Long-Term Mortality and Its Risk Factors in Stroke Survivors

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Background: Stroke is one of the leading causes of mortality worldwide. Understanding the risk factors associated with stroke mortality is important to improve patient management. Few studies have examined long-term mortality and its associated predictive risk factors. *Methods:* We examined long-term mortality in 1137 patients with acute stroke and compared it to a geographically age- and sex-matched, stroke-free control group. We followed the stroke patients for as long as 16.4 years. In 1018 of these patients we assessed the effect of demographic, clinical, and hematological factors on mortality. *Results:* At the end of the study period, 51.7% of the patients and 32.7% of the stroke-free control individuals had died (hazard ratio 2.2, confidence interval 1.9-2.5, $P < .001$). A total of 72.5% of the patients and 53% of the controls with 12 years' follow-up (n = 570) had died ($P < .001$). Regression analyses indicate that, in addition to known risk factors such as age, diabetes, and stroke severity, both low cholesterol ($P < .001$) and hemoglobin ($P < .002$), hyperhomocysteinemia ($P = .005$), and elevated serum creatinine ($P < .001$) at index stroke are associated with increased long-term mortality. *Conclusions:* Stroke patients surviving the first year after stroke have a markedly increased mortality rate as seen in long-term follow-up. Furthermore, the results from this study indicate that changes in creatinine, homocysteine, and hemoglobin should be followed more carefully as standard practice after acute stroke. **Key Words:** Stroke—long-term—mortality—risk factors—homocysteine—creatinine.

Introduction

Stroke is one of the leading causes of mortality worldwide with about 6 million people dying annually.[1] The risk of death from stroke is greatest in the first few weeks after the stroke. The resulting brain injury and secondary complications, due in part to immobilization,[2-5] are the main causes for this short-term mortality.

The risk factors for long-term mortality after stroke are less investigated,[6,7] but existing evidence suggests that they differ in part from the short-term risk factors. Stroke severity, age, and cardiovascular risk factors[2,4,7-9] are prominent predictors for mortality within the first year after stroke, whereas age, male gender, smoking, and diabetes are predictors for long-term mortality.[10-12] Few studies[6,7] have investigated long-term mortality and compared the mortality rates of stroke patients with a stroke-free, age- and sex-matched control group from the general population living in the same geographical area. In young stroke survivors (18-50 years), the cumulative 20-year mortality compared to the general population exceeded expected mortality for decades after the initial stroke.[13] Awareness of long-term mortality and its clinical predictors offers the opportunity to better regulate these risk factors in poststroke follow-up.

In the present study, we analyzed the long-term mortality rates in 1137 stroke patients hospitalized for stroke in the county of Rogaland, Norway, from 1996 to 2004. The patients were followed up for up to 16.4 years and

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the mortality rates were compared to a stroke-free, age- and sex-matched group from the general population derived from the same geographical area. The risk factors predicting mortality were identified in the stroke patient group.

Materials and Method

Patients and Controls

All patients admitted to the stroke unit at Stavanger University Hospital between January 1, 1996, and March 31, 2004, were included in the study (n = 1472). At this time, the stroke unit was composed of 6 acute stroke beds that were continuously occupied by consecutive patients. If there was no capacity for new patients at the stroke unit, these patients were admitted to a general medical ward, but due to a lack of structured follow-up, these patients were not included in the study.

Demographic variables, medical history, and results of the radiological, laboratory, and clinical investigations were recorded on study inclusion (baseline) (Table 1). Neurological deficit was assessed clinically using the Scandinavian Stroke Scale (SSS).[14]

Information on death was collected through linkage to the National Population Register of Statistics (Statistics Norway) and the National Registry of Death, Norway, until May 31, 2012.

The control group was obtained from the National Population Register of Statistics. Reference individuals were acquired arbitrarily from the general population but were individually matched 1:1 according to sex, age (born on the same year as the index patient), and residency on the same year the patient was hospitalized for stroke.

Initially, 1472 acute stroke admissions were recorded. In case of repeated admissions during the study period, only the index stroke was taken into account. Thus, 82 multiple registrations were removed. Thirteen patients of foreign nationality were excluded as they were not registered in the National Population Register of Statistics. Furthermore, we excluded the patients who died within the first year of the stroke (n = 72) and their matched control persons as we aimed to assess long-term mortality (Fig 1).

To have a stroke-free control group for the mortality analysis, we examined the hospital files of the control

Table 1. *Demographic and clinical variables at baseline according to analysis*

Variables	Factors	Mortality analysis n = 1137	Missing n	Risk factor analysis n = 1018	Missing n
All patients	Mean age at inclusion (years)	66.8 (SD 14.3)	0	67.6 (SD 14.4)	0
	Dead at study end (%)	51.7	0	50.6	0
	Male (%)	54.6	0	54.1	0
	SSS score at admission (mean)	46.3 (SD 13.8)	409	46.0 (SD 14)	154
	SSS score at discharge (mean)	50.4 (SD 11.8)	424	50.2 (SD 12)	215
Cerebrovascular subtype	Infarct (%)	73.5	0	73.2	0
	Hemorrhage (%)	10.7	0	10.7	0
	TIA (%)	15.8	0	16.1	0
Risk factors	Previous cardiovascular event (%)	40.8	0	44.1	0
	Cardiovascular heredity (%)	18.3	245	18.4	7
	Hypercholesterolemia (%)	27.8	0	27.0	0
	Diabetes (%)	12.3	0	10.4	0
	Hypertension (%)	51.8	0	50.3	0
	Smoking (current or previous) (%)	39.8	47	41.2	47
	Atrial fibrillation (%)	9.3	238	10.9	140
	Carotid stenosis (%)	24.6	9	27.2	8
	Hyperhomocysteinemia (%)	22.0	239	23.5	1
Mean values (SD)	Cholesterol value (mmol/L)	5.5 (1.2)	247	5.5 (1.2)	12
	HDL cholesterol (mmol/L)	1.3 (.4)	282	1.3 (.4)	51
	Triglyceride value (mmol/L)	1.4 (.7)	259	1.4 (.7)	25
	Creatinine value (μmol/L)	86.9 (25)	239	87.2 (25)	1
	CRP at admission (mg/L)	16.3 (26)	238	16.7 (29)	0
	Glucose value (mmol/L)	5.9 (1.5)	288	5.9 (1.5)	24
	Cobalamine value (pmol/L)	328 (219)	371	330 (223)	154
	Homocysteine value (μmol/L)	13.6 (8)	400	13.9 (9.1)	183
	Hemoglobine value (g/dL)	13.9 (1.5)	240	13.9 (1.5)	2

Abbreviations: CRP, C-reactive protein; HDL, high-density lipoprotein; SSS, Scandinavian Stroke Scale; TIA, transient ischemic attack; SD, standard deviation.