Long-Term Survival and Causes of Death After Stroke

Henrik Brønnum-Hansen, MSc; Michael Davidsen, MSc; Per Thorvaldsen, MD, DMSc;
for the Danish MONICA Study Group

Background and Purpose—As part of the Danish contribution to the World Health Organization (WHO) MONICA (Monitoring Trends and Determinants in Cardiovascular Disease) Project, a register of patients with stroke was established in 1982. The purpose of the present study was to analyze long-term survival and causes of death after a first stroke and to compare them with those of the background population.

Methods—The study population comprised all subjects aged 25 years or older who were resident in a geographically defined region in Copenhagen County. All stroke events in the study population during 1982–1991 were ascertained and validated according to standardized criteria outlined for the WHO MONICA Project. After completion of the stroke registry at the end of 1991, all patients were followed up by record linkage to official registries. Standardized mortality ratios were calculated for various causes of death and periods after the stroke.

Results—The estimated cumulative risks for death at 28 days, 1 year, and 5 years after onset were 28%, 41%, and 60%, respectively. Compared with the general population, nonfatal stroke was associated with an almost 5-fold increase in risk for death between 4 weeks and 1 year after a first stroke and a 2-fold increase in the risk for death subsequent to 1 year. The excess mortality rate in stroke patients was due mainly to cardiovascular diseases but also to cancer, other diseases, accidents, and suicide. The probability for long-term survival improved significantly during the observation period for patients with ischemic or ill-defined stroke.

Conclusions—Stroke is a medical emergency associated with a very high risk for death in the acute and subacute phases and with a continuous excess risk of death. Better prevention and management of strokes may improve the long-term survival rate. (*Stroke*. 2001;32:2131-2136.)

Key Words: cause of death ■ cerebrovascular disorders ■ Denmark ■ epidemiology ■ survival

Knowledge of the epidemiology of stroke has increased over the last decades, although it is well established that stroke is associated with a high risk for death, especially in the first few weeks after the attack. Studies of incidence and mortality have shown that case fatality rates vary considerably among populations.[1,2] Few studies have been published on the long-term prognosis after stroke, and they are somewhat heterogeneous as regards study objectives, design, and the subjects investigated.

Studies of the determinants and probabilities of survival and at various times after the index stroke have included all strokes,[3] first stroke,[4–6] or ischemic stroke,[7–10] with emphasis on stroke subtype,[11] age,[12] or place of management.[13] The absolute risk for death after a stroke is an appropriate variable in analyses of prognostic factors, but the inferences to be drawn from the absolute survival probability may be limited because most stroke patients were in their 70s or 80s. Few community-based studies have included comparisons of mortality rates after stroke with the mortality rates and causes of death in the general population of the same age and sex.[4–6,14]

In this article we describe the long-term absolute and relative risks for death and the causes of death of a large, unselected, community-based cohort of stroke patients registered in the Danish portion of the World Health Organization (WHO) MONICA (Monitoring Trends and Determinants in Cardiovascular Disease) Project and compare them with the background population from which the cohort was drawn.

Subjects and Methods

A stroke register was established within the Glostrup Population Studies in 1982, with the objective of monitoring stroke events in the community over a 10-year period[15] and contributing data to the WHO MONICA Project.[1,2]

The Danish MONICA population was defined as all residents (approximately 330 000) of 11 municipalities in Copenhagen County. Stroke events were registered among the subpopulation aged 25 years or older (approximately 210 000), and validated, irrespective of survival status and place of occurrence and management. Multiple and overlapping sources were used to identify strokes among both hospitalized and nonhospitalized patients. The details of case ascertainment were described recently.[15]

Stroke was defined as rapidly developing signs of focal (or global) disturbance of cerebral function lasting >24 hours (unless inter-

Stroke is available at http://www.strokeaha.org

TABLE 1.   Fatal and Nonfatal First Strokes in the Danish MONICA Population 1982–1991, by Sex and Age

| | Men | | | | | | Women | | | | | |
| | 25–69 y | | ≥70 y | | ≥25 y | | 25–69 y | | ≥70 y | | ≥25 y | |
Stroke	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Fatal	237	18.1	296	33.8	533	24.4	169	22.6	470	38.3	639	32.4
Nonfatal	1073	81.9	581	66.2	1654	75.6	580	77.4	756	61.7	1336	67.6
All	1310	100.0	877	100.0	2187	100.0	749	100.0	1226	100.0	1975	100.0

rupted by surgery or death), with no apparent nonvascular cause; the study population included patients presenting with clinical signs and symptoms suggestive of subarachnoid hemorrhage, intracerebral hemorrhage, or cerebral infarct.

At the end of 1991, when the stroke register was completed, 5262 stroke events had been registered prospectively for the 10 years. The events were subdivided into first or recurrent and into fatal or nonfatal, a fatal stroke being defined as one in which death occurred within 28 days. All patients were followed up for vital status for at least 5.5 years (range, 5.5 to 15.5 years) and for causes of death for at least 4 years (range, 4 to 14 years). Data were obtained by record linkage to the Danish Civil Registration System and the Cause of Death Registry on the basis of the unique individual person number (a 10-digit code including the date of birth). Data on deaths and causes of death in the general population covered by the stroke register (the Danish MONICA population), distributed by sex, age, and calendar year, were derived from the same official registries. The expected number of deaths in the general population was estimated for each sex by calculating the age- and time-specific person-years of observation multiplied by the similar age- and time-specific population death rate. Standardized mortality ratios (SMRs) and excess death rates (EDRs) were estimated and 95% confidence limits were established after it was assumed that the numbers of deaths followed a Poisson distribution. The SMR is the quotient of the observed to the expected numbers of deaths, and the EDR is the observed minus the expected number of deaths per 1000 person-years. The SMR is suitable for comparing mortality rates among stroke patients with those of the general population, whereas EDR is a measure of the excess number of deaths due to the disease over that expected. SMRs and EDRs were calculated for all causes of death, and SMRs were calculated for specific causes of death: cardiovascular diseases, cancer, other diseases, accidents, and suicide. Information on the cause of death after a nonfatal stroke (ie, among 28-day survivors) was available for 1828 patients who died before January 1, 1996; no information was available in 11 such cases.

For patients who survived for at least 28 days but for whom the exact date of onset of stroke was not specified, it was assumed to have occurred on the 15th day of the month. One hundred seventy-three patients with fatal stroke were randomly assigned a survival time between 0 and 27 days when only month of onset was known and death occurred before the 28th day in the following month.

Stroke was clinically defined in the protocol of the MONICA Project. The stroke subtype was recorded for patients with fatal stroke who were examined postmortem and for patients examined by neuroimaging techniques within 28 days of onset. Cases with insufficient data on stroke subtype were labeled "acute but ill-defined stroke." Since stroke was defined as an event lasting 28 days, we chose to regard stroke as the cause of death in fatal events. Hence, we analyzed short-term survival in relation to the subtype of stroke but did not further explore the direct cause of death in these cases. Because the protocol of the MONICA Project did not include clinical data on the severity of stroke or on comorbidity in individual patients, our data do not permit analyses of determinants of survival.

Time trends in survival probability up to 5 years after a stroke were analyzed in a Cox regression model that included the covariates sex, age at stroke onset, and time. Changes in mortality rates in the general population were taken into account by including the expected number of deaths in the model with the "offset variable" facility in the "proc phreg" procedure in the SAS software package.[16]

Results

A total of 4162 patients with a first stroke were eligible for the analyses. Table 1 shows the proportions of fatal and nonfatal stroke by sex and age group.

Short-Term Survival by Stroke Subtype

Valid information on stroke subtype was available for 1887 (45.3%) of the patients. The subtypes were cerebral infarct in 1318, primary intracerebral hemorrhage in 331, and subarachnoid hemorrhage in 238. The remaining 2275 were classified as ill-defined stroke. The patients with subarachnoid hemorrhage were younger than the other patients (mean age, 53.1 years), whereas patients with documented cerebral infarct or primary intracerebral hemorrhage were of similar ages, the mean ages being 61.4 years and 62.8 years, respectively. Sufficient information on stroke subtype was more frequently available for younger than for older patients: the mean age of patients with ill-defined stroke was 74.0 years. Figure 1 shows the Kaplan-Meier estimates of the survival probability for each stroke subtype and ill-defined stroke. The short-term survival probability was clearly best for cerebral infarct and poorest for primary intracerebral hemorrhage. The patients with ill-defined stroke had survival
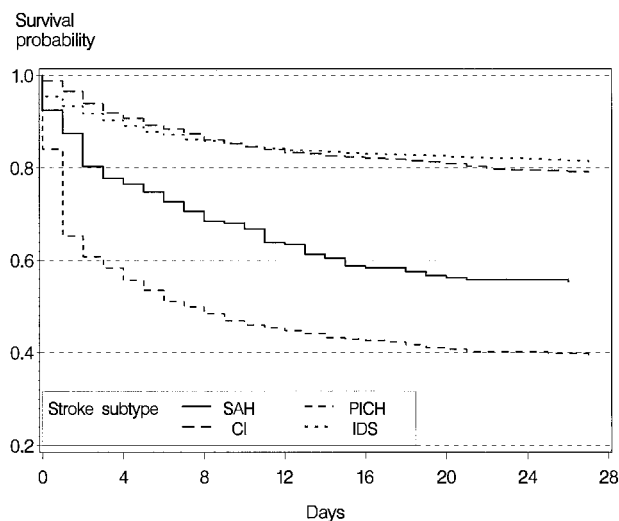

Figure 1. Short-term survival probability (Kaplan-Meier estimates) after a first stroke by subtype. SAH indicates subarachnoid hemorrhage; PICH, primary intracerebral hemorrhage; CI, cerebral infarct; and IDS, ill-defined stroke.
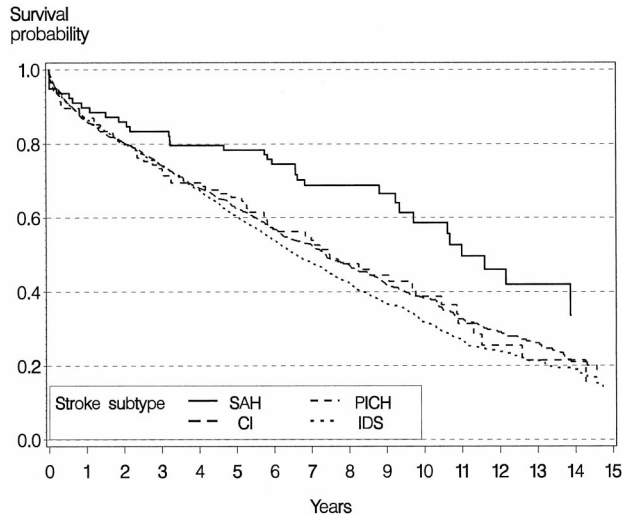
Figure 2. Long-term survival probability for patients aged 65 years at first nonfatal stroke by subtype (Cox regression). Abbreviations are as defined in Figure 1.

Figure 3. Long-term survival probability for patients aged 65 years at first cerebral infarct or ill-defined stroke by period of attack (Cox regression).

probabilities similar to those with known cerebral infarct, despite their markedly greater age.

Long-Term Survival

A total of 2990 patients (72%) survived their first stroke by >27 days, and 2448 (59%) were still alive 1 year after the stroke; thus, 41% died after 1 year. The risk for death between 4 weeks and 12 months after the first stroke was 18.1% (95% CI, 16.7% to 19.5%). After the first year, the annual risk for death was approximately 10% and remained almost constant.

The estimated cumulative risk for death was 60%, 76%, and 86% at 5, 10, and 15 years after index stroke, respectively.

Figure 2 shows the long-term survival probability for a person aged 65 at the time of a first nonfatal stroke. The prognosis was better for subarachnoid hemorrhage than for the other 3 categories ($P<0.001$, adjusted for the effect of sex
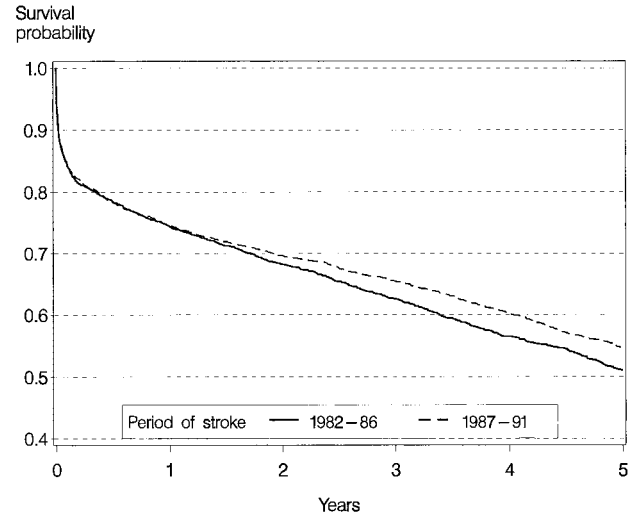
and age). There were no differences in long-term survival for the other 3 categories ($P=0.16$).

Table 2 shows the SMRs and EDRs for men and women by age group for various periods after a nonfatal stroke. Those who had survived their initial stroke by 4 weeks had an almost 5-fold greater risk for dying within 1 year after the stroke than persons of the same age and sex in the general population in the same geographic area. The excess risk for death was significantly higher for women than for men during the first year after a stroke but did not differ significantly between sexes after the first year.

The mean age at stroke was 67.2 years during 1982–1986 and 68.7 years during 1987–1991. The survival probability improved significantly during the observation period for patients with infarcts or ill-defined stroke. Figure 3 shows, as an example, the survival probability for a person aged 65 years with onset of cerebral infarct or ill-defined stroke

TABLE 2. SMRs* and EDRs† by Sex and Age for Patients After a First Nonfatal Stroke

Age Group, y	Years After Stroke	SMR (95% CI)			EDR (95% CI)		
		Men	Women	All	Men	Women	All
25–69	0–1	4.64 (3.71–5.72)	9.27 (6.94–12.1)	5.72 (4.81–6.75)	66.7 (49.8–86.6)	86.8 (62.4–117)	73.7 (59.5–89.8)
	1–5	3.01 (2.63–3.43)	3.52 (2.80–4.35)	3.14 (2.80–3.50)	43.3 (35.1–52.3)	31.1 (22.3–41.4)	38.9 (32.7–45.7)
	5–10	2.75 (2.39–3.15)	3.32 (2.66–4.09)	2.90 (2.58–3.25)	49.9 (39.5–61.3)	38.6 (27.6–51.4)	45.6 (37.9–54.0)
	10–15	2.50 (1.94–3.18)	2.45 (1.60–3.59)	2.49 (2.01–3.05)	55.5 (34.7–80.4)	31.2 (13.0–55.8)	45.7 (30.9–62.8)
≥70	0–1	3.70 (3.15–4.32)	5.18 (4.54–5.87)	4.46 (4.04–4.92)	245 (195–301)	328 (278–383)	291 (255–329)
	1–5	1.92 (1.68–2.18)	2.05 (1.81–2.30)	1.99 (1.82–2.17)	93.3 (69.2–120)	92.9 (71.8–116)	93.1 (77.0–110)
	5–10	1.89 (1.56–2.27)	1.99 (1.67–2.36)	1.94 (1.71–2.20)	117 (73.8–166)	104 (69.6–142)	109 (82.1–139)
	10–15	2.49 (1.48–3.93)	1.67 (1.08–2.47)	1.94 (1.40–2.61)	253 (80.7–498)	98.0 (12.1–214)	143 (61.6–246)
≥25	0–1	3.98 (3.50–4.51)	5.62 (5.00–6.30)	4.73 (4.34–5.15)	124 (104–145)	213 (184–244)	162 (145–180)
	1–5	2.34 (2.13–2.56)	2.27 (2.04–2.52)	2.31 (2.15–2.47)	56.1 (47.4–65.5)	57.9 (47.4–69.2)	56.9 (50.1–64.0)
	5–10	2.37 (2.11–2.64)	2.37 (2.07–2.70)	2.37 (2.17–2.58)	60.0 (49.0–72.0)	57.1 (44.5–71.0)	58.8 (50.4–67.7)
	10–15	2.50 (2.00–3.09)	2.00 (1.49–2.63)	2.28 (1.92–2.70)	66.4 (44.2–92.6)	42.7 (20.9–69.7)	56.1 (40.0–74.3)

*Quotient of observed to expected numbers of deaths.

†Observed minus expected number of deaths per 1000 person-years.

TABLE 3. Causes of Death of Patients With Nonfatal Stroke Who Died Before January 1, 1996

	Men		Women		All	
Cause of Death*	No.	%	No.	%	No.	%
Cardiovascular diseases *ICD-8*: 390–458; *ICD-10*: I00–I99	626	63.4	608	72.3	1234	67.5
Ischemic heart disease *ICD-8*: 410–414; *ICD-10*: I20–I25	242	24.5	173	20.6	415	22.7
Cerebrovascular disease *ICD-8*: 430–438; *ICD-10*: I60–I69	268	27.2	318	37.8	586	32.1
Cancer *ICD-8*: 140–209; *ICD-10*: C00–D09	133	13.5	83	9.9	216	11.8
Other diseases *ICD-8*: 0–136, 210–389, 460–796; *ICD-10*: A00–B99, D10–H95, J00–R99	205	20.8	130	15.4	335	18.3
Accidents and suicide *ICD-8*: E800–E999; ICD-10: V00–Y99	23	2.3	20	2.4	43	2.4
Total	987	100	841	100	1828	100

International Classification of Diseases (*ICD*) codes: 8th edition for deaths before January 1, 1994; 10th edition for deaths after January 1, 1994.

*Unknown in 11 cases.

during 1982–1986 compared with 1987–1991. The difference is statistically significant ($P<0.01$). The survival curves show that the risks for acute and early death did not differ, but the probability of long-term survival increased after the first year beyond the index stroke.

Causes of Death

Two thirds of the patients with nonfatal stroke subsequently died from vascular diseases (Table 3). The mortality rate due to all cardiovascular diseases was almost 4 times higher than that in the background population (Table 4). More patients died from cerebrovascular disease than from heart disease, particularly women. The risk for cerebrovascular death was 8 to 9 times that of the general population, but the excess mortality was not confined to vascular diseases since the rates for cancer, other diseases, accidents, and suicide were also significantly higher than expected. Ischemic heart disease and other vascular diseases were more than twice as often the cause of death than expected, but vascular diseases other than stroke contributed only slightly more than other diseases to the overall excess mortality. The frequency of other diseases, accidents, and suicide as the cause of death was approximately double that for the general population, and stroke survivors also had a statistically significant 26% increase in the risk for dying from cancer.

Discussion

In this community-based study, in which we followed up unselected patients with a first stroke for a sufficient length of time and in sufficiently large numbers for accurate statistics on the absolute and relative long-term risks for death, our results are in agreement with those of previous investigations, showing that the highest risk for death is in the acute phase of a stroke and then gradually declines. More than 1 year after a first stroke, the excess mortality appears to level off, the risk for death being approximately twice that of the general

TABLE 4. SMRs* by Sex and Causes of Death of Patients After a First Nonfatal Stroke

	SMR (95% CI)					
	Men			Women		
Cause of Death	Cerebral Infarct	Ill-Defined Stroke	All Strokes†	Cerebral Infarct	Ill-Defined Stroke	All Strokes†
Cardiovascular diseases	4.01 (3.43–4.66)	3.62 (3.29–3.98)	3.75 (3.46–4.06)	5.77 (4.67–7.06)	3.77 (3.44–4.12)	4.03 (3.71–4.36)
Ischemic heart disease	2.85 (2.22–3.60)	2.62 (2.24–3.06)	2.64 (2.32–2.99)	3.64 (2.42–5.26)	2.41 (2.03–2.84)	2.50 (2.14–2.90)
Cerebrovascular disease	9.07 (7.07–11.5)	7.70 (6.62–8.91)	8.32 (7.35–9.37)	12.1 (8.89–16.0)	8.19 (7.20–9.27)	8.89 (7.94–9.92)
Other cardiovascular diseases	2.99 (2.03–4.25)	2.58 (2.04–3.21)	2.70 (2.23–3.24)	3.98 (2.40–6.21)	2.41 (1.95–2.94)	2.54 (2.10–3.05)
Cancer	1.40 (1.03–1.86)	1.15 (0.92–1.43)	1.22 (1.02–1.44)	1.87 (1.21–2.76)	1.17 (0.87–1.53)	1.33 (1.06–1.65)
Other diseases	2.17 (1.64–2.82)	2.24 (1.89–2.64)	2.20 (1.91–2.52)	2.48 (1.63–3.60)	1.74 (1.41–2.11)	1.83 (1.53–2.18)
Accidents and suicide	2.60 (1.25–4.78)	1.44 (0.72–2.58)	1.88 (1.19–2.83)	2.86 (0.93–6.68)	1.72 (0.97–2.84)	1.82 (1.11–2.81)
Total	2.68 (2.38–3.01)	2.55 (2.36–2.75)	2.58 (2.43–2.75)	3.58 (3.03–4.19)	2.73 (2.53–2.95)	2.85 (2.66–3.05)

*Quotient of observed to expected numbers of deaths.

†Subarachnoid hemorrhage, primary intracerebral hemorrhage, cerebral infarct, and ill-defined stroke.

population. In the Oxfordshire Community Stroke Project,[5] 675 patients with a first stroke were followed up for up to 6.5 years, and the relative risk of death was found to vary between 1.1 and 2.9 at 2 to 6 years after the stroke. In the Perth Community Stroke Study,[4] in which 362 patients with a first stroke were followed up for 5 years, the relative risk for death beyond 1 year after the stroke was between 2.0 and 2.3. Loor et al[6] followed up 221 patients up to 3 years and reported the relative risk for death to be 2.0 in the interval 2 to 3 years after the stroke. We found a SMR ≥2.0 for as long as 10 to 15 years after the initial stroke. Hence, we conclude that persons who survive a stroke have a continuing excess risk of death, which remains at least double that of the background population.

Case fatality rates vary considerably among populations,[1] and it has been found frequently that the age-standardized case fatality rates are higher for women than for men. We found that, after 4 weeks, women continued to have a higher risk for death than men for as long as 1 year after the stroke. The female stroke victims were older than the men, but the effect of age was controlled for in the analyses, and our data do not offer any explanation for the difference. A similar difference was found in a study in the Netherlands[6]; in other community-based studies, risk estimates were not reported by sex.

The most frequent cause of death in patients with nonfatal strokes was cardiovascular disease (either cerebrovascular disease or heart disease). The distribution of causes of death is similar to that found among 30-day survivors in other studies: cerebrovascular diseases accounted for 43% and other vascular causes for 26% of deaths in the Netherlands,[6] and the corresponding figures were 36% and 34% in Oxfordshire[5] and 27% and 31% in Perth, Australia.[4] We found that 32.1% of deaths after nonfatal stroke were due to cerebrovascular disease and 22.7% to ischemic heart disease. In comparison with the background population, the risk for death from cardiovascular diseases other than stroke was more than double that expected (Table 4), and the estimated risk for death from cerebrovascular disease was more than 8-fold that expected. Ischemic heart disease and vascular diseases other than stroke contributed little more than did the category "other diseases" to the overall excess mortality. The relative distribution of causes of death may, however, be biased. Since our analyses were based on official death statistics, it is likely that the SMRs for cerebrovascular disease are overestimated, because certifying doctors may more readily have recorded "cerebrovascular disease" as the cause of death when there was a history of stroke and no more obvious specific cause. The ratios for heart disease and other diseases may be underestimated for the same reason, whereas the registration of cancer deaths, accidents, and suicide is less likely to be influenced.

The finding that death from cancer was more frequent may reflect an association with stroke as a result of shared risk factors such as smoking. There was a tendency to excess mortality from lung cancer among male but not among female stroke patients (data not shown), whereas deaths from chronic bronchitis and emphysema were more frequent among female patients but not among male patients (data not shown).

A degree of disability after a stroke that made the patient ineligible for antineoplastic therapy may also have played a role in the excess mortality from cancer, and this factor may similarly have limited the possibilities for effective treatment of any other condition, thereby accounting in part for the excess death rates. In the study in Perth, physical disability before a stroke increased the risk for death of stroke patients; we assume that poststroke disability may have a similar effect.

Disabled persons may also have a higher risk for accidents, in particular falls. In the study of Loor et al,[6] it was found that 5 of 62 deceased patients (8%) died of complications after a fracture of the femur. It can only be speculated that poststroke depression might lead to suicide.

In view of the definition in the protocol of the WHO MONICA Project of a stroke event, we analyzed survival probability after a fatal stroke by stroke subtype and not by direct or indirect causes of death. In studies in which the direct cause of death within 30 days after a first stroke was examined,[4–6] death was due to cerebrovascular disease in 91% of patients in the Oxfordshire Community Stroke Project and in 85% in the Perth Community Stroke Study. Loor et al[6] found that only 1 of 58 patients did not die of the index stroke. A study in Rochester, Minn, [10] included stroke of uncertain type in the analyses of cerebral infarct because it was assumed that the overwhelming majority of patients had had a cerebral infarct. We were tempted to reach a similar conclusion for our category of ill-defined stroke because the survival curves for verified cerebral infarct and ill-defined stroke were almost identical. However, the cohort was established during a period when neuroimaging was less frequently used than today. An exact diagnosis was established more frequently in younger than in older patients, and a complete workup was assumed to have been done more often for patients presenting with severe symptoms and suspected to have intracranial bleeding.

Because some diagnoses were established postmortem, the short-term survival rates for patients with particular stroke subtypes are biased. The short-term prognosis was assumed to be better for all patients with cerebral infarct than for those in whom this subtype was diagnosed. Only the survival rates for patients with subarachnoid hemorrhage can be considered to be unbiased. These patients constituted 6% of the total, and we consider it unlikely that there were many cases of this subtype among the ill-defined strokes.

Our findings clearly show that stroke is a medical emergency with a high risk for death shortly after onset. The selection bias in the risk estimates for subtypes of stroke do not alter the fact that hemorrhagic stroke is more often fatal than cerebral infarct, illustrating why relatively few cases of bleeding complications can balance the therapeutic gain of rapid treatment of cerebral infarct.

Our findings suggest that the probability of long-term survival was significantly better for patients with ischemic or ill-defined stroke during 1987–1991 than for patients with stroke onset at the beginning of the study period. A similar improvement in survival over time was found in northern Sweden.[17] In previous analyses of all strokes,[15] we found no positive time trend in short-term survival: the age-adjusted

28-day case fatality rates did not change significantly during 1982–1991, and the improvement was restricted to those who survived longer. Our data do not offer any specific explanation because we had no information on stroke severity or comorbidity. We know, however, that the incidence rates of stroke declined.[15] We consider this to be in part the result of improved primary prevention, in particular control of hypertension. Awareness of means for preventing cardiovascular diseases in general increased during the 1980s, and it was at the end of this decade that warfarin was shown to be effective in preventing stroke in patients with arterial fibrillation; this was also the time when the concept of dedicated stroke units was introduced. No such unit was available to the patients included in the present study, but we strongly believe that the focus on appropriate stroke management has had a positive influence on patient care.

We have pointed to stroke-related disability as a possible explanation for the excess mortality from other diseases, cancer, accidents, and suicide. If this assumption is true, it emphasizes the need for improved rehabilitation to minimize poststroke disability. The most important risk of stroke survivors is recurrent cerebrovascular disease, which was >8 times higher than that of the background population and much more pronounced than the excess risk for death from other causes, including ischemic heart disease. In our opinion, this is a strong argument in favor of continuing and increasing efforts in the field of secondary stroke prevention.

The incidence of stroke declined,[15] and the present results suggest that long-term survival improved in Denmark during a time when it became clear that stroke is a public health issue. This improvement may be the result of better prevention, better management or, more likely, a combination of the two.

Acknowledgments

References

1. WHO MONICA Project (prepared by Thorvaldsen P, Asplund K, Kuulasmaa K, Rajakangas AM, Schroll M). Stroke incidence, case fatality, and mortality in the WHO MONICA Project: World Health Organization Monitoring Trends and Determinants in Cardiovascular Disease. *Stroke*. 1995;26:361–367.
2. WHO MONICA Project (prepared by Thorvaldsen P, Kuulasmaa K, Rajakangas AM, Rastenyte D, Sarti C, Wilhelmsen L). Stroke trends in the WHO MONICA Project. *Stroke*. 1997;28:500–506.
3. Scmidt EV, Smirnov VE, Ryabova VS. Results of the seven-year prospective study of stroke patients. *Stroke*. 1988;19:942–949.
4. Hankey GJ, Jamrozik K, Broadhurst RJ, Forbes S, Burvill PW, Anderson CS, Stewart-Wynne EG. Five-year survival after first-ever stroke and related prognostic factors in the Perth Community Stroke Study. *Stroke*. 2000;31:2080–2086.
5. Dennis MS, Burn JP, Sandercock PA, Bamford JM, Wade DT, Warlow CP. Long-term survival after first-ever stroke: the Oxfordshire Community Stroke Project. *Stroke*. 1993;24:796–800.
6. Loor HI, Groenier KH, Limburg M, Schuling J, Meyboom-de Jong B. Risks and causes of death in a community-based stroke population: 1 month and 3 years after stroke. *Neuroepidemiology*. 1999;18:75–84.
7. Matsumoto N, Whisnant JP, Kurland LT, Okazaki H. Natural history of stroke in Rochester, Minnesota, 1955 through 1969: an extension of a previous study, 1945 through 1954. *Stroke*. 1973;4:20–29.
8. Turney TM, Garraway WM, Whisnant JP. The natural history of hemispheric and brainstem infarction in Rochester, Minnesota. *Stroke*. 1984;15:790–794.
9. Broderick JP, Phillips SJ, O'Fallon WM, Frye RL, Whisnant JP. Relationship of cardiac disease to stroke occurrence, recurrence, and mortality. *Stroke*. 1992;23:1250–1256.
10. Petty GW, Brown RD Jr, Whisnant JP, Sicks JD, O'Fallon WM, Wiebers DO. Survival and recurrence after first cerebral infarction: a population-based study in Rochester, Minnesota, 1975 through 1989. *Neurology*. 1998;50:208–216.
11. Petty GW, Brown RD Jr, Whisnant JP, Sicks JD, O'Fallon WM, Wiebers DO. Ischemic stroke subtypes: a population-based study of functional outcome, survival, and recurrence. *Stroke*. 2000;31:1062–1068.
12. Marini C, Totaro R, Carolei A, for the National Research Council Study Group on Stroke in the Young. Long-term prognosis of cerebral ischemia in young adults. *Stroke*. 1999;30:2320–2325.
13. Indredavik B, Bakke F, Slordahl SA, Rokseth R, Hâheim LL. Stroke unit treatment: 10-year follow-up. *Stroke*. 1999;30:1524–1527.
14. Sacco RL, Wolf PA, Kannel WB, McNamara PM. Survival and recurrence following stroke: the Framingham Study. *Stroke*. 1982;13:290–295.
15. Thorvaldsen P, Davidsen M, Brønnum-Hansen H, Schroll M. Stable stroke occurrence despite incidence reduction in an aging population: stroke trends in the Danish Monitoring Trends and Determinants in Cardiovascular Disease (MONICA) population. *Stroke*. 1999;30:2529–2534.
16. SAS Institute. *SAS/STAT User's Guide, Version 6.12*. Cary, NC: SAS Institute Inc; 1991.
17. Peltonen M, Stegmayr B, Asplund K. Time trends in long-term survival after stroke: the Northern Sweden Multinational Monitoring of Trends and Determinants in Cardiovascular Disease (MONICA) study, 1985–1994. *Stroke*. 1998;29:1358–1365.