



Long-term survival and prognostic determinants in stroke patients in western Iran: A retrospective cohort study using landmark analysis

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Keywords

Hemorrhagic Stroke; Ischemic Stroke; Landmark; Risk Factors; Stroke; Survival; Iran

Abstract

Background: The purpose of this study was to estimate the long-term survival of patients with stroke and identify prognostic factors associated with mortality.

Methods: This retrospective cohort study included 2744 patients with stroke admitted to Farshchian (Sina) Hospital in Hamadan City, Iran, between 2014 and 2019, who were followed until 2022. Data on demographic characteristics, clinical history, vital signs at admission, post-stroke complications, and stroke severity were collected. The primary outcome was

survival time from stroke admission to death. Two Cox proportional hazards models were developed: a baseline prognostic and a landmark analysis model.

Results: Of the 2744 patients included in the study, 1433 (52.22%) died during the follow-up period. The survival rates were 67.2% at 1 year (901 deaths), 51.3% at 5 years (1296 deaths), and 37.6% at 9 years (1433 deaths).

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In the landmark analysis, mortality risk was significantly higher for patients with acute kidney injury [adjusted hazard ratio (HR): 1.86; 95% confidence interval (CI): 1.28–2.70], diabetes (adjusted HR: 1.29; 95% CI: 1.00–1.68), and Glasgow Coma Scale (GCS) scores ≤ 8 (adjusted HR: 1.74; 95% CI: 1.09–2.75) compared to the corresponding reference groups. Respiratory failure and pneumonia occurring after 7 days were associated with significantly increased mortality risk with adjusted HRs of 1.88 (95% CI: 1.33–2.67) and 2.00 (95% CI: 1.28–3.13), respectively.

Conclusion: The findings highlight the importance of secondary prevention and rehabilitation in improving long-term outcomes among stroke survivors. In addition, several potentially modifiable prognostic factors associated with mortality were identified. The results further suggest that landmark analysis may improve the accuracy and stability of risk estimates in stroke survival studies.

Introduction

Central nervous system (CNS) infarction is defined as brain, spinal cord, or retinal cell death attributable to ischemia, based on neuropathological, neuroimaging, and/or clinical evidence of permanent injury. Ischemic stroke refers to CNS infarction accompanied by overt symptoms, whereas silent infarction causes no known symptoms. Broadly, stroke is classified into ischemic and hemorrhagic subtypes, with the latter including intracerebral hemorrhage (ICH) and subarachnoid hemorrhage (SAH).¹ Stroke is the second leading cause of death worldwide after ischemic heart disease (IHD), with survivors often suffering from various physical disabilities as well as mood disorders such as depression.^{2,3} The global economic burden of stroke exceeds US\$890 billion, representing 0.66% of global gross domestic product (GDP). Between 1990 and 2021, stroke incidence, prevalence, and mortality rose substantially, with low- and middle-income countries (LMICs) accounting for 87% of stroke-related deaths and 89% of disability-adjusted life years (DALYs).⁴

Risk factors for stroke can be broadly categorized into non-modifiable factors – including age, sex, race, and genetic predisposition – and modifiable factors, such as hypertension (HTN), smoking, diabetes mellitus, and hyperlipidemia.⁵

International population-based studies have indicated substantial long-term consequences of stroke. For instance, a study from Joinville, Brazil, reported a 5-year survival rate of 52%, with 68% of

patients being either deceased or disabled.⁶ In the United Kingdom, data from the South London Stroke Register revealed that only 21% of patients survived up to 15 years post-stroke, with high rates of disability, depression, and cognitive impairment among long-term survivors.⁷ In contrast, data from Iran remain limited. A large-scale registry-based study in Iran on 1345 patients diagnosed with stroke reported a one-year survival rate of 72.1%, with predictors of one-year survival being older age, diabetes, a history of stroke or transient ischemic attack (TIA), and prior use of warfarin. Further, hospital complications such as hemorrhage, sepsis, and hydrocephalus significantly elevated the risk of death.⁸ Increasing age, lower educational level, and greater stroke severity have been identified as predictors of long-term mortality in patients.⁹ Notably, recent findings from the Global Burden of Disease (GBD) study demonstrated that high body mass index (BMI) was the most rapidly increasing risk factor for stroke between 1990 and 2019. In 2019, high BMI contributed to 34.9 million (24.3%) of global stroke-related DALYs.¹⁰

Given the significant outcomes of stroke, including both disability and mortality, it is essential to understand its prevalence and associated risk factors for healthcare planning, prevention, and rehabilitation. Nevertheless, there exists a substantial knowledge gap regarding population-specific prognostic indicators, especially in developing countries where the burden of stroke is disproportionately high. Understanding these factors is critical for developing targeted interventions and effective public health strategies. Moreover, comprehensive studies exploring long-term outcomes and disparities in healthcare access are especially needed in resource-constrained settings. Although numerous studies from high-income countries have ascertained predictors of post-stroke survival, data from LMICs remain limited. Iran, as an upper-middle-income country with diverse healthcare infrastructures and regional disparities, represents a vital setting for such investigations. The aim of this study was to estimate the long-term survival rate among patients with ischemic or hemorrhagic stroke admitted to a tertiary hospital in Hamadan, western Iran, as well as to identify key prognostic factors over a 5-year follow-up period. This analysis addresses a critical evidence gap and supports context-sensitive stroke care strategies in LMICs.

Materials and Methods

This retrospective cohort study included all patients diagnosed with stroke who were referred to and admitted to Farshchian (Sina) Hospital in Hamadan City between 2014 and 2019 and had complete medical records. In this manuscript, the term stroke refers specifically to ischemic and hemorrhagic stroke. Other cerebrovascular events, such as TIA, SAH, and cerebral venous thrombosis (CVT), were not considered within the scope of this study. During the study period, a total of 2744 eligible patients were followed up until 2022. Farshchian Hospital serves as the main tertiary referral center for acute stroke care in Hamadan Province. Stroke was diagnosed based on the presence of acute-onset focal neurological deficits, such as hemiparesis, aphasia, or visual disturbances, and evidence of corresponding brain lesions on neuroimaging [computed tomography (CT) or magnetic resonance imaging (MRI)], in accordance with established international clinical guidelines, such as those of the American Heart Association/American Stroke Association (AHA/ASA).¹

Inclusion criteria were as follows: residence in Hamadan City, age 18 years or older, and a definitive diagnosis of acute ischemic or hemorrhagic stroke based on clinical presentation as well as either CT or MRI findings. For patients with multiple stroke admissions along the study period, only the first admission was included. Exclusion criteria were incomplete medical records, a history of previous stroke prior to the study period, or a final diagnosis of TIA, traumatic brain injury, brain tumor, or subdural hematoma.

Data source

Data were retrospectively extracted from medical records using a predetermined and standardized checklist developed based on existing clinical guidelines and documentation practices. Trained reviewers performed the data collection, ensuring consistency and minimizing potential measurement bias. Data were categorized into the following domains:

- Demographic variables: age, gender, education (illiterate, below diploma, diploma, or university degree), occupation (homemaker, employee, industrial/construction worker, self-employed, retired, other), residence (urban/rural), marital status (single, married), history of smoking, history of opiate use.
- Clinical history: stroke subtype (ischemic vs. hemorrhagic) and treatment modality (medical

vs. surgical), underlying diseases such as gastrointestinal (GI) diseases, respiratory failure, acute kidney injury, obesity, diabetes, HTN, cardiovascular diseases (CVDs), neurological diseases, and surgical history.

- Vital signs at admission: history of blood transfusion, fever status, blood pressure categories based on the American Heart Association (AHA) guidelines,¹¹ heart rate [normal: 60–99 beats per minute (bpm), bradycardia: < 60 bpm, tachycardia: ≥ 100 bpm], respiratory rate (normal: 12–20, elevated: > 20), and level of consciousness appraised both qualitatively (full consciousness, lethargy, and obtundation) and quantitatively using the Glasgow Coma Scale (GCS) (categorized as 13–15, 9–12, and ≤ 8). The qualitative consciousness variable was based on initial clinical observation, while GCS provided a structured and validated assessment.
- Post-stroke complications: seizure, pneumonia, blunted affect, respiratory failure, CVDs (heart failure/IHD), bedsores, hematologic disorder, recurrent stroke, and peripheral edema which is defined as swelling of the extremities due to fluid accumulation and may occur in survivors of ischemic or hemorrhagic stroke, particularly in those with reduced mobility and limb weakness. Although it is not a direct neurological consequence of stroke, it can negatively affect rehabilitation and quality of life (QoL).
- Stroke severity-related clinical manifestations at admission: aphasia, dysarthria, hemianopia, vertigo, consciousness, hemianesthesia, facial nerve [cranial nerve 7 (CN VII)] palsy (specifically central motor weakness), hemiplegia, paresis, impaired balance, urinary incontinence at admission, delusion, memory impairment, GI symptoms (nausea, vomiting, and abdominal distension) at admission.

Outcomes: The main outcome of this study was overall survival, defined as the interval between the initial stroke admission and death. The vital status of the deceased patients was documented via hospital records. The mortality status of discharged patients was obtained from death certificates using the patients' national identification code through Iranian Legal Medicine Organization database; this provided a reliable method for capturing mortality for at least 3 years following initial stroke. The end of follow-up was December 20, 2022; patients who were still alive at this time were considered as censored.

Ethics: Institutional permission was obtained from Farshchian (Sina) Hospital for data access. All patient data were anonymized and handled in compliance with institutional and national guidelines for retrospective studies. The study protocol was approved by the Institutional Ethics Committee of Hamadan University of Medical Sciences (approval ID: IR.UMSHA.REC.1399.1055), and all relevant ethical standards were observed carefully.

Life tables were created to estimate early survival (every two months during the first year), long-term survival (annually from year one to year nine), and overall survival throughout the follow-up period (0–5 years and 0–9 years). The chi-square test was applied to compare categorical variables between deceased and surviving patients at the end of follow-up. In addition, Kaplan-Meier survival curves were plotted based on gender, age, and GCS category, and compared by log-rank tests.

In this study, a penalized regression method was used with Least Absolute Shrinkage and Selection Operator (LASSO) to identify key predictors of survival among all covariates. In order to address the potential bias associated with in-hospital complications such as pneumonia and respiratory failure, which may occur post-admission, two separate models were employed. The first model incorporated only baseline prognostic factors measured at admission, while the second model analyzed in-hospital complications and baseline prognostic factors using a landmark analysis approach.^{12,13} The landmark model included only patients who were still at risk at day 7, ensuring that the evaluation of prognostic factors reflected baseline characteristics and complications occurring after the landmark.

Unadjusted and adjusted hazard ratios (HRs) for mortality, with 95% confidence intervals (CIs), were estimated using Cox proportional hazards regression models in both study models. Furthermore, two statistical assumptions were evaluated: the proportionality of hazards in the Cox model and the collinearity between the variables. The goodness of fit in the models was evaluated using the Akaike information criterion (AIC) and reported for both models as well. To address potential immortal time bias introduced by applying hospital admission as the start point for the primary outcome, a sensitivity analysis was conducted defining the time-to-event interval as the duration from symptom onset to death. Full

details about LASSO, landmark analysis, testing the assumptions, and sensitivity analysis are provided in the Supplementary Materials.

All analyses were conducted at a significance level of 0.05 using R 4.4.2 (the glmnet package) and Stata (version 17, Stata Corporation, College Station, TX, USA) software.

Results

Of 4317 patients admitted to the hospital, 2781 met the inclusion criteria (Figure 1). After excluding 37 patients due to insufficient follow-up data, the final analytical cohort comprised 2744 patients who experienced an initial stroke and were admitted to the hospital between 2014 and 2019.

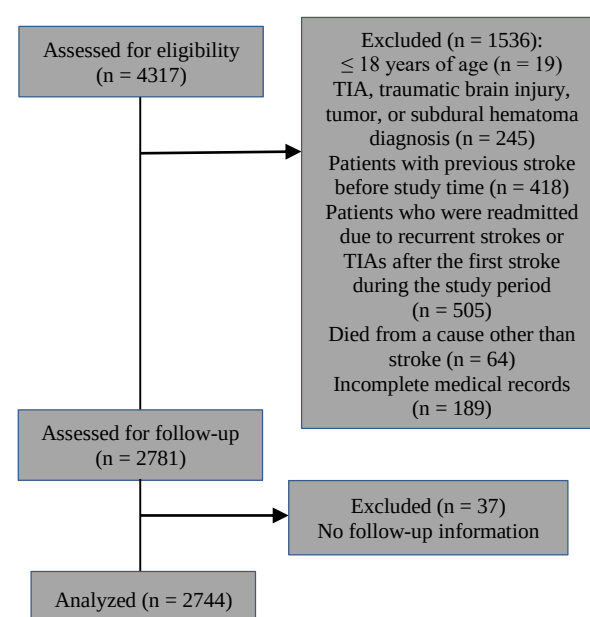


Figure 1. Flow diagram of patient selection for the study cohort

The median follow-up duration was 41 months [interquartile range (IQR): 2–70], with a mean duration of 40.84 ± 33.58 months. In general, out of 2744 patients, 1433 (52.22%) patients were deceased at the end of follow-up time, and 450 (16.40%) deaths occurred in the hospital after admission to the hospital owing to the initial stroke.

As reported in table 1, for baseline analysis, the survival rates at 1, 3, and 6 months post-stroke were 81.4%, 74.3%, and 71.3%, respectively. For landmark analysis, these rates were 84.9%, 80.3%, and 77.4%, respectively. Further, the results in table 1 and figure 2 indicate that the survival rates for baseline analysis at 1, 2, 3, 5, and 9 years were 67.2%, 62.6%, 58.5%, 51.3%, and 37.6%, respectively.

Table 1. Survival rate for patients with stroke: Comparison between baseline (hospital admission) and a 7-day landmark analysis using life table

	Time	Duration	Number of patients	Number of deaths	Number of censored	Survival rate	SE	95% CI
Baseline	Month	0-1	2744	509	1	0.814	0.007	0.799-0.829
		1-3	2234	195	0	0.743	0.008	0.727-0.759
		3-6	2039	82	0	0.713	0.009	0.696-0.730
	Year	0-1	2744	901	1	0.672	0.009	0.654-0.689
		1-2	1842	124	2	0.626	0.009	0.608-0.644
		2-3	1716	110	55	0.585	0.009	0.567-0.604
		3-5	1551	161	500	0.513	0.010	0.494-0.532
Landmark	Month	0-1	2493	376	1	0.849	0.007	0.834-0.863
		1-3	2116	116	0	0.803	0.008	0.786-0.818
		3-6	2000	70	0	0.774	0.008	0.758-0.790
	Year	0-1	2493	661	1	0.735	0.009	0.717-0.752
		1-2	1831	121	2	0.686	0.009	0.668-0.704
		2-3	1708	116	71	0.633	0.010	0.619-0.657
		3-5	1521	150	502	0.563	0.010	0.543-0.583
		5-9	869	134	735	0.412	0.013	0.386-0.439

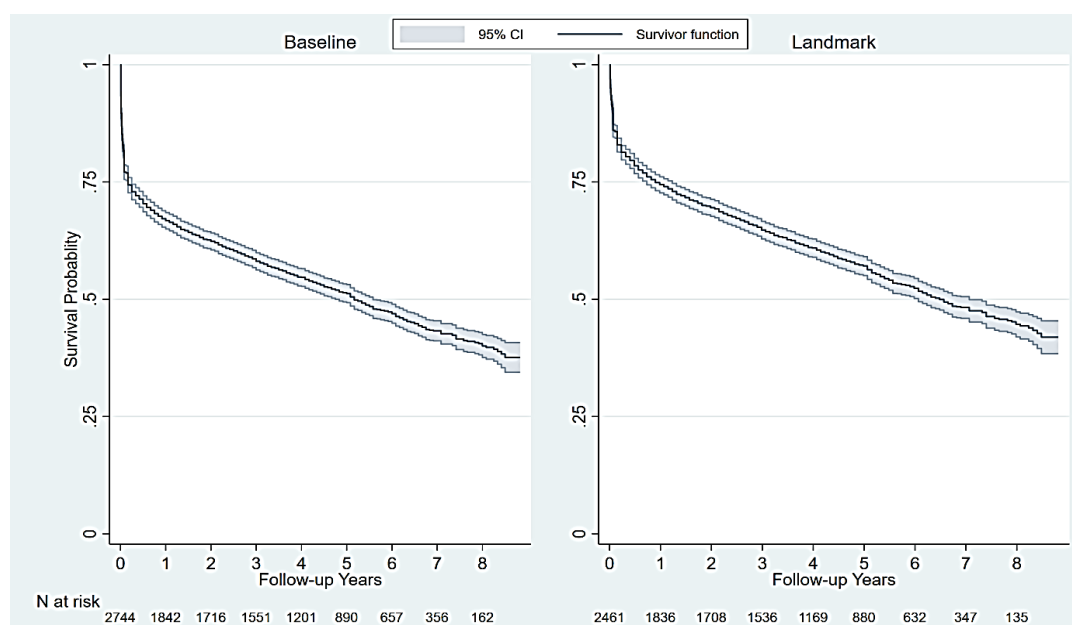
SE: Standard error; CI: Confidence interval

The corresponding survival rates at these time points for landmark analysis were 73.5%, 68.6%, 63.3%, 56.3%, and 41.2%. The 9-year survival rate was estimated based on 888 observations for the baseline analysis and 869 observations for the landmark analysis.

According to figure 3, the survival rate in patients aged 18–54 years, those with an ischemic stroke diagnosis, and those with a GCS score of 13–15 was longer compared to other groups ($P < 0.001$). Although the survival rates were

slightly higher in men than in women, this difference was not statistically significant ($P = 0.116$). Moreover, the survival curves for both sexes showed converging trends toward the end of the follow-up period.

Baseline characteristics, including demographics, clinical history, underlying diseases, vital signs at admission, post-stroke complications, and stroke severity are presented in table S1 (Supplementary Materials) for all patients, as well as for those alive and deceased.

**Figure 2.** Survival time from stroke diagnosis to death in Hamadan Province, Iran (2014–2022) using Kaplan-Meier curve based on baseline and landmark analyses

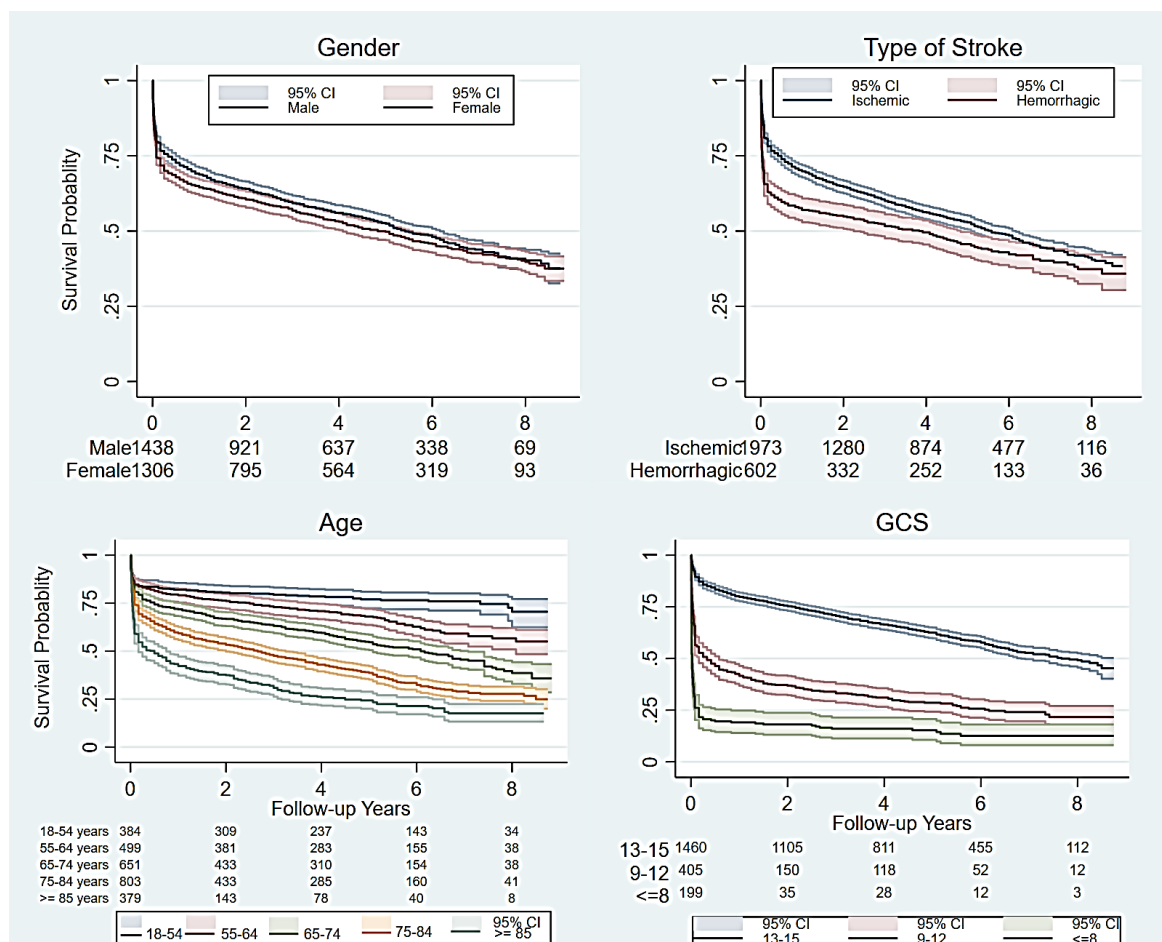


Figure 3. Survival time from stroke diagnosis to death in Hamadan Province, Iran (2014-2022) using Kaplan-Meier curve compared by gender, type of stroke, age, and Glasgow Coma Scale (GCS)

Briefly, patients who died were significantly older (over 55 years), had hemorrhagic stroke, and had higher prevalence of underlying diseases such as GI diseases, respiratory failure, acute kidney injury, diabetes, HTN, and CVD. They also were more likely to present with abnormal vital signs, specifically fever, tachycardia, respiratory rate exceeding 20 breaths per minute, and altered consciousness (GCS score < 12, lethargy, or obtundation). Additionally, patients who were non-ambulatory at admission (those arriving by wheelchair or stretcher, compared with ambulatory patients who walked with or without assistive devices), those with recurrent stroke, pneumonia, respiratory failure, or hematologic disorder during hospitalization had higher risks of mortality compared to other groups. Symptoms such as aphasia, dysarthria, urinary incontinence, unconsciousness, and GI symptoms were also associated with increased mortality. The unadjusted HRs for mortality, associated with demographic characteristics, clinical history,

underlying diseases, vital signs at admission, post-stroke complications, and stroke severity, are outlined in table S2 (Supplementary Materials). These results align with the patterns observed in the previous table, further supporting the associations identified in our analysis.

Assessment of model assumptions: After identifying key predictors of survival among all covariates by LASSO, the proportional hazard assumption was assessed using the Schoenfeld residuals test. Since the test was not significant for baseline and landmark models ($P = 0.058$ and $P = 0.063$, respectively), the proportional hazards assumptions were justified with no multicollinearity observed for variables. The results of checking assumption, including Schoenfeld residuals test and variance inflation factors (VIFs), are provided in table S3 (Supplementary Materials).

Demographic variables: The influence of potential risk factors on mortality was ascertained by the first and the second model and reported by adjusted HRs in table 2.

Table 2. Adjusted hazard ratios (HRs) for mortality by patient characteristics using Cox proportional hazards model

Covariates		Landmark model	Baseline model	Landmark model	Baseline model
		HR (95% CI)	P	HR (95% CI)	P
Gender		0.90 (0.72–1.13)	0.341	0.83 (0.66–1.05)	0.121
Demographic variables	Age (year)				
	18–54 (Ref)	-	-	-	-
	55–64	2.07 (1.16–3.67)	0.013	2.74 (1.46–5.15)	0.002
	65–74	3.90 (2.27–6.69)	< 0.001	4.31 (2.36–7.87)	< 0.001
	75–84	6.17 (3.64–10.47)	< 0.001	6.49 (3.58–11.77)	< 0.001
Clinical history	≥ 85	10.64 (6.09–18.58)	< 0.001	9.73 (5.24–18.06)	< 0.001
	Opiate (Ref: Yes)	0.79 (0.59–1.05)	0.112	0.82 (0.61–1.12)	0.216
	Type				
	Ischemic (Ref)	-	-	-	-
	Hemorrhagic	1.15 (0.89–1.49)	0.282	1.23 (0.93–1.63)	0.150
	Urinary incontinence before stroke (Ref: No)	1.86 (1.28–2.70)	0.001	1.54 (1.02–2.33)	0.040
	Diabetes (Ref: No)	1.29 (1.00–1.68)	0.048	1.39 (1.06–1.83)	0.016
	Obesity (Ref: No)	0.76 (0.51–1.13)	0.173	0.83 (0.55–1.25)	0.375
	Neurological diseases (Ref: No)	1.20 (0.89–1.63)	0.235	1.26 (0.90–1.76)	0.172
	High blood pressure (Ref: No)	1.12 (0.89–1.41)	0.318	1.18 (0.93–1.52)	0.180
Vital signs at admission	Surgery (Ref: No)	-	-	1.16 (0.92–1.47)	0.216
	History of blood transfusion (Ref: No)	-	-	1.74 (1.08–2.79)	0.022
	Fever (Ref: No)	1.34 (1.01–1.82)	0.046	1.18 (0.83–1.67)	0.353
	Blood pressure				
	Normal	-	-	1.34 (0.82–2.20)	0.239
	Elevated	-	-	1.71 (0.88–3.30)	0.111
	Stage 1 (hypertension)	-	-	1.04 (0.68–1.59)	0.851
	Stage 2 (hypertension)	-	-	0.88 (0.59–1.32)	0.554
	Hypertensive crisis (Ref)	-	-	-	-
	Heart rate				
	Normal (Ref)	-	-	-	-
	Bradycardia (< 60 bpm)	1.35 (0.65–2.83)	0.422	1.02 (0.46–2.25)	0.960
	Tachycardia (≥ 100 bpm)	0.65 (0.38–1.13)	0.125	0.59 (0.33–1.04)	0.073
	Respiratory rate (Ref: 12-20 breaths/min)				
	> 20	1.74 (1.09–2.75)	0.019	2.02 (1.26–3.24)	0.004
	GCS				
	13–15 (Ref)	-	-	-	-
	9–12	1.02 (0.77–1.36)	0.865	1.47 (1.11–1.94)	0.007
	≤ 8	1.67 (1.07–2.61)	0.023	1.60 (1.01–2.73)	0.048
Post-stroke complications	Initial entrance				
	Ambulatory (Ref)	-	-	-	-
	Wheelchair	1.29 (0.90–1.87)	0.158	1.18 (0.79–1.75)	0.424
	Stretcher	2.40 (1.64–3.51)	< 0.001	2.44 (1.61–3.69)	< 0.001
	Recurrent stroke (Ref: No)	1.13 (0.87–1.48)	0.341	1.07 (0.80–1.44)	0.633
	Respiratory failure (Ref: No)	1.88 (1.33–2.67)	< 0.001	-	-
	Pneumonia (Ref: No)	2.00 (1.28–3.13)	0.002	-	-
Stroke severity	Dysarthria (Ref: No)	0.84 (0.63–1.12)	0.231	0.82 (0.61–1.11)	0.203
	Facial nerve palsy (Ref: No)	1.25 (0.99–1.59)	0.059	1.20 (0.93–1.54)	0.162
	Urinary incontinence (Ref: No)	1.28 (0.91–1.81)	0.160	1.35 (1.00–1.94)	0.047
	Digestive (Ref: No)	-	-	1.30 (1.00–1.69)	0.049
	Sensory (Ref: No)	-	-	0.76 (0.52–1.10)	0.152
	Organ force loss (Ref: No)	-	-	1.26 (0.90–1.75)	0.166
	AIC	4136.63		4671.11	

HR: Hazard ratio; CI: Confidence interval; AIC: Akaike information criterion

The first model included 2744 patients and analyzed only baseline prognostic factors measured at admission. The second model included 2493 patients (only patients who were still at risk at 7 days post-admission) and analyzed in-hospital complications and baseline prognostic factors using a landmark analysis approach. Accordingly, in both models, the risk of mortality was significantly elevated in patients aged more than 55 years compared to 18–54 age group. In the first model, the increased risk was 2.74-fold for 55–64 years ($P = 0.002$), 4.31-fold for 65–74 years ($P < 0.001$), 6.49-fold for 75–84 years ($P < 0.001$), and 9.73-fold for more than 85 years ($P < 0.001$). Similarly, in the second model, the risk was 2.07-fold for 55–64 years ($P = 0.001$), 3.90, 6.17, and 10.64-fold for 65–74 years, 75–84 years, and more than 85 years, respectively ($P < 0.001$).

Clinical history and vital signs at admission:

Underlying diseases such as acute kidney injury and diabetes at admission were significantly associated with increased mortality in the first model, with HRs of 1.54 ($P = 0.040$) and 1.39 ($P = 0.016$), respectively. In the second model, the corresponding HRs were 1.86 ($P = 0.001$) and 1.29 ($P = 0.048$). At the time of admission, the respiratory rate higher than 20 breaths/min and the use of a stretcher for non-ambulatory status were significantly associated with increased mortality by 2.02 (95% CI: 1.26–3.24) and 2.44 (95% CI: 1.61–3.69) times in the first model and 1.74 (95% CI: 1.09–2.75) and 2.40 (95% CI: 1.64–3.51) times in the second model compared to the reference groups. At admission, GCS scores of 9–12 and ≤ 8 were factors that significantly elevated the risk of mortality 1.47-fold ($P = 0.007$) and 1.60-fold ($P = 0.048$), respectively. However, at the landmark approach, only $GCS \leq 8$ significantly raised the risk of death by 1.67 (95% CI: 1.07–2.61) times.

Stroke severity and post-stroke complications:

A history of blood transfusion, urinary incontinence, and GI symptoms were associated with increased mortality by 1.74 (95% CI: 1.08–2.79), 1.35 (95% CI: 1.00–1.94), and 1.30 (95% CI: 1.00–1.69) times, respectively, in the first model. However, there was no statistically significant association between these factors and the risk of mortality in the second model. Based on table 2, occurrence of respiratory failure and pneumonia after 7 days was associated with a significantly higher hazard of mortality by 1.88 (95% CI: 1.33–2.67) and 2.00 (95% CI: 1.28–3.13) times, respectively. According to these findings,

there was no statistically significant association between other factors and the risk of mortality. The CIs for the parameter estimates in the second model (landmark analysis) were shorter than the baseline model, revealing smaller standard errors (SEs) and greater precision in the estimates at the specified landmark time points. Moreover, the AIC value in baseline and landmark models was 4671.11 and 4136.63, respectively.

Of the 2744 patients in the cohort, 2517 (91.8%) had valid symptom-onset data and were included in the sensitivity analysis. The sensitivity analysis using symptom onset as the time origin in the first model yielded HR estimates in line with the primary analysis, indicating that the choice of time origin did not significantly affect the findings. Specifically, the adjusted HRs for GCS scores of 9–12 and ≤ 8 at the time of admission were 1.44 (95% CI: 1.08–1.90) and 1.74 (95% CI: 1.01–2.93) when measured from symptom onset, compared to 1.44 (95% CI: 1.07–1.93) and 1.92 (95% CI: 1.11–3.31) when measured from hospital admission. The results of analysis using symptom onset as the time origin are detailed in table S4 (Supplementary Materials).

Discussion

The aim of this extensive retrospective cohort study was to evaluate long-term survival rates and identify prognostic factors associated with ischemic and hemorrhagic stroke in a large group of patients with stroke admitted to a single center in the west of Iran. Our analysis revealed that more than half of the patients (52.22%) died during the follow-up period, with survival rates recorded at 67.3% for one year, 51.4% for five years, and 37.7% for nine years. Key prognostic factors for heightened mortality included older age, hemorrhagic stroke subtype, diabetes, and lower GCS scores at admission. Specifically, patients with $GCS \leq 8$ had a significantly higher hazard of mortality, while GCS score of 9–12 presented a non-significant trend in the landmark model. In-hospital complications such as respiratory failure, facial nerve palsy, urinary incontinence, and GI diseases were significantly associated with elevated mortality risk.

In our cohort, the one-year survival rate was 67.3%, which is comparable to the 65.5% reported by Novbakht et al.¹⁴ These results align with findings from another study conducted in the northeast of Iran.¹⁵ In addition, a study in Shahrour, Iran, reported a one-year survival rate

of 78.4%.¹⁶ However, when compared to international studies, significant discrepancies emerge. For example, a study by Chang et al. in Taiwan reported mortality rates of 12.2%, 15.8%, 20.5%, and 25.6% for patients with ischemic stroke at 1 to 4 years post-stroke,¹⁷ which are substantially lower than our findings. In contrast, a Danish study reported one-year and five-year mortality rates of 41% and 60%, respectively,¹⁸ both one-year and five-year survival rates of the present study are higher than those of the Danish study. Additionally, a Brazilian study noted cumulative mortality rates of 27.8%, 31.2%, and 33.4% at one, two, and three years, respectively,¹⁹ which also suggests lower mortality compared to our cohort. These variations in mortality rates may be attributed to discrepancies in patient characteristics, healthcare systems, and treatment protocols across different regions. In our setting, limited access to specialized stroke units, especially in smaller cities and rural areas, can delay initiation of appropriate acute care interventions such as thrombolysis or neurosurgical evaluation. Furthermore, post-stroke rehabilitation services are often underdeveloped or inconsistently available in Iran's public healthcare system, which may negatively affect long-term outcomes. Moreover, disparities in regional health resources, variations in staffing, high cost of the tissue plasminogen activator (tPA) drug, lack of priority for triage, and limited infrastructure for follow-up care contribute to unequal stroke management across different provinces.²⁰⁻²²

Advanced age was identified as the strongest independent predictor of mortality risk in this study. Patients aged 55–64 years had a 2.08-fold higher HR compared to those aged 18–54, which rose to 10.64-fold for those over 85 years old. This finding is in line with numerous studies that have consistently shown age to be a critical non-modifiable risk factor for poor outcomes following stroke.^{15-17,23,24} Older patients are more likely to have multiple comorbidities, reduced physiological reserves, and diminished functional capacity, all contributing to their heightened vulnerability to stroke-related complications and mortality.

Hemorrhagic stroke was linked to a 1.28-fold higher mortality risk compared to ischemic stroke in this cohort. This finding accords with the results from other studies that have also reported a significantly higher mortality risk for hemorrhagic stroke compared to ischemic stroke.^{25,26} ICH is known to have a worse prognosis than ischemic stroke owing to the rapid development of mass

effect, perihematomal edema, and elevated intracranial pressure, which can result in early neurological deterioration and death.²⁶

The presence of diabetes was found to be a significant predictor of mortality risk in our study, with a HR of 1.47 for patients with diabetes compared to non-diabetic patients. In a study by Akhtar et al., patients with diabetes and acute ischemic stroke experienced more in-hospital complications, poorer discharge outcomes, and higher rates of mortality as well as stroke recurrence at 90 days compared to patients with prediabetes or those without diabetes.²⁷ This finding is further supported by a systematic review which included 66 eligible articles, estimating the prevalence of diabetes among patients with stroke to be approximately 28%. The review revealed that acute hyperglycemia and diabetes were consistently associated with poorer outcomes following both ischemic and hemorrhagic strokes, including higher mortality rates, worse neurological and functional outcomes, longer hospital stays, elevated readmission rates, and higher rates of stroke recurrence.²⁸

The present research found that patients with GCS scores ≤ 8 or between 9–12 had a higher risk of mortality compared to those with GCS scores of 13–15. The GCS is a widely used tool for assessing the level of consciousness and serves as a proxy for stroke severity.²⁹ Lower GCS scores indicate more extensive brain injury and are linked to higher rates of complications, such as aspiration pneumonia, deep vein thrombosis (DVT), and pressure ulcers, which can further compromise outcomes. The identification of GCS ≤ 8 as a significant predictor of mortality has important implications for clinical triage as well as intensive care unit (ICU) prioritization, especially in low-resource settings. In Iranian hospitals where access to intensive neurological care is limited, early GCS assessment upon admission could help prioritize patients for close monitoring, airway protection, and targeted supportive care. Likewise, the elevated hazard associated with diabetes suggests the need for routine screening of glycemic control and tighter inpatient glucose management among stroke admissions.

Our study findings are practical for both clinical practice and public health policy. Identifying key prognostic factors can guide clinicians in evaluating patient prognosis and prioritizing interventions. Further, understanding the demographic and clinical characteristics associated

with mortality can aid in the development of targeted educational campaigns and resource allocation to ameliorate stroke care.

To evaluate the robustness of our findings and minimize potential bias related to the choice of the time origin, a sensitivity analysis was conducted using symptom onset as the start point for survival analysis. The results from this alternative analysis were in accordance with our primary findings, indicating that the choice of time origin (symptom onset vs. hospital admission) did not significantly alter the estimated association between pre-hospital delay and early mortality. These findings strengthen our confidence that the observed lack of an independent association between delay and mortality is not an artifact of immortal time bias. Nonetheless, we acknowledge that the accuracy of symptom onset data depends on reliable documentation, and potential variability or missing data could affect the analysis. Future studies with prospective collection of symptom onset data are warranted to further validate these results.

Our study found that landmark analysis provided more precise estimates. This advantage stems from analyzing patients at specific time points, which lowers variability and better models changing risks in stroke survival. Nevertheless, our study had several limitations that warrant consideration. It was conducted at a single center, which may limit the generalizability of the findings to other populations or healthcare settings. Further, owing to the retrospective cohort design, the study relied on existing medical records, which are subject to potential inaccuracies, missing data, and inconsistent documentation. Even though we attempted to adjust for key confounders, residual confounding because of unmeasured variables remains possible. In addition, although stroke subtyping was based on clinical presentation and neuroimaging (CT/MRI) according to standard guidelines, all diagnoses were extracted from routine clinical records without central re-adjudication by the research team. Given the long study period (2014–2019) and variability in imaging reports across different radiologists, this may introduce some degree of misclassification bias, though the distinction between ischemic and hemorrhagic stroke is generally reliable in clinical practice.

Considering the outcome assessment, although we employed national legal medicine databases and hospital records to ascertain death events, potential inaccuracies in death certificate data, particularly in determining the exact cause of

death, cannot be ruled out. This study lacked standardized stroke severity measures such as National Institutes of Health Stroke Scale (NIHSS), and did not model recurrent strokes or competing risks. Lastly, while our sensitivity analysis – using symptom onset as the time origin – supports the robustness of our findings, we acknowledge that documentation of symptom onset is often incomplete or imprecise, which may introduce additional uncertainty. Given these limitations, we recommend developing prospective, multicenter stroke registries in Iran that incorporate standardized severity assessments, cause-specific outcomes, and long-term follow-up. Such registries could validate and extend our findings while supporting more precise risk stratification as well as policy planning.

Conclusion

The findings revealed that more than half of the patients with stroke died during the follow-up period, with highest mortality observed in the early years after stroke. Older age, hemorrhagic subtype, diabetes, low GCS scores at admission, and post-stroke complications such as respiratory failure and urinary incontinence were key predictors of death. These findings underscore the need for actionable interventions, including optimizing glycemic control and systematic management of diabetes in patients with stroke, implementing protocols for early GCS assessment as well as monitoring to identify high-risk individuals, and prioritizing in-hospital care to prevent or promptly manage complications, such as respiratory failure and urinary conditions. Integrating these measures into clinical practice and hospital care pathways could ameliorate long-term survival among patients with stroke, particularly in LMICs.

Conflict of Interests

The authors declare no conflict of interest in this study.

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