ORIGINAL ARTICLE

One-year survival and prognostic factors for survival among stroke patients: The PROVE-stroke study

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Background: Survival and prognostic factors following stroke occurrence differ between world regions. Studies investigating stroke features in the Middle-east region are scarce. We aimed to investigate 1-year survival and related prognostic factors of stroke patients in Central Iran. **Materials and Methods:** It is an observational analytical study conducted on patients registered in the Persian Registry of Cardiovascular Disease-Stroke (PROVE-Stroke) database. Records of 1703 patients admitted during 2015–2016 with the primary diagnosis of stroke in all hospitals of Isfahan, Iran were reviewed. Information regarding sociodemographic characteristics, clinical presentations, medications, and comorbidities were recorded. The living status of patients after 1 year from stroke was considered as 1-year survival. **Results:** Among 1345 patients with the final diagnosis of stroke, 970 (72.1%) were alive at the 1 year follow-up and the mean survival time based on Kaplan–Meier procedure was estimated 277.33 days. The hemorrhagic and ischemic types of stroke were reported in 201 (15.0%) and 1141 (84.8%) patients, respectively. Age (hazard ratio [HR] = 1.07, 95% confidence interval [CI] = 1.05–1.09), diabetes (HR = 1.49, 95% CI = 1.07–2.06), history of stroke or transient ischemic attack (HR = 1.81, 95% CI = 1.30–2.52), history of warfarin usage (HR = 1.73, 95% CI = 1.11–2.71), hospital complications of hemorrhage (HR = 3.89, 95% CI = 2.07–7.31), sepsis (HR = 1.78, 95% CI = 1.18–2.68), and hydrocephalus (HR = 3.43, 95% CI = 1.34–8.79), and modified Rankin Scale (mRS) ≥3 at the time of hospital dicharge (HR = 1.98, 95% CI = 1.27–3.07), were predictors of 1-year survival. **Conclusion:** Predictors of 1-year survival can be categorized into unchangeable ones, such as age, diabetes, previous stroke, and mRS. The changeable factors, such as hospital complications of infection and hemorrhage, guide physicians to pay greater attention to reduce the risk of mortality following stroke.

Key words: Hemorrhagic stroke, Iran, ischemic stroke, prognosis, survival analysis

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INTRODUCTION

Stroke is the second most common cause of disability adjusted life-years, and the second leading cause of mortality in the world. It is reported as the most prevalent neurological disease with a prevalence of 80.1 million cases globally in 2016.[1] Studies suggest an increase in the estimated global lifetime risk of stroke in the recent years.[2] Identifying factors that reduce stroke complications and improve the stroke outcome can increase patients' survival and enhance their quality of life.[3,4] Accordingly, many studies have investigated positive and negative predictive factors important in the survival of stroke patients. Intermittent claudication, urinary incontinence, and previous history

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of ischemic attack are some of the independent baseline factors suggested to predict adverse outcomes such as death in 5 years in stroke patients.[5] Another extensive epidemiological study reported stroke type, prestroke index and history of hypertension, ischemic heart disease and diabetes, as the most important predictors of stroke-induced death in a year from hospital admission.[6] There are evidences that these positive and negative predictive factors may differe between world regions considering differences in race, ethnicity, sociodemographic and economic factors, and type of the life style, highlighting the importance of conducting studies on stroke patients in different world regions.[6,7] Studies investigating factors associated with a faviorable or poor stroke outcome and the stroke features in the Middle east region are scarce. Meanwhile, the incidence rate of stroke has been reported to be 22.7–250 per 100,000 population per year in the middle east, with an increasing trend in the incidence and mortality during the last decades.[8] To the best of our knoweledge, no study has comprehensively investigated different predictive factors among stroke patients in Iran, hitherto. Iran is the second largest country in the Middle East and has an incidence rate of approximately 128–149 stroke cases per 100,000 individuals per year.[3,9]

The main objective of the present study was to determine 1-year survival rate and different positive and negative predictive factors affecting survival among stroke patients in Central Iran.

MATERIALS AND METHODS

The present study is an observational study conducted using the information of patients recorded in the Persian Registry of Cardiovascular Disease-Stroke (PROVE-Stroke) database. PROVE is an open-label registry, established in Isfahan province, Iran from 2014 and covers a total population of over 2,000,000 inhabitants. The design and methodology of the PROVE pilot study has been published in detail previously.[10] In brief, records of stroke patients admitted to two hospitals with specialized stroke units, and seven general hospitals in the city of Isfahan were reviewed. Definite diagnosis of acute ischemic or hemorrhagic stroke based on the clinical presentation and computed tomography (CT)/magnetic resonance imaging (MRI) findings was the inclusion criterion in the present study The exclusion criteria were a diagnosis of iatrogenic stroke or transient ischemic attack (TIA), an incomplete medical record regarding the final diagnosis and type of stroke, and lack of informed consent. Information on sociodemographic characteristics, medical history, underlying diseases, history of cigarette/hookah smoking, history of medication usage (before stroke, during hospitalization, and at the time of discharge), laboratory findings, electrocardiogram, echocardiogram, carotid Doppler sonogram, brain CT/MRI findings, and degree of disability using modified Rankin Scale (mRS) were collected. mRS is a well-known scale which is consisted of seven scores (from 0 to 6) that describe the level of patient's disability as recorded by the clinician. Score 0 indicates the absence of any symptoms and score 6 indicates death, while other scores describe various degrees of disability.[11]

Two board certified neurologists classified patients with ischemic type stroke based on their medical records, using the Trial of Org 10172 in Acute Stroke Treatment classification in to five subtypes of large-artery atherosclerosis (LAA), cardioembolism (CE), small-vessel occlusion (SVO), stroke of other determined etiology, and stroke of undetermined etiology.[12] Patients with stroke of undetermined etiology were further divided into two groups of those with negative standard evaluations and those with inadequate standard assessments. Patients with hemorrhagic type stroke were classified into two groups of intracerebral hemorrhage and subarachnoid hemorrhage. Living status of patients after 1 year from stroke occurrence was assessed by telephone interview with a first-degree family member of the patient and recorded as 1-year survival. The time of survival during the 1st year was considered as survival time.

The study was approved by the ethics committee of Isfahan University of Medical Sciences.

Statistical analysis

We reported continuous and categorical data as mean ± standard deviation (or median [inter quartile range]) and frequency (percentages), respectively. We compared categorical data using Chi-square or Fisher exact test, where appropriate. We compared continuous data using independent sample *t*-test or Mann–Whitney U test. Normality assumption was checked using the Kolmogrov–Smirnov test. We used simple proportional hazard cox regression analysis to determine crude hazard ratios (HRs) for 1-year survival of patients. We used multiple cox propportional hazard regression analysis to evaluate the adjusted HRs for 1-year survival of patients using stepwise method (forward selection). The proportional hazard assumptions was checked using Schoenfeld residuals test. We also draw the Kaplan Mayer graph by type of stroke. Statistical analysis was performed using the Statistical Package for the Social Sciences version 25 (SPSS Inc., Chicago, IL, USA) and STATA14 (StataCorp, MP-Parallel Edition, College Station, Texas, USA). $P < 0.05$ was considered as statistically significant.

RESULTS

Among 1703 patients admitted to the hospital during 2015–2016 with the initial diagnosis of stroke in the primary

evaluation, 358 (21.0%) patients were further diagnosed with another medical condition after more comprehensive evaluations and implementing other diagnostic tests. Thus, information regarding 1345 patients with a definite diagnosis of stroke was analyzed in the present study. Survival time for patients was between 0 and 365 days. The mean survival time based on Kaplan–Meier procedure was estimated as 277.33 days (95% confidence interval [CI]: 269.47, 285.20). Figure 1 presents Kaplan–Meier survival curves by type of the stroke.

Patients' sociodemographic characteristics, past medical history and drug history before stroke based on the living status on 1-year follow up and type of the stroke could be found in Table 1. In general, 710 (52.8%) patients were male and the mean age of patients, regardless of type of the stroke was 69.63 ± 13.81 years. Based on the type of the stroke, the mean age of patients in the hemorrhagic and ischemic groups was 64.85 ± 14.52 and 70.51 ± 13.50 years, respectively. No statistically significant difference was observed in the gender distribution of patients between two hemorrhagic and ischemic groups.

Among 1345 patients with the final diagnosis of stroke, 970 (72.1%) were alive at the 1-year follow-up. The mean age of patients who died from stroke was significantly higher than the mean age of patients who survived the condition (75.14 [12.61] and 67.50 [13.67] years, respectively [$P < 0.001$]). No statistically significant differences were observed between the proportion of males and females among dead and alive patients ($P = 0.18$).

As shown in Table 1, 17% of all patients reported the history of cigarette or hookah smoking and 8.8% reported history of drug abuse. Previous history of stroke was the only underlying condition that was statistically significantly different between alive and dead patients (18.6% compared to 26.1% for alive and dead patients, respectively [$P = 0.002$]). Hypertension (66.4%) and diabetes (33.1%) were the most reported underlying diseases among all patients.

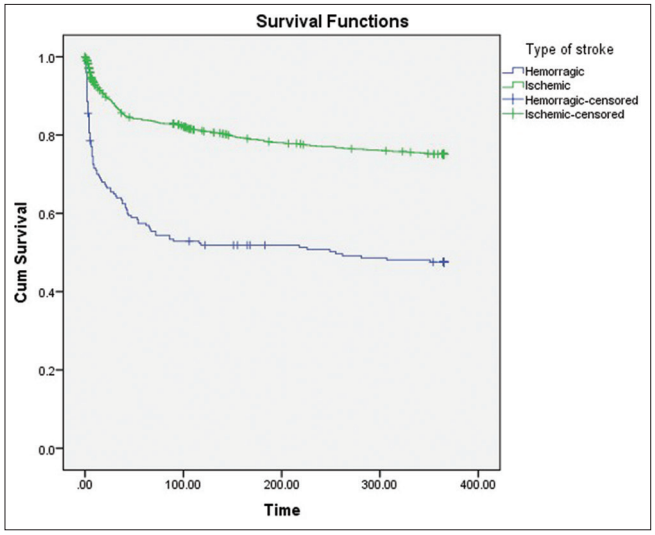

Figure 1: Kaplan-Meier survival curves by type of the stroke

Table 2 represents patients' clinical presentations, hospital complications, and drug history during hospitalization and after hospital discharge based on the living status on the 1-year follow-up and type of the stroke. The mean duration of hospitalization was significantly higher in those who expired following stroke compared to patients who survived the condition ($P < 0.001$). The duration of hospitalization was also higher in patients with hemorrhagic type stroke compared to those with ischemic stroke ($P < 0.001$) [Table 2].

Regarding the type of the stroke, 201 (15%) patients had hemorrhagic type, with intracerebral hemorrhage in 177 (88.1%) and subarachnoid hemorrhage in 24 (11.9%) patients. The most reported underlying condition among patients with intracerebral and subarachnoid hemorrhages were hypertension (75.6%) and aneurysm (27%), respectively. Ischemic type stroke was diagnosed in 1141 (84.8%) patients. SVO was present in 281 (24.6%) patients, CE in 230 (20.1%) patients, and LAA in 89 (7.8%) patients. Stroke of other determined etiology and stroke of undetermined etiology were responsible for 21 (1.8%) and 520 (45.76%) cases, respectively. Type of the stroke was not reported in 3 (0.2%) patients. Patients' risk factors, clinical presentations, and mRS at the time of hospital discharge among patients with ischemic stroke could be found in Supplementary File Table 1. Furthermore, the effects of subtypes on patients' survival among ischemic stroke patients are tabulated as Supplementary File Table 2.

As could be seen in Table 2, evaluating hospital complications revealed that infectious complications (pneumonia, sepsis, and urinary tract infection), hydrocephalus, and hemorrhagic transformation were statistically significantly higher in patients who further died from stroke compared to those who survived the condition ($P < 0.001$ for all). Cerebral edema was also more common among dead patients ($P = 0.023$). Furthermore, stroke presenting symptoms were significantly different among dead and alive patients and those with hemorrhagic or ischemic type strokes. Lack of consciousness was more common in patients who died following stroke compared to alive patients ($P < 0.001$). While alive patients compared to those who were dead a year following stroke happening, showed more symptoms of hemiparesis ($P = 0.042$), aphasia ($P = 0.012$), dysarthria ($P < 0.001$), diplopia ($P = 0.027$), dizziness ($P < 0.001$), imbalance ($P = 0.003$), and headache ($P = 0.004$).

Table 1: Patients' sociodemographic characteristics, past medical history and drug history before stroke based on the living status on 1-year follow up and type of the stroke

Variable	Total	Dead	Alive	*P**	Ischemic type	Hemorrhagic type	*P**
Sex (male)†	710 (52.8)	523 (53.9)	187 (49.9)	0.182	112 (55.7)	597 (52.3)	0.373
Age‡	69.63±13.81	75.14±12.61	67.50±13.67	<0.001	70.51±13.50	64.85±14.52	<0.001
Education							
Never been in school/elementary school	949 (78.7)	247 (84.0)	702 (77.0)	0.005	847 (80.6)	100 (65.8)	<0.001
Undergraduate	192 (15.9)	41 (13.9)	151 (16.6)		144 (13.7)	47 (30.9)	
Graduate degree	65 (5.4)	6 (2)	59 (6.5)		60 (5.7)	5 (3.3)	
Occupational status							
Unemployed	539 (44.8)	140 (47.6)	399 (43.9)	0.540	476 (45.2)	63 (41.7)	0.532
Retired	408 (34.0)	94 (32.0)	314 (34.6)		357 (34.1)	51 (33.8)	
Employed	255 (21.2)	60 (20.4)	195 (21.5)		217 (20.7)	37 (24.5)	
Family history							
Positive family history of stroke	114 (14.2)	30 (13.6)	84 (14.5)	0.732	100 (14.5)	14 (12.5)	0.575
Past medical history							
Cigarette/hookah smoking	195 (17.0)	47 (14.4)	148 (18.0)	0.137	158 (16.2)	37 (21.6)	0.082
Drug abuse	100 (8.8)	28 (8.6)	72 (8.9)	0.899	87 (9)	12 (7.4)	0.515
Type 2 diabetes	443 (33.1)	130 (34.8)	313 (32.3)	0.390	387 (34)	56 (27.9)	0.089
Hypertension	891 (66.4)	262 (70.2)	629 (64.9)	0.064	754 (66.3)	135 (67.2)	0.802
Dyslipidemia	202 (15.1)	45 (12.0)	157 (16.2)	0.054	190 (16.7)	12 (6.0)	<0.001
Ischemic heart disease	300 (22.3)	91 (24.3)	209 (21.6)	0.287	271 (23.8)	28 (13.9)	0.002
Atrial fibrillation	45 (3.3)	18 (4.8)	26 (2.7)	0.050	42 (3.7)	2 (1.0)	0.049
Valvular heart disease/rheumatic heart disease	85 (6.3)	25 (6.7)	60 (6.2)	0.745	78 (6.8)	7 (3.5)	0.072
Prosthetic heart valve	34 (2.5)	9 (2.4)	25 (2.6)	0.853	27 (2.4)	7 (3.5)	0.353
Previous stroke	278 (20.7)	98 (26.1)	180 (18.6)	0.002	242 (21.2)	36 (17.9)	0.287
Drug history before stroke occurrence							
Aspirin	348 (25.9)	91 (24.6)	257 (26.8)	0.413	301 (26.8)	46 (22.9)	0.250
Warfarin	119 (8.8)	51 (13.8)	68 (7.1)	<0.001	103 (9.2)	16 (8)	0.583
Insulin	103 (7.7)	26 (7)	77 (8)	0.529	90 (8)	13 (6.5)	0.455
Antihypertensive	798 (59.3)	232 (62.5)	566 (59)	0.241	678 (60.2)	119 (52.9)	0.788
Clopidogrel	67 (5.0)	16 (4.3)	51 (5.3)	0.456	59 (5.2)	8 (4)	0.449
Statins	268 (19.9)	61 (16.5)	207 (21.6)	0.038	242 (21.5)	25 (12.4)	0.003
Oral hypoglycemic agents	313 (23.3)	99 (26.7)	214 (22.3)	0.092	268 (23.8)	45 (22.4)	0.664
Dipyridamole	4 (0.3)	1 (0.3)	3 (0.3)	>0.999	3 (0.3)	1 (0.5)	0.483
Ticlopidine	6 (0.4)	1 (0.3)	5 (0.5)	>0.999	6 (0.5)	0	0.599
Oral contraceptive	5 (0.4)	0	5 (0.5)	0.330	4 (0.4)	1 (0.5)	0.561
Migraine medications	2 (0.1)	1 (0.3)	1 (0.1)	0.480	2 (0.2)	0	>0.999

*P<0.05 was considered as statistically significant, †Data are shown as frequency (%), ‡Data are shown as mean±SD. Chi-square or Fisher's exact test was used. Independent sample *t*-test was done. For 139 (10.3%) patients, education was not reported and the occupational status of 143 (10.6) of patients was unknown. Also, the family history of stroke was not clear for 542 (40.3%) patients. For 197 (14.0%) and 210 (15.6%) patients, smoking and drug abuse status were not reported, respectively. History of type 2 diabetes, hypertension and ischemic heart disease were unknown in 3 (0.2%) patients. Medications used before stroke were missing for 18 (1.3%) patients. SD=Standard deviation

Number of cases that were using warfarin and statins before stroke occurrence was significantly different among dead and alive patients ($P < 0.001$ and $P = 0.038$ for warfarin and statin use, respectively) [Table 2]. Overall, antihypertensives, aspirin, and oral hypoglycemic agents were the most prevalent drugs patients reported to use before stroke onset. The prescription of aspirin, clopidogrel, and statins during hospitalization was significantly higher for patients who were alive after 1 year from stroke happening compared to dead patients ($P \leq 0.001$).

During hospitalization, 199 (14.79%) patients died from stroke or related hospital complications. Furthermore, during 1st year after stroke, 176 patients died. Results from mRS revealed that almost 84% of the patients who died during 1st year after hospital admission, were discharged from hospital with mRS score ≥3. Considering type of the stroke, mRS scores were significantly higher among patients with hemorrhagic type stroke compared to patients with ischemic type stroke, and most of the ischemic stroke patients were discharged from hospital with mRS score ≤3 [Table 3].

Results from the simple Cox regression analysis is found in Supplementary File Table 3. The factors identified to be effective based on the simple Cox regression analysis were used to perfrom multiple cox regression analysis. As could be seen in Table 4, the predictive variables of death

Table 2: Patients' clinical presentations, hospital complications, and drug history during hospitalization and after hospital discharge based on the living status on 1-year follow up and type of the stroke

Variable	Total	Dead	Alive	*P**	Ischemic type	Hemorrhagic type	*P**
Stroke presenting symptoms†							
Hemiparesis	833 (38.1)	216 (57.6)	617 (63.6)	0.042	760 (66.6)	73 (36.3)	<0.001
Aphasia	98 (7.3)	38 (10.1)	60 (6.2)	0.012	95 (8.3)	3 (1.5)	0.001
Dysarthria	401 (29.8)	84 (22.4)	317 (32.7)	<0.001	368 (32.3)	33 (16.4)	<0.001
Diplopia	59 (4.4)	9 (2.4)	50 (5.2)	0.027	53 (4.6)	6 (3)	0.290
Lack of consciousness	244 (18.1)	152 (40.5)	92 (9.5)	<0.001	149 (13.1)	93 (46.3)	<0.001
Dizziness	187 (13.9)	24 (4/6)	163 (8/16)	<0.001	172 (1/15)	15 (5/7)	0.004
Imbalance	122 (9.1)	20 (3/5)	102 (5/10)	0.003	114 (10)	8 (4)	0.006
Nausea and vomiting	154 (11.4)	46 (1/11)	108 (3/12)	0.559	96 (4/8)	57 (4/28)	<0.001
Dysphagia	40 (3.0)	11 (9/2)	29 (3)	0.956	39 (4/3)	1 (5/0)	0.0.025
Headache	129 (9.6)	22 (9/5)	107 (11)	0.004	72 (3/6)	56 (9/27)	<0.001
Incontinence	56 (4.2)	22 (9/5)	34 (5/3)	0.052	44 (9/3)	12 (6)	0.167
Hemi sensory	19 (1.4)	5 (1.3)	14 (1.4)	0.878	13 (1/1)	6 (0.3)	0.052
Hospital complications†							
Recurrent stroke	10 (0.7)	3 (0.8)	7 (0.7)	>0.999	9 (0.8)	1 (0.5)	>0.999
Heart failure	5 (0.4)	2 (0.5)	3 (0.3)	0.622	4 (0.4)	1 (0.5)	0.556
Hemorrhagic transformation	55 (4.1)	35 (9.3)	20 (2.1)	<0.001	20 (1.8)	35 (17.4)	<0.001
Cerebral edema	5 (0.4)	4 (1.1)	1 (0.1)	0.023	3 (0.3)	2 (1)	0.164
Seizure	31 (2.3)	14 (3.7)	17 (1.8)	0.030	22 (1.9)	8 (4.0)	0.070
Hydrocephalus	35 (2.6)	21 (5.6)	14 (1.4)	<0.001	8 (0.7)	26 (12.9)	<0.001
MI	7 (0.5)	4 (1.1)	3 (0.3)	0.100	7 (0.6)	0	0.603
DVT	4 (0.3)	3 (3.8)	1 (0.1)	0.068	2 (0.2)	2 (1)	0.109
Pulmonary embolism	6 (0.4)	5 (1.3)	1 (0.1)	0.008	3 (0.3)	3 (1.5)	0.047
Sepsis and UTI and pneumonia)	155 (11.5)	91 (24.3)	64 (6.6)	<0.001	121 (10.6)	33 (16.4)	0.017
Duration of hospitalization‡	6.9 (8.5)	10.11 (13.4)	5.6 (5.1)	<0.001	6.03 (7.19)	11.19 (12.45)	<0.001
Median (Q1-Q3)	5 (3.7)	6 (3.11)	4 (3.7)		4 (3.7)	7 (4.14)	
Minimum-maximum	0-111	0-111	0–62		0-111	0–65	
Drug history during hospitalization†							
Aspirin	850 (63.2)	188 (50.1)	662 (68.2)	<0.001	839 (73.5)	11 (5.5)	<0.001
Warfarin	252 (18.7)	58 (15.5)	194 (20)	0056	239 (20.9)	13 (6.5)	<0.001
Insulin	240 (17.8)	75 (20)	165 (17)	0.199	199 (17.4)	41 (20.4)	0.313
Antihypertensive	764 (56.8)	208 (55.5)	556 (57.3)	0.538	653 (57.2)	109 (54.2)	0.428
Clopidogrel	581 (43.2)	134 (35.7)	447 (46.1)	0.001	575 (50.4)	6 (0.3)	<0.001
Statins	820 (61.0)	187 (49.9)	633 (65.3)	<0.001	771 (67.6)	48 (23.9)	<0.001
Drug history after discharge from hospital†							
Aspirin	624 (46.4)	92 (24.9)	532 (56.4)	<0.001	619 (55.7)	5 (2.5)	<0.001
Warfarin	203 (15.1)	29 (7.9)	174 (18.4)	<0.001	195 (17.5)	8 (4)	<0.001
Antihypertensive	579 (43.0)	101 (27.3)	478 (50.6)	<0.001	520 (46.7)	59 (29.8)	<0.001
Clopidogrel	451 (33.5)	63 (17.1)	388 (41.1)	<0.001	450 (40.5)	1 (0.5)	<0.001
Statins	696 (51.7)	103 (27.9)	593 (62.8)	<0.001	667 (60)	29 (14.6)	<0.001

*P<0.05 was considered as statistically significant, †Data are shown as frequency (%), ‡Data are shown as mean±SD, median (IQR). Chi-square or Fisher's exact test was used. Mann-Whitney *U*-test was done. Medications used after discharge from hospital were missing for 32 (2.4%) patients. MI=Myocardial infarction; DVT=Deep vein thrombosis; UTI=Urinary tract infection; SD=Standard deviation; IQR=Interquartile range

in a year from stroke occurance were age (HR = 1.07, 95% CI = 1.05–1.09), diabetes (HR = 1.49, 95% CI = 1.07–2.06), history of stroke or TIA (HR = 1.81, 95% CI = 1.30–2.52), history of warfarin usage (HR = 1.73, 95% CI = 1.11–2.71), hospital complications of hemorrhage (HR = 3.89, 95%CI = 2.07–7.31), sepsis (HR = 1.78, 95% CI = 1.18–2.68), and hydrocephalus (HR = 3.43, 95% CI = 1.34–8.79), and mRS ≥ 3 compared to ≤ 2 at the time of hospital dicharge (HR = 1.98, 95% CI = 1.27–3.07).

DISCUSSION

In the present study, examination of the profiles of 1345 stroke patients from the PROVE-Stroke database showed that by a year from stroke occurence, 375 (27.9%) patients were died. Age but not gender was a mortality predictor and the mean age of dead patients was higher than those who survived the cindition. The presence of diabetes, history of stroke or TIA, using warfarin before hospitalization,

Table 3: Degree of disability using modified Rankin Scale at the time of hospital discharge based on the living status in a year from stroke and type of the stroke

mRS score	1-year survival statues		*P*	Type of stroke		*P*	Total
	Dead	Alive		Ischemic	Hemorrhagic		
0	1 (0.3)	23 (2.37)	<0.001*	21 (1.8)	3 (1.5)	<0.001*	24 (1.78)
1	5 (1.4)	65 (6.72)		60 (5.)	10 (4.97)		70 (5.21)
2	18 (4.8)	165 (17.06)		154 (13.5)	29 (14.42)		183 (13.63)
3	70 (18.6)	553 (57.18)		579 (50.7)	44 (21.89)		623 (46.42)
4	35 (9.3)	82 (8.47)		105 (9.2)	12 (5.97)		117 (8.71)
5	42 (11.2)	55 (5.68)		73 (6.4)	24 (11.94)		97 (7. 2)
6	199 (53.0)	0 (0.0)		123 (10.78)	76 (37.81)		199 (14.82)
Not reported	5 (1.3)	24 (2.48)	-	26 (2.27)	3 (1.5)	-	29 (1.71)

**P*<0.05 was considered as statistically significant. Data are shown as frequency (%). Chi-square test was used. mRS=Modified Rankin Scale

Table 4: Adjusted hazard ratio (95% confidence interval) to predict patients's 1 year survival

	HR†	95% CI for HR	*P**
General characteristics			
Age	1.07	1.05-1.09	<0.001
Past medical history			
Diabetes mellitus	1.49	1.07-2.06	0.017
Previous stroke/TIA	1.81	1.30-2.52	<0.001
Drug history before stroke occurrence			
Warfarin	1.73	1.11-2.71	0.017
Hospital complications			
Hemorrhage	3.89	2.07-7.31	<0.001
Sepsis	1.78	1.18-2.68	0.005
Hydrocephalus	3.43	1.34-8.79	0.010
mRS at the time of hospital discharge (≥3 compared to≤2)	1.98	1.27-3.07	0.002

**P*<0.05 was considered as statistically significant, †Data are shown as HR and 95% CI for HR. Multiple cox-regression analysis was done using stepwise method. HR=Hazard ratio; CI=Confidence interval; TIA=Transient ischemic attack; mRS=Modified Rankin Scale

hospital complications of hemorrhage, sepsis, and hydrocephalus, and mRS ≥3 compared to ≤2 at the time of hospital dicharge were identified as mortality predictors. History of hypetension and hyperlipidemia were similar among dead and alive patients.

The factors affecting recovery and survival of stroke patients are of great importance and not completely understood yet.[13,14] Here, we found a survival rate of 72.1% on 1-year follow-up among patients with the final diagnosis of stroke. In the Nanjing stroke registry, 1-year survival rate of Chinese patients with a first time stroke was reported to be 86.4%.[15] In another study in Brazil evaluating 75,000 patients with stroke, 69% were reported to be alive in a year from stroke occurance.[16] Differences between stroke survival rates reported in our study and others are suggested to be mainly due to the different sociodemographic characteristics of the patients, as well as patients' past medical histories. Age has been reported to be an imprtant factor in determining the chance of mortality in stroke patients.[15] It is suggested that the mortality rate increases among older patients due to the poor physical ability to compensate the lesion and less social support in them.[17] One study reported more than three times higher risk of death among patients over 65 years compared to younger patients.[18] Another study showed that those over 75 years would face death five times more than other stroke patients.[15]

In the present study, there was no statistically significant differences in the survival rate between men and women. Results from the Dijon stroke registry on stroke survival also showed no difference between genders,[19] although there are studies suggesting the survival following stroke may be affected by the patient's sex.[20] Extensive registry-based studies have reported that some factors including adherence to the treatment after hospital discharge and factors affecting rehabilitation were more responsible for different survival rates observed between genders in these studies.[21,22]

Regarding the type of the stroke, in the present study, 201 (14.94%) patients were diagnosed with hemorrhagic type and 1141 (84.83%) patients with ischemic type strokes. Patients with hemorhagic type stroke showed higher hazard of mortality compared to the ischemic stroke patients. In a study conducted in Denmark on 40,000 stroke patients, 10% were diagnosed with hemorrhagic type and 90% with the ischemic type strokes. The authors reported that the likelihood of death among patients with hemorrhagic type stroke was 1.56 times higher than the other type.[23] In another study, 1-month mortality rate of patients with hemorrhagic type stroke was reported to be about 70.8%, which is considerably high.[15] Hence, it can be concluded that although the percentage of patients with hemorrhagic type stroke is lower than those with ischemic type stroke, their mortality rate is higher. This can be due to the higher prevalence of some risk factrors such as hypertension, aneurysm, and alcohol consumption in the hemorrhagic type stroke patients, which can lead to severe brain damages.[24] Furthermore, we found longer mean duration of hospitalization in these patients compared to the individuals with ischemic type stroke. The longer

duration of hospitalization in patients with hemorrhagic type stroke substantially indicates worse condition of them at the time of hospital admission, as well as higher hospital complications among them which both increase the chance of mortality.

The presence of specific underlying diseases including diabetes, and previous history of stroke or TIA as the predictors of mortality was the other finding of the current study. In a study on chines patients, diabetes, smoking, and previous history of stroke were found to be associated with the increased risk of death after a first-ever stroke.[15] Furthermore, a previous study in Iran showed that diabetes, smoking, history of previous stroke, and myocardial infarction were all the predictors of mortality in stroke patients.[25] The increased risk of stroke mortality observed in diabetic patients may be due to the microvascular complications of diabetes, which can cause fibrinoid necrosis and subcortical myocardial infarction.[24] On the other hand, although the history of high blood pressure/hypertension and dyslipidemia are suggested to be associated with reduced survival of stroke patients, we found no relationships in our study.[15,25] This could be due to the differences in the definition of high blood pressure and abnormal lipid profile among studies, as well as patients' recall bias.

Among the controlable factors found to increase hazard of mortality, we found that the hospital complications of hemorrhage, sepsis, and hydrocephalus had the highest HR. It emphasizes the importance of proper management of stroke patients during hospitalization. Another population-based study in Denmark also reported the relationship between hospital complications, especially pneumonia and increased risk of mortality and length of hospitalization among stroke patients.[26]

Another important finding of the present study is the effect of patiens' drug histories on their survival. We found higher prevalence of warfarin usage and lower prevalence of statin usage among dead patients compared to the patients who were alive 1 year poststroke. No significant differences were observed regarding other types of used medications between dead and alive patients. These findings are in the same vein with findings from other studies that reported higher risk of mortality among stroke patients using warfarin.[27] The reduced rate of mortality observed with statin usage among our patients could be due to the specific functions these medications impose. Statins have been widely used to reduce cardiovascular accidents and stroke complications. These medications, not only directly affect the level of cholestrol, also reduce the risk of atherosclerosis due to their anti-inflammatory effects and have plaque stabilizing effects.[28,29]

There are some limitations to the present study; first, as these patients were recruited from 9 hospitals in the city of Isfahan, differences in medical examinations and imaging studies present which may affect the results. Second, we reviewed patients' medical records retrospectively and some biases may happen in the retrospective evaluation of patients records. Third, we should note the possibility of patients' recall biases regarding their past medical histories, which was inevitable.

CONCLUSION

Here we reported the 1-year survival and mean survival time of patients with stroke, based on PROVE-Stroke, which can help researchers and clinicians predict the outcome of Iranian patients following stroke. Comparing the statistics with the global reports shows that the stroke features and survival following stroke in the present study were not much different from the other world regions. Studying the predictors of 1-year survival showed two distinct factors; changeable and unchangeable. The unchangeable ones, such as age, diabetes, previous stroke, and mRS, show which factors the physician should consider more precisely in the medical history of patients for more intense treatment and closer follow-up. The changeable factors, such as hospital complications of infection and hemorrhage, can guide physicians to the factors that require greater attention for more appropriate treatment to reduce these complications and the risk of mortality following stroke. According to the results of the present study, we recommend to implement screening programs for identifying the factors that can increase the risk of mortality in patients following stroke.

Availability of data and material

The data that support the findings of this study are available on request from the corresponding authors upon reasonable request. The data are not publicly available due to privacy and ethical restrictions.

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Conflicts of interest

There are no conflicts of interest.

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Supplementary File Table 1: Past medical history, stroke clinical presentations, and Modified Rankin Scale at the time of hospital discharge among ischemic stroke subtypes

	Ischemic type (total)	LAA	SVO	CE	Stroke of other determined etiology	Stroke of undetermined etiology	*P**
Family history							
Positive family history of stroke	100 (14.5)	3 (6.1)	28 (15.6)	19 (14.7)	0 (0.0)	50 (15.7)	0.223
Past medical history							
Cigarette/hookah smoking	158 (16.2)	17 (24.6)	31 (13.0)	27 (13.9)	4 (21.1)	79 (17.4)	0.134
Drug abuse	87 (9.0)	11 (16.2)	19 (7.9)	19 (9.6)	0 (0.0)	38 (8.5)	0.163
Type 2 diabetes	387 (34.0)	37 (41.6)	117 (41.8)	60 (26.1)	4 (19.0)	169 (32.6)	0.001
Hypertension	754 (66.3)	56 (62.9)	213 (75.8)	144 (62.6)	4 (19.0)	337 (65.2)	<0.001
Dyslipidemia	190 (16.7)	18 (20.2)	55 (19.6)	39 (17.0)	0 (0.0)	78 (15.0)	0.100
Ischemic heart disease	271 (23.8)	17 (19.1)	48 (17.1)	100 (43.5)	0 (0.0)	106 (20.4)	<0.001
Atrial fibrillation	42 (3.7)	0 (0.0)	0 (0.0)	38 (16.5)	0 (0.0)	4 (0.8)	<0.001
Valvular heart disease/rheumatic heart disease	78 (6.8)	2 (2.2)	11 (3.9)	38 (16.5)	0 (0.0)	27 (5.2)	<0.001
Prosthetic heart valve	27 (2.4)	1 (1.1)	1 (0.4)	14 (6.1)	0 (0.0)	11 (2.1)	0.001
Previous stroke	242 (21.2)	18 (20.2)	61 (21.7)	50 (21.7)	1 (4.8)	112 (21.5)	0.468
Stroke presenting symptoms							
Hemiparesis	760 (66.6)	54 (60.7)	188 (66.9)	164 (71.3)	5 (23.8)	349 (67.1)	<0.001
Aphasia	95 (8.3)	7 (7.9)	4 (1.4)	35 (15.2)	0 (0.0)	49 (9.4)	<0.001
Dysarthria	368 (32.3)	39 (43.8)	103 (36.7)	72 (31.3)	2 (9.5)	152 (29.2)	0.004
Diplopia	53 (4.6)	5 (5.6)	15 (5.3)	5 (2.2)	4 (19.0)	24 (4.6)	0.009
Lack of consciousness	149 (13.1)	10 (11.2)	13 (4.6)	47 (20.4)	3 (14.3)	76 (14.6)	<0.001
Dizziness	172 (15.1)	19 (21.3)	54 (19.2)	33 (14.3)	1 (4.8)	65 (12.5)	0.026
Imbalance	114 (10)	12 (13.5)	33 (11.7)	20 (8.7)	3 (14.3)	46 (8.8)	0.436
Nausea and vomiting	96 (8.4)	7 (7.9)	20 (7.1)	17 (7.4)	8 (38.1)	44 (8.5)	<0.001
Dysphagia	39 (3.4)	8 (9.0)	11 (3.9)	8 (3.5)	1 (4.8)	11 (2.1)	0.023
Headache	72 (3.6)	7 (7.9)	12 (4.3)	9 (3.9)	13 (61.9)	31 (6.0)	<0.001
Incontinence	44 (3.9)	5 (5.6)	7 (2.5)	10 (4.3)	0 (0.0)	22 (4.2)	0.502
Hemi sensory	13 (1.1)	2 (2.2)	3 (1.1)	2 (0.9)	1 (4.8)	5 (1.0)	0.445
mRS score at the time of hospital discharge							
0	21 (1.9)	0 (0.0)	12 (4.4)	4 (1.8)	1 (5.6)	4 (0.8)	<0.001
1	60 (5.4)	3 (5.0)	23 (8.4)	12 (5.3)	3 (16.7)	19 (3.7)	
2	154 (13.8)	19 (22.6)	37 (13.5)	21 (9.3)	7 (38.9)	70 (13.6)	
3	579 (51.9)	42 (50.0)	159 (58.0)	100 (44.4)	6 (33.3)	272 (52.9)	
4	105 (9.4)	9 (10.7)	29 (10.6)	23 (10.2)	0 (0.0)	44 (8.6)	
5	73 (6.5)	7 (8.3)	8 (2.9)	22 (9.8)	1 (5.6)	35 (6.8)	
6	123 (11.0)	4 (4.8)	6 (2.2)	43 (19.1)	0 (0.0)	70 (13.6)	

**P*<0.05 was considered statistically significant. LAA=Large-artery atherosclerosis; mRS=Modified Rankin Scale; SVO=Small-vessel occlusion; CE=Cardioembolism

Supplementary File Table 2: The effects of ischemic stroke subtypes on patients' survival at the time of 1-year follow-up

	HR (95% CI)	*P**
Subarachnoid hemorrhage	1.18 (0.63-2.21)	0.601
Hemorrhagic type stroke	2.82 (2.25-3.53)	<0.001
Ischemic stroke subtypes		
LAA (reference)	1	
CE	2.76 (1.54-4.95)	0.001
SVO	0.66 (0.34-1.27)	0.216
Stroke of other determined etiology	0.63 (0.14-2.79)	0.542
Stroke of undetermined etiology	2.03 (1.15-3.58)	0.015

**P*<0.05 was considered as statistically significant. LAA=Large-artery atherosclerosis; SVO=Small-vessel occlusion; CE=Cardioembolism; HR=Hazard ratio; CI=Confidence interval

Supplementary File Table 3: Crude hazard ratio (95% confidence interval) to predict patient's 1 year survival

Variable	Crude		
	HR	95% CI	*P**
General characteristics			
Age	1.04	1.03-1.05	<0.001
Male	0.88	0.72-1.07	0.20
Hemorrhagic type stroke	2.81	2.24-3.53	<0.001
Cigarette/hookah smoking	0.82	0.60-1.11	0.20
Past medical history			
Hypertension	1.24	0.99-1.55	0.05
Diabetes mellitus	1.09	0.88-1.35	0.39
Ischemic heart disease	1.10	0.87-1.40	0.40
Atrial fibrillation	1.59	0.99-2.56	0.05
Prosthetic heart valve	0.94	0.48-1.82	0.85
Previous stroke/TIA	1.40	1.11-1.76	0.004
Drug history before stroke			
Aspirin	0.86	0.68-1.09	0.23
Warfarin	1.73	1.28-2.32	<0.001
Insulin	0.88	0.59-1.31	0.54
Antihypertensive	1.14	0.92-1.40	0.22
Clopidogrel	0.84	0.50-1.38	0.49
Statins	0.75	0.57-0.99	0.04
Oral hypoglycemic agents	1.19	0.94-1.5	0.13
Hospital complications			
Recurrent stroke	1.05	0.34-3.30	0.92
Heart failure	1.40	0.34-5.62	0.63
Hemorrhagic transformation	3.21	2.26-4.54	<0.001
Thromboembolism (PTE, DVT)	3.99	1.98-8.07	<0.001
Sepsis	3.13	2.46-3.96	<0.001
Hydrocephalus	3.04	1.96-4.7	<0.001
Stroke presenting symptoms			
Hemiparesis	1.28	1.04-1.57	0.01
Aphasia	1.50	1.07-2.10	0.01
Unconsciousness	4.63	3.76–5.69	<0.001
Nausea and vomiting	1.13	0.83-1.54	0.42
mRS at the time of hospital discharge (≥3 compared to≤2)	2.17	1.41-3.34	<0.001

**P*<0.05 was considered statistically significant. HR=Hazard ratio; CI=Confidence interval; DVT=Deep-vein thrombosis; PTE=Pulmonary thromboembolism; TIA=Transient ischemic attack; mRS=Modified Rankin Scale