript{166} (I, III) in order to analyze the relative importance of clinical variables for the risk. Factor analysis calculations were based on a matrix of Pearson's correlation coefficients (IV). Simple cross-tabulations ($\chi^2$-test) were used for testing differences between proportions (II, V).
RESULTS

Survival and risk factors for death after stroke (I)

The survival rate of the 409 patients with cerebrovascular disease was 77% after 3 months, 69% after one year, 52% after three years and 37% after five years. An excess mortality rate among patients was seen during the first six months after stroke the prognosis, thereafter, being relatively good.

The most important prognostic factor for death was impairment of consciousness on admission, with a standard coefficient of 8.09 (p<0.001), while the second most important factor was age, 5.94 (p<0.001). History of previous cardiac failure and diabetes mellitus worsened the prognosis. Previous TIA indicated a reduced risk of death. Other earlier diseases had no effect on outcome. The prognosis for men was worse than for women. The only CVD diagnosis which was a risk factor for death was intracerebral hemorrhage.

Autopsy findings after stroke (II)

The accumulated probability of death during the first three months after stroke was 23% and, thereafter, 7-10% annually. In the first week after the stroke, death was ascribed directly to the cerebrovascular accident in 90% of patients. From the second to fourth weeks, pulmonary embolism was the most common cause of death, bronchopneumonia in the 2-to-3-month interval and cardiac disease thereafter. There were no significant differences in the cause of death between men and women nor between age groups <75 and ≥75 years within the first three months, although the older group appeared to die more often from bronchopneumonia.

As expected, for the majority (76%) of patients with intracerebral hemorrhage the cause of death was their cerebral disease. In 55% of patients with non-embolic cerebral infarction the cause of death was non-cerebral; the corresponding proportion was 64% in embolic cerebral infarctions.

A potential source of emboli was found at 18 of the 82 autopsies performed in patients who died within 3 months of having a stroke, and, of them, 15 were in the heart.

The causes of death in the 128 patients who died later than three months
after stroke during the follow-up period were cerebrovascular events 27%, cardiac disorder 32%, bronchopneumonia 18%, pulmonary embolism 5% and other/uncertain causes 18%.

Of 12 patients who died of pulmonary embolism, four had been capable of walking without assistance.

Recurrent strokes, myocardial infarction and epilepsy after stroke (III)

During the follow-up, recurrent stroke occurred in 93 patients. The risk of recurrent stroke was highest during the first year after admission and thereafter remained fairly constant (5-8% annually). High age and congestive heart failure were predictors of increased risks of recurrent stroke. A history of previous stroke (before inclusion in this study) did not achieve statistical significance but may be a possible risk factor. Previous TIA, hypertension, myocardial infarction, angina pectoris, atrial fibrillation and diabetes mellitus (for definition see Methods) and male sex were of less importance for recurrent stroke.

Fifty-seven patients developed myocardial infarction, the greatest estimated proportion occurring during the first two months after stroke. High age, diabetes mellitus and angina pectoris were associated with significantly increased risks. The other factors (see above) did not increase the risk of myocardial infarction.

Only 15 out of the 347 patients who survived more than one month developed epileptic seizures. The greatest risk of onset of epilepsy appeared to be between 6 and 12 months after stroke.

Impairment and disability in long-term stroke survivors (IV)

The factor analysis grouped motor and perceptual functions into three distinct groups. One of these represented motor function only, which was impaired in 36% of long-term survivors. The perceptual items fell into the two remaining groups. Applying the principles of ecological perception 167,168, one of these characterized low level perception. Deficits within this level of perception prevailed in 8%. The other factor adequately characterized high-level perception which was impaired in 57%. Finally, self-care disability (in terms of dependency) prevailed in 32%. The joint effect of the three impairments (one motor and two perceptual) factors on self-care
ability was analyzed using a multiple linear regression model. With this model, 71% of the variance in self-care ADL capacity could be explained.

Life satisfaction 4-6 years after stroke (V)

Decreased general and/or domain specific satisfaction with life was found in 61% of the 62 communicable patients with completed stroke. Twelve subjects (15%) experienced a decrease in four or more out of the 7 aspects and 14 (18%) had decreased life satisfaction in only one aspect. Most often, subjects felt a decrease in global life satisfaction (42%) followed by diminished satisfaction with sexual life (38%) for the 42 married subjects. Reduced satisfaction in leisure and self care ADL was found in about one third of interviewees.

Subjects with motor impairment had significantly more frequently changes in global, leisure and sexual satisfaction than individuals with normal motor function. Decreased global satisfaction, self care ADL-satisfaction and sexual satisfaction were found significantly more often in subjects with ADL-disability. However, a fair proportion of unimpaired patients reported negative changes in life satisfaction.

No statistical differences in life satisfaction were found between the two age groups of reference subjects. Life satisfaction level prior to stroke in the patients did not differ significantly for any items from those of the reference group. But after stroke, satisfaction with life in general, self-care ADL, leisure and sexual life were significantly lower for the patients than for the reference subjects.
DISCUSSION

In this thesis, a sample of a stroke population was analyzed and followed up. The sample could be regarded as representative of the total hospitalized stroke population except that patients with subarachnoidal hemorrhage were excluded.

The patients in nursing homes and at the Department of Geriatric Medicine were not generally admitted to the Department of Medicine and therefore some events of stroke were missed in patients with several risk factors for stroke and death (high age, cardiac failure and diabetes mellitus). Some patients with TIA and minor stroke may be assumed to receive treatment at home, especially in rural areas. It can be assumed that these groups are so small that they would not influence the results as Terent\textsuperscript{13} showed that 90\% of Swedish patients suffering from stroke turned to their hospital for care.

In the present study, age was a risk factor for death (I), as was also recurrent stroke and myocardial infarction (III). In the population study H-70 in Gothenburg, Sweden, Svanborg and co-workers\textsuperscript{169} demonstrated that the more recent cohort was more healthy and had fewer diseases. This may mean that biological age represents a group of factors that is genetically linked but can be affected by external factors such as eating habits, smoking, alcohol and leisure activities. This can result in the mean age of stroke patients increasing in subsequent cohorts.

The impairment of consciousness was the most important risk factor for death in the acute stage after stroke. As shown in study II and by Ulbrich\textsuperscript{170} and Bounds and co-workers\textsuperscript{171}, for most patients who died during the first week after stroke cerebral disease was the primary cause of death, indicating that the brain damage per se, its dimension and/or localisation is the determinant that causes the poor outcome.

Hypertension per se was neither a risk factor for death (I) nor for myocardial infarction after stroke (III). The risk of recurrent stroke increased in hypertensives with embolic cerebral infarction (III). High systolic blood pressure has been shown to be significantly associated with stroke mortality in patients aged 65-84 years\textsuperscript{172}. In studies made in the 1960's, hypertension increased the risk of death\textsuperscript{173,174} and recurrent stroke\textsuperscript{175} but in studies in the 1970-80's no significance was found for hypertension as a risk factor for death after stroke\textsuperscript{8,124,127,128}. This may be the effect of hypertension treatment which has changed the patterns of risk
factors. In the study by Solzi and co-workers\textsuperscript{130} all patients treated at a Rehabilitation Center, from 1958 to 1977, were recorded and hypertension was found to be a risk factor for death. However, no division was made between patients observed in different decades.

Cardiac failure was a risk factor for recurrent stroke (III) and for death (I). In earlier times, cardiac failure was often caused by hypertension and arteriosclerosis but today it is most frequently a sequel to coronary artery disease\textsuperscript{176}. Sacco and co-workers\textsuperscript{130} found that risk of death or recurrent stroke was influenced by male sex, cardiac comorbidity and hypertension. It may be possible with new medical therapies to further reduce the effect of hypertension on arteriosclerosis and cardiac failure and also to improve the treatment of cardiac failure and so reduce the negative effect of this risk factor.

The risk of myocardial infarction was highest in the first weeks after stroke (III), which may indicate that cerebral damage can cause myocardial damage\textsuperscript{138} by increasing the level of plasma catecholamines.

Cardiac diseases caused death in 32\% of patients up to three months after stroke (II) and similar results are reported in several other studies\textsuperscript{128,173,175,177}. The accumulated risk of myocardial infarction was 7\% one year and 19\% five years after stroke (III). It has been shown in selected stroke patients\textsuperscript{144} that there are about 1\% annually "silent" myocardial infarctions of lesser clinical importance. Such patients may have been missed in the present study because electrocardiograms were not taken during the follow-up. As expected in patients of high age\textsuperscript{178,179}, 40\% of those with post-stroke myocardial infarctions in our study died (III). Prevention of major cardiac events by using betablockers may be a possible way to improve the late prognosis, as shown in subarachnoidal hemorrhages\textsuperscript{180} and also in a recent study in stroke patients\textsuperscript{181}. High dose acetylsalicylic acid had no preventive effect on myocardial infarction in patients with cerebral infarction\textsuperscript{144}.

Our patients were followed up and conventional therapy was applied to attain good secondary prevention. Comparisons between earlier and recent studies are difficult to make as the distribution of CVD diagnoses has changed and mortality decreased. The risk of recurrent strokes was 14\% after one year and 38\% after five years (III). In previous studies, the recurrence rate was reported to be 8-13\% in the natural history of cerebrovascular disorder (for review see\textsuperscript{58}). Chen and Ling\textsuperscript{16}, in a recent study reported a cumulative
recurrence rate after cerebral thrombosis at one year of 13% and after 3 years 33%. These results are similar to those found in the present study.

Recurrent strokes are a further risk of death in a later phase. Miah and co-workers\(^{128}\) reported that, in 17% of unselected patients, recurrent stroke was the underlying cause of death during a three year follow-up and in the Swedish Cooperative Study of ASA\(^{144}\) recurrent stroke caused death in 25% of selected patients during a two-year follow-up. No differences were found between the ASA and placebo groups regarding recurrent stroke.

Diabetes mellitus was a risk factor for death (I) and myocardial infarction after stroke but not for recurrent stroke (III). Several other studies have shown poor outcome for diabetic stroke patients\(^{58,130,182}\) and also for patients with hyperglycaemia\(^{183}\) or abnormal HbA\(_1c\)\(^{184,185}\) and other studies have shown no effect on the outcome\(^{124,127}\). In the Framingham study, diabetes mellitus and glucose intolerance constituted greater risks of myocardial infarction than of stroke\(^{186}\). After myocardial infarction, the patients with diabetes mellitus had a poorer outcome than the control population\(^{187}\). Stroke causes myocardial damage\(^{138}\) and the hearts of diabetics may be more vulnerable due to general arteriosclerosis. Another explanation may be that patients with hyperglycemia in stroke develop more pronounced cerebral edema\(^{188}\), and hyperglycemia was shown to decrease the regional cerebral blood flow\(^{189}\). It was also demonstrated that incomplete cerebral ischemia may be more harmful than complete. This could be explained by the high levels of lactic acidosis which is in turn due to on the level of blood glucose\(^{190}\).

In our study, previous TIA (see definition under methods) constituted neither a risk of recurrent stroke nor a risk factor for myocardial infarction (III) and, surprisingly, previous TIA indicated a reduced risk of death in this stroke population (I), which may be an effect of the small population or that all patients with TIA in the present study were treated with acetylsalicyclic acid. Other studies\(^{124,129}\) confirm that TIA is not a risk factor for death and that patients without other risk factors for death had the same survival rate as the age-matched population. On the other hand TIA patients who had 3 or more risk factors for death, had a greatly reduced survival rate. Patients with multiple TIA had a significantly greater risk of TIA recurrence and stroke or death than patients with single TIA\(^{72}\). Young and middle aged TIA patients had no stroke during the 55 months follow-up\(^{191}\). In earlier studies (for review see ref\(^{192}\)) the major cause of death in TIA patients was myocardial
infarction. Asymptomatic coronary artery disease was found in 28% of 83 consecutive patients with TIA compared with 6% for controls. It is suggested therefore that TIA may be a marker of asymptomatic coronary artery disease. An active investigation of coronary heart disease should be performed in TIA patients in order to plan optimal comprehensive management.

After the first week, complications of stroke were the primary causes of death both in study II and other studies. Pulmonary embolism is difficult to diagnose because of its varying symptomatology. That is why a prophylactic low-heparin regime may reduce the occurrence of venous thromboembolic events, which are common after stroke, as demonstrated by the fibrinogen uptake test by Prasad et co-workers and Mellbring and co-workers. The first study showed that pneumatic compression of the calf in elderly hemiplegics (mean age 78 years) had no positive effect. However, it is possible that prophylactic treatment with anticoagulants and an intensified clinical observation could be of great importance here.

Of the 347 patients (85% of the whole population studied) who survived more than one month (III), 15 (4%) developed epileptic seizures during the follow-up. The risk factors could not be calculated because of the small number of patients with epilepsy. The highest risk was from 6 to 12 months after stroke and this interval was confirmed by Skyhøj Olsen. He found epilepsy in 33% of patients with cortical infarcts and that only one out of 33 patients with subcortical infarcts developed epilepsy. These findings were also verified by Hornig and co-workers who also found the localization of the lesion in the brain area supplied by the medial cerebral artery. Lesser and co-workers did not accept that the initial reduction of blood flow per se caused the epileptic seizures but that it probably arose from subsequent cytotoxic effects which they could not specify.

There are few studies in the literature which evaluate the prevalence of impairment and disability in long-term survivors, as most investigators are concerned with selective series. Moreover, the motor function after stroke has been measured using different methods. The observed occurrence rate found in this investigation (IV) is close to that reported by Petlund. It should, though, be remembered that only cooperative patients were included. Hence, the observed occurrence of motor impairment, ADL-disability and decreased life satisfaction may constitute an under- rather than an overestimation of the real occurrence. It can also reasonably be assumed that
the occurrence of perceptual disturbances is greater than that reported here: Eleven non-communicable (and therefore nonassessed) patients with cognitive disturbances were classified as suffering from (multiinfarct) dementia and most probably had perceptual disturbances.

Usually symptom-oriented approaches are used for characterizing perceptual deficits, which many authors regard as deficits of cerebral integration. According to the definitions of Gibson and followers\textsuperscript{167,168}, perception is immediate and can, therefore, be seen as a sensing quality. The present findings (IV) of two distinct perceptual factors of which one represents low-order and the other represents higher-order perception appear to substantiate Gibson's theoretical model. In this context it is important to emphasize that, in a sample of patients examined within two weeks after stroke, the identical model of two perceptual factors emerged\textsuperscript{201}.

It is well-known that motor function is a powerful predictor of capacity to manage self-care. With the methods used here for measuring motor function and ADL-capacity, Fugl-Meyer and Jääskö\textsuperscript{202} demonstrated a close correlation between these parameters in six-year survivors of first stroke. The present results (IV) confirm those findings but, in addition, perceptual function is also of considerable importance as a predictor of the degree of disturbances in self-care ADL. A search of the literature revealed no other reports demonstrating the long-term joint effect of motor and perceptual impairments on abilities/disabilities after stroke.

The majority of communicable (non-demented, non-aphasic) stroke subjects reported decreases in life satisfaction (V). The 42\% decrease in global life satisfaction is clearly lower than that reported by Ahlsiö and co-workers\textsuperscript{17} in their two-year follow-up study. This discrepancy may partly be explained by methodological differences. For instance, Ahlsiö and co-workers\textsuperscript{17} used a visual analogue scale to characterize one item, that of global life satisfaction, while the present investigation incorporated a total of seven items. Moreover, selection criteria and follow-up time differed between the two investigations which do, however, agree that satisfaction with life is long-lastingly (permanently?) reduced after stroke. Evidently impairment and also disability are of importance for the continuation of the premorbid quality of life, as illustrated by significant associations between motor impairment vs decreases in satisfaction with life in general, with leisure and with sexuality, and also between reduced self-care ability and decreases in satisfaction with life in general, experienced ADL and sexuality. That these decreases are the
long-term effects of stroke is supported by the virtually stable levels of life satisfaction throughout a 20-year period in non-apoplectic, clinically healthy, elderly subjects. However, a considerable proportion of non-impaired and non-self-care disabled subjects reported decreased life satisfaction due to stroke. Such decreases which may best be explained by the psychological impact of stroke per se, including fear and anxiety.

It could be argued that non-normative, "subjective" measures, such as that used for measuring life satisfaction, are insufficient because of low validity. Judging from the generally close correspondence of levels of life satisfaction between patients' retrospective reports of satisfaction prior to the stroke and the actual reported life satisfaction of reference subjects, it would appear that self-reported changes can be used as valid and reproducible measures.

Satisfaction with family life and friends changed little (V), which may indicate that these stroke patients experienced good support from their family and friends. However, the decreases, not only in global but also in sexual and leisure satisfaction, point equally strongly to many patients' ending up frustrated and passive spectators of life. This postulation is supported by Sjögren's findings of close correlations between decreased levels of leisure and sexual activity and decreases in the respective levels of satisfaction. The conclusion is, therefore, that much attention should be focused on patients' premorbid values, interests and life-roles.

Stroke is a major - often catastrophic - life event for the victims and those close to them. Hence, throughout treatment of completed stroke, the patient, and his relatives should be seen as social human beings. If that is forgotten, we may, with our more or less intensive medical and rehabilitation interventions, well-intentioned though they might be, help to create a population of formally well-functioning (in terms of impairment and disability) stroke survivors among whom the majority of whom have lost a considerable part of the meaningfulness of their lives.
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