Five-Year Case Fatality Following First-Ever Stroke in the Mashhad Stroke Incidence Study: A Population-Based Study of Stroke in the Middle East

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Background and Purpose: Despite recent declines in stroke mortality in high-income countries, the incidence and mortality of stroke have increased in many low- and middle-income countries. Population-based information on stroke in such countries is a research priority to address this rising trend. This study was designed to evaluate 5-year stroke mortality and its associated factors. *Methods:* During a 12-month period beginning from November 2006, 624 patients with first-ever stroke (FES) living in Mashhad, Iran, were recruited and followed longitudinally. Kaplan-Meier analyses were used to determine the cumulative risk of death. Prognostic variables associated with death were assessed using a Cox proportional hazard, backward logistic regression model. *Results:* The 5-year cumulative risk of death was 53.8% for women and 60.5% for men (log rank = .1). The most frequent causes of death were stroke (41.2%), myocardial infarction/vascular diseases (16.4%), and pneumonia (14.2%). In multivariable Cox proportional hazard analysis, male gender (hazard ratio [HR]: 1.29, 95% confidence interval [CI]: 1.01-1.64), age (HR: 1.04, 95% CI: 1.03-1.05, per 1-year increase), National Institute of Health Stroke Scale score at admission (HR: 1.11, 95% CI: 1.09-1.12, per 1-point increase), atrial fibrillation (HR: 1.78, CI: 1.24-2.54), and education < 12 years (HR: 1.61, 95% CI: 1.08-2.4) were associated with greater 5-year case fatality. *Conclusions:* Long-term case fatality following stroke in Iran is greater than that observed in many high-income countries. Targeting

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strategies to reduce the poor outcome following stroke, such as treating AF, is likely to reduce this disparate outcome. **Key Words:** Stroke—population based—mortality—Middle East.
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Introduction

Little is known about the stroke case fatality and factors associated with death in low- to middle-income countries.[1] In a population-based study of stroke in Iran, the Mashhad Stroke Incidence Study (MSIS), we have shown both an excessive incidence of stroke[2] and greater 1-year stroke case fatality compared with those observed in most Western countries.[1]

The current study was designed to evaluate long-term survival, factors associated with death, and causes of death after a first-ever stroke (FES) in participants from the MSIS.

Methods

The methodology of the MSIS has been previously described.[2] Briefly, using a standard verbal autopsy,[3] we identified causes of death at 5 years and then classified them according to the 10th version of the International Classification of Diseases (ICD-10).

Data Collection and Analysis

Prognostic variables associated with death were assessed using a Cox proportional hazard, backward logistic regression analysis. Kaplan–Meier analyses were used to determine the cumulative risk of death by subtype and gender. A P value of ≤.05 (2 sided) was considered statistically significant. SPSS statistical software (version 16, SPSS Inc., Illinois, USA) was used for all statistical analyses.

Results

Case Fatality

A total of 624 patients with FES (mean age 64.6 ± 14.8) were registered in the MSIS. Among the patients with FES, 330 died during the 5-year follow-up period. The mean age at the time of the index stroke was older in those who died than in survivors (69.6 ± 13.5 versus 58.8 ± 14.2 years, $P < .001$). The cumulative risk of death during the 5-year period was 57.3%, with the greatest risk during the first month (20.8%) and the first year (37.3%) (Fig 1, Table 1).

Association between Subtype of Index Stroke and Case Fatality

Among patients with FES, case fatality was significantly greater in patients with intracerebral hemorrhage (ICH) than in patients with ischemic stroke (IS), subarachnoid hemorrhage, and undefined stroke (Table 1). In patients with ICH, most deaths occurred during the first 30 days, increasing from 41.2% in the first month to 62.9% at 5 years. In those with IS, case fatality increased steadily during the follow-up period (first month: 17.3%, first year: 30.2%, 5 years: 57.5%) (Fig 2).

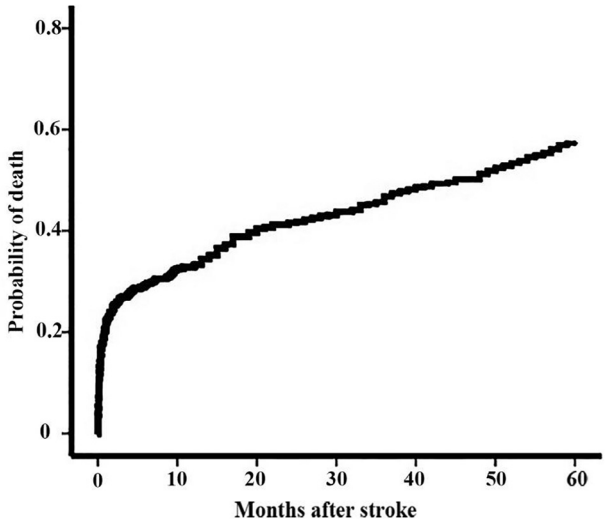

Figure 1. *Kaplan–Meier curve showing the probability of death after the index stroke during the 5-year follow-up of patients with first-ever stroke in the MSIS.*

Causes of Death

Death most commonly resulted from the direct impact of the stroke itself (41.2%). Vascular diseases other than stroke, including coronary artery disease and peripheral vascular disorders (deep vein thrombosis and pulmonary emboli), contributed to 16.4% of deaths. Among all causes of death, the shortest mean interval time between FES and death was observed for stroke (7.4 ± 1.2 months, 95% CI: 5-10), whereas those with other causes died later (24.2 ± 2.5 months, 95% CI: 19-29).

Factors Associated with Death at 5 Years

The results of univariable Cox proportional hazard analyses of factors associated with death are summarized in Supplementary Table S1. After adjustment for vascular and demographic variables in multivariable Cox proportional regression modeling, male gender (hazard ratio [HR]: 1.29, 95% confidence interval [CI]: 1.01-1.6), increasing age (HR: 1.04, 95% CI: 1.03-1.05, per year lived), National Institutes of Health Stroke Scale (NIHSS)

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