Five Year Survival after Stroke, and Related Prognostic Factors in Israel

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ABSTRACT: **Background:** In many countries information regarding long-term survival after stroke is scarce.

Objectives: To both assess 5 year survival after stroke in the Israeli population and determine its independent prognostic factors.

Methods: We followed 616 people with acute stroke who were admitted consecutively to seven large general hospitals in Israel. The data were collected on admission to the hospital, at discharge, at 3, 6 and 12 months thereafter, and 5 years after the stroke.

Results: The 5 year cumulative probability of survival was 49.2% (95% CI 45.0–53.7%). In the multivariate Cox analysis, lower age and functioning independently before the event were associated with a lower risk of death, while other demographic characteristics and cardiovascular risk factors were not found to be associated with mortality.

Conclusions: Five year survival after stroke in Israel, though high, is similar to other western countries. There is a need to ensure early, active and sustained implementation of strategies for preventing stroke events.

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KEY WORDS: stroke, five year follow-up, survival, prognostic factors

Stroke survivors often face ongoing chronic morbidity and disability. Having survived the immediate aftermath of a stroke, patients and their families are concerned about the patient's potential long-term survival and independence and therefore seek information that will enable them to make short and long-term plans and rational decisions [1,2]. Such information is also of interest to health care planners and providers since stroke patients exact a heavy toll in disability and constitute a significant economic burden on the health system [3,4].

The incidence of stroke is well documented in western countries [5,6], but information on long-term survival after stroke is more limited. According to recent studies the risk of death ranged from 38% during the first 4 years after the event [7] to 68% five years after the event [8], exceeding the 40–54% rates reported in earlier studies [9-11]. These figures underline the importance of measuring long-term survival rates and risk factors for dying following a stroke, in different countries and among different ethnic groups [12].

In Israel, as in most western countries, stroke is the third leading cause of death and a major cause of disability, especially in the elderly [13]. In 1997, stroke accounted for 8.1% of total deaths – 7.5% among men, with a crude mortality rate of 48.3/100,000, and 8.6% among women, with a crude mortality rate of 51.7/100,000 [14]. However, information regarding long-term survival after stroke is scarce. The aims of this study, therefore, were to describe 5 year survival after stroke in the Israeli population and to determine the factors at the onset of stroke that are independently related to an increased probability of surviving for 5 years.

PATIENTS AND METHODS

The study was conducted among a national representative sample of patients who had been admitted with a diagnosis of stroke (ICD-CM9 43–433, 436) to seven of Israel's large hospitals (i.e., those with over 500 beds). Two large hospitals in the center of the country were not included in the study due to their similarity to two others in the same geographic area that were included. The study included all patients who arrived consecutively at the emergency room of one of the seven hospitals from mid-October 1998 to mid-January 1999 and were admitted to the hospital with a diagnosis of stroke. The diagnosis of stroke was made for 97% of the study population by clinical and radiological evaluation (computed tomography scan) [15]. The study population included first-ever and recurrent stroke patients. Patients who died in the emergency room and those who were discharged without being hospitalized were not included in the study.

Data on patients who were hospitalized were collected on admission to hospital in face-to-face interviews and from a review of medical records within 48 hours of admission and at discharge from hospital. The patients were interviewed five more times using standardized structured questionnaires: at discharge from the hospital and 3 months thereafter in face-to-face interviews, and at 6 months, 12 months and 5 years after the stroke through telephone interviews. Information collected in the study included patients' sociodemographic

Table 1. Kaplan-Meier estimates of the risk of death within defined time intervals after the stroke

	From admission to discharge from the hospital (7 days on average)	From discharge to up to 3 months after the event	Between 3 and 6 months after the event	Between 6 and 12 months after the event	Between 1 and 5 years after the event
Risk (%)	16.6	10.7	3.0	3.8	29.3
95% CI	13.6–19.5	8.0–13.4	1.4–4.6	1.9–5.6	24.6-33.9
Cumulative risk (%)	16.6	25.5	27.7	30.4	50.8
95% CI	13.9–19.7	22.2–29.1	24.4–31.5	27.0–34.3	46.7-55.0
At risk (n)	616	514	431	399	369
Death (n)	102	55	13	15	108
Censured (n)		28	19	11	33
Cumulative death (n)	102	157	170	185	293

The percentage risk each year (first row in table) is calculated on the basis of death/at risk.

characteristics, functioning in activities of daily living, instrumental ADL, and mobility before the event, existence of cardiovascular risk factors, and previous history of stroke. Where it was not possible to interview patients at every stage of the study, we interviewed a family member known to be the patient's main caregiver. Data on mortality were compiled during the period of hospitalization and thereafter through interviews with family caregivers; in the case of patients whom we were unable to locate, the information was completed from Ministry of the Interior records.

At admission to these seven hospitals, 616 patients were included in the study – 75% of those who arrived at one of the relevant emergency rooms with a diagnosis of stroke. The main reasons for non-inclusion in the study were refusal to participate and logistic pitfalls (e.g., the brevity of the patient's stay in the emergency room or the interviewer's temporary absence from his/her post). Comparison of age, gender, type of stroke, and death during hospitalization between patients who were admitted to the hospitals but were not included in the study and those who were included revealed no statistically significant differences between the two groups. The study was approved by an institutional review board (Helsinki Committee) at each of the seven hospitals included in the study.

Statistical analysis was conducted using SPSS software. Crude associations between the occurrence of death and each of the independent categorical variables recorded at baseline were assessed by cross-tabulations using the chi-square test. The Kaplan-Meier product limit technique was used to generate survival probabilities and survival curves based on the deaths within the 5 years. We used multiple regression Cox proportional hazards analysis to develop statistical models predicting occurrence of death within 5 years of the stroke. We included in the model only variables with a log-rank test value of $P < 0.05$. This set of variables was reduced by backward elimination until only those significant at $P < 0.05$ remained in the model.

RESULTS

The average age of the patients was 72 on admission to hospital; 56% of them were men. Most (73%) of the patients had ischemic stroke, 16% with brain hemorrhage, and 11% had experienced some other type of event. Most of the patients suffered from illnesses and had risk factors prior to the stroke, and one-third of them had suffered a previous stroke.

Of the 616 patients who were included in the study, 102 died during hospitalization; they represent 16.6% (95% confidence interval 13.6–19%) of all stroke patients admitted to hospital. During the first 3 months after the event an additional 55 people died, representing 10.7% (95% CI 8.0–13.4%); between 3 and 6 months after the event another 13 people died (95% CI 1.4–4.6); and during the subsequent 6 months 15 more people died representing 3.8% (95% CI 1.9–5.6). In all, in the period between admission to the hospital and one year following the event, 185 people died, representing 30.4% (95% CI 27.0–34.3) of the stroke patients who had been admitted to the hospitals. An additional 108 people died between 1 and 5 years after the stroke, representing 29.3% (95% CI 24.6–33.9) of the survivors one year after the stroke. Another 91 patients (15% of the original study population) dropped out of the study, either because they moved to a new location and could not be found or because they refused to continue being interviewed.

The cumulative probability of 5 years survival was 49.2% (95% CI 45.0–53.7). The risk of death was highest in the first year after the stroke (36.5%, 95% CI 31.5–41.4). Stratification by age showed that the prognosis for older patients was

ADL = activities in daily living

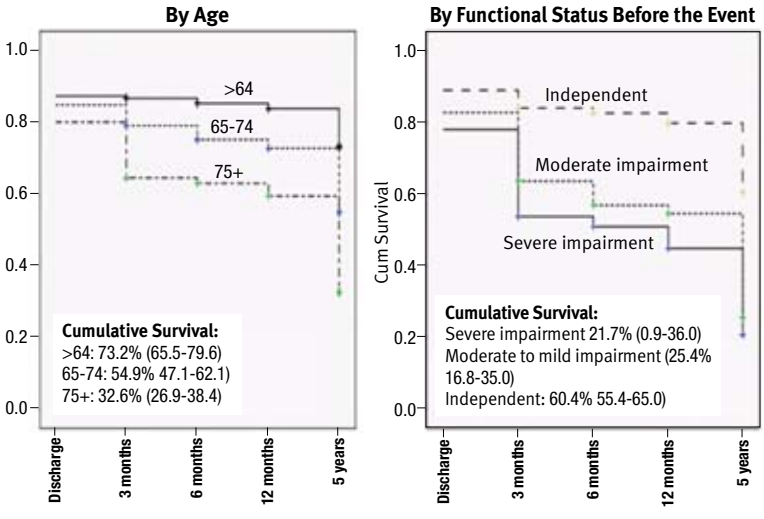
CI = confidence interval

Table 2. Patients' characteristics by 5 years survival (%)

	Alive 5 years after stroke	Died	Total
Gender: men	56	58	57
Age (yrs)**			
≥ 64	35	13	25
65–74	34	27	30
75+	31	60	45
Living alone	21	24	22
Place of birth			
Israel	19	10	15
Europe/America	25	36	30
Asia/Africa	30	28	29
Former Soviet Union	27	26	26
Education*			
None	12	16	14
1–9 yrs	32	39	35
10+ yrs	56	45	51
Cardiovascular disease	33	42	38
IHD**	27	37	32
CHF**	8	19	13
AF**	16	26	21
ADL before the stroke**			
Total impairment	4	11	7
Moderate impairment	10	27	17
Independent	86	62	76
IADL before the stroke**			
Total impairment	13	49	29
Moderate Impairment	21	20	20
Independent	66	32	50

* $P < 0.05$
** $P < 0.01$

Figure 1. Survival during 5 years after stroke. Kaplan-Meier estimates of the risk of death



worse. Figure 1 shows that the cumulative probability of 5 years survival was 73.2% (95% CI 65.5–79.6) for patients aged 64 or younger at the occurrence of the stroke, 54.9% (95% CI 47.1–62.1) for patients aged 65–74, and 32.6% (95% CI 26.9–38.4) for patients aged 75 or over at the occurrence of the stroke. Stratification by functional status in ADL shows that the cumulative probability of 5 years survival was 60.4% (95% CI 55.4–65.0) for patients who had been independent in ADL before the event; 25.4% (95% CI 16.8–35.0) for those who suffered with moderate to mild impairment, and 21.7% (95% CI 0.9–36.0) for those patients with severe impairment before the event.

The average length of stay in the hospital for all patients was 11 days; about 49% of them were hospitalized for less than one week. Table 2 shows a relationship between the patients' characteristics and 5 years survival. Lower age, being Israeli-born rather than an immigrant, and having a higher education were positively and significantly associated with 5 years survival. Independence in ADL and IADL before the stroke was also positively and significantly associated with 5 years survival. Non-existence of cardiovascular disease, such as ischemic heart disease, congestive heart failure, and atrial fibrillation before the stroke was also positively and significantly associated with 5 years survival.

In the Cox proportional hazards model, only two variables were found to be independently related to 5 year mortality from admission to the hospital: age > 75 years old (odds ratio 2.03, 95% CI 1.58–2.61) and being disabled in ADL before the event (OR 2.36, 95% CI 1.82–3.07). Functioning in IADL before the event was not entered into the model because of multicollinearity with ADL. None of the cardiovascular risk factors (IHD, CHF and AF) were found to have a significant relation to 5 years survival in our model.

DISCUSSION

The principal findings of this study were that the cumulative risk of death within 5 years after a stroke in Israel is about 50%, with the risk of death beyond the first year being approximately 7% per year. These findings are consistent with other studies that found the risk of death elevated in the longer term, and the annual risk of dying after stroke about 7–10%

IADL = instrumental activities of daily living
OR = odds ratio
IHD = ischemic heart disease
CHF = congestive heart failure
AF = atrial fibrillation

[10,11,16]. Other studies in Europe and the United States also found high long-term mortality rates following stroke. The cumulative mortality rate in the Northern Manhattan study was 41% [17]; in the Perth study 58% of the patients died at 5 years [11,18]. The cumulative risk of mortality at one year was 30.4% in our study, which is slightly lower than in the Perth study, which was 36.5% [11], but similar to the finding of Modrego and colleagues [9]. However, in the study by Modrego et al., overall mortality was 38% after a mean follow-up of 4 years, while ours was 50.8%. It should also be mentioned that the mortality rate for Chinese patients after one year was 15.6%, which is much lower than the figure for western countries [18]. The difference in the cumulative mortality rates between studies reflects the importance of examining long-term mortality in each country separately, making it possible to consider the needs of the survivors and their families in accordance with their specific epidemiology and the health services in that country and to prepare a specific intervention program.

Searching for patients' characteristics and risk factors that are related to higher mortality revealed that in a univariate analysis, higher age, immigrating to Israel rather than being born there, lower education, and dependency in ADL and IADL before the stroke (pre-stroke low Barthel Index) were significantly related to higher risk of 5 years mortality. These findings are similar to previous Israeli studies. Tanne and co-authors [19] found regional-ethnic variations in stroke mortality among subjects included in the cohort of the Israeli Ischemic Heart Disease Project. Immigrants to Israel from the Middle East, North Africa and Asia exhibited higher age-adjusted ischemic stroke mortality rates than those born in Europe. Zeidman et al. [20] also found that the rate of Israeli stroke patients younger than 65 was much higher among subjects born in Asia and Africa than among other ethnic groups. Other researchers also found that advanced age was associated with a greater risk of death in the long-term period after stroke [8,10,11]. As in other studies, we also found in the univariate analysis that existence of IHD, CHF and AF before the stroke was significantly related to a high rate of long-term mortality [13,23].

However, in the multivariate analysis we found that only increasing age and poor functional status before the event were independently associated with a greater risk of death in a multivariate analysis. Other demographic and cardiovascular risk factors were not found to be associated independently with mortality in the multivariate model. While most studies found that higher age and pre-stroke disability were independently related, our findings are incompatible with other studies in which intermittent claudication was also independently associated with a higher death rate [24]. These differences may be attributed to differences in the populations studied, as well as differences in the research methods, as fatality rates vary according to lifestyle behaviors, nutrition, environmental and living conditions, health behaviors and accessibility of health services [25].

This study has several limitations that should be mentioned. First, our study did not include people who died in the emergency room since their number is unknown. Yet it appears that a similar situation was found in other studies, particularly in light of the fact that most of these patients are not given a clear, valid diagnosis of stroke. Therefore, mortality estimates might be biased. Second, we did not include in our univariate and multivariate analysis the type and severity of the stroke on admission. Although this information exists in our database, we could not enter it into the model because of the small number of intracerebral hemorrhage stroke patients who survived the first stage of the event [15]. Third, we did not include in our univariate and multivariate analysis several variables that could contribute to our knowledge of prognostic factors of stroke mortality. These include variables such as first-ever or recurrent stroke, and health behaviors such as smoking or alcohol consumption. This is because we are not sure that we obtained information about all the patients and there may therefore be a problem of validity. Finally, for logistic reasons, our study did not include Arabs. Koton et al. [14] showed differences in stroke mortality in Israel between Jews and Arabs and risk factor distribution. There is a need, therefore, for additional studies to provide a deeper understanding of short- and long-term mortality in different groups in the Israeli population.

In conclusion, we believe this study is one of the first to provide information about long-term survival after stroke in the Israeli population. Although our findings did not show an independent relation between stroke and cardiovascular risk factors, long-term secondary prevention in stroke patients can certainly be improved. It is necessary to augment preventive measures, address risk factors, and treat the early stages of stroke, as is done in other countries, in order to reduce the numbers of cerebral stroke patients and those who suffer in the long term and to enhance the implementation of preventive strategies.

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