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Investigating the in-hospital mortality rate of stroke and its related factors at Ali-Ibn-Abi Talib Hospital of Rafsanjan

Alireza Vakilian[1], Zahra Kamiab[2], Sakineh Afzal[3], Amir Moghadam-Ahmadi[1], Nazanin Jalali[1]

[1]Department of Neurology, Faculty of Medicine, Non-communicable Diseases Research Center, Rafsanjan University of Medical sciences, Rafsanjan, Iran

[2]Department of Family Medicine, Faculty of Medicine; Clinical Research Development Unit, Ali-Ibn Abi-Talib Hospital, Rafsanjan University of Medical Sciences, Rafsanjan, Iran

[3]General physician, Clinical Research Development Unit, Ali-Ibn Abi-Talib Hospital, Rafsanjan University of Medical Sciences, Rafsanjan, Iran

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Corresponding Author:
Zahra Kamiab, Asst. M.D., Prof., Department of Family Medicine, Faculty of Medicine; Clinical Research Development Unit, Ali-Ibn Abi-Talib Hospital, Rafsanjan University of Medical Sciences, Rafsanjan, Iran
ORCID:
orcid.org/0000-0001-6670-1828

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ABSTRACT

Aims: Stroke is the third leading cause of disability and the second leading cause of death worldwide. Due to the effects of different factors on stroke mortality, the present study aims to determine the in-hospital mortality rate of stroke and its related factors at Ali-Ibn-Abi Talib Hospital of Rafsanjan.

Methods: In this cross-sectional descriptive study, the records of all dead patients with the diagnosis of stroke at Ali-Ibn-Abi Talib Hospital of Rafsanjan were studied for the period of 2012-2017. The inclusion criteria were the definite diagnosis of stroke not longer than 72 hours from the onset of symptoms and being older than 18 years at the time of stroke. The exclusion criteria included other fatal cerebral lesions, having incomplete information for the records, death at the time of admission, and having an indefinite cause of death.

Results: From among 2,199 stroke patients (the mean age was 68.46±15.67, 46% male, 54% female) who were hospitalized, 9.04% (199 patients) died during the hospitalization period. The in-hospital mortality rate was 7.54% (n=142) and 17.98% (n=57) in ischemic stroke and cerebral hemorrhage, respectively. The major risk factor percentages in died patients were 68.3% hypertension, 35.7% diabetes mellitus, 18.6% cholesterolemia. The most common fatal complications in died patients included neurological complications (48.7%, n=97), infections (23.1%, n=46), cardiac complications (18.1%, n=36), and thromboembolism (5.5%).

Conclusions: Our findings are consistent with other studies about risk factors and complications of a stroke. We should focus on the prevention of complications in stroke patients by controlling important risk factors.

Introduction

Stroke is a syndrome characterized by the acute onset of neurological symptoms for at least 24 hours, which is caused by a central nervous system condition resulting from a disorder in the cerebral blood flow. Thus, the syndrome is characterized by the four main manifestations of acute onset, the duration of disorder, vascular origin, and the local complication (1). Stroke is the third leading cause of disability and the second leading cause of death after heart diseases worldwide (2,3). About 70% of stroke cases and 87% of its related deaths and disabilities occur in low- and middle-income countries (3). The prevalence of risk factors for stroke and the related deaths is higher in Asian countries than in Western countries; it is also higher in Iran as one of the middle-income countries in the Middle East (4,5). In Iran, stroke is one of the major causes of mortality and disability (6). Identifying the risk factors of stroke and its incidence increase life expectancy (7). Risk factors for stroke include male gender, smoking, and high levels of alcohol consumption (1,8). The mortality rate of stroke in every country depends on various factors, such as the social class and geographical area of the affected people. The incidence of stroke in developed countries is 5 cases per 1,000 persons. However, the incidence rate in developing countries is about 5-10 cases per 1,000 individuals (9). In the study conducted by Mazdeh and Seif Rabiei (10), the

overall mortality rate of stroke patients was determined to be 59.19%. Stroke patients are susceptible to many neurological and non-neurological complications. Neurological complications are less common than non-neurological ones but occur sooner (11). Post-stroke complications are the leading causes of death in the acute and subacute stroke phases (12). These complications, though not life-threatening, lead to prolonged hospitalization, adverse functional outcomes, and delayed rehabilitation. Most of these complications occur within the first weeks of stroke (13). According to studies conducted in the first trimester of stroke, mortality rates within the first week of stroke are very high but gradually decrease (14). The major risk factors of post-stroke complications include being of an older age, experiencing highly severe stroke, having a previous disability, as well as related diseases, such as diabetes mellitus (DM), hypertension (HTN), and ischemic heart diseases (IHD) (15). The prognosis and mortality of stroke patients depend on stroke complications and the interaction among age, sex, stroke severity, and its type (16). Since mortality is an important health indicator, and stroke is preventable, it is vital to know more about its risk factors so as to analyze the stroke rate and its related burden (9,17).Therefore, this study was conducted to determine the in-hospital mortality rate of stroke and its related factors at Ali-Ibn-Abi Talib Hospital of Rafsanjan.

Methods

In this retrospective cross-sectional study, the records of patients who died at Ali-Ibn-Abi Talib Hospital of Rafsanjan from March 2012 to March 2017 due to stroke were investigated. In all patients, stroke (as defined by the World Health Organization) indicates the onset of localized neurologic symptoms that last longer than 24 hours, result in death, or are confirmed by a neurologist based on the evidence of stroke in computed tomography (CT) scans or magnetic resonance imaging (MRI) scans (18). The study was approved by the Ethics Committee under the code: (IR.RUMS.REC.1395.145), in accordance with the Helsinki Criteria. The inclusion criteria were the definitive diagnosis of stroke by a neurologist, experiencing an acute stroke occurrence (not longer than 72 hours from the onset of symptoms to the patient referral), and being older than 18 years at the time of stroke. In contrast, the exclusion criteria included having cerebral lesions, such as tumors, infections, and traumatic brain injuries that were potentially fatal, having incomplete information for the records, experiencing death at the time of admission to the cardiopulmonary resuscitation room, and having an indefinite cause of death. This study was conducted based on the data present in the files of stroke patients using a checklist. The checklist included general patient information, such as age, sex, smoking habits, as well as the presence or absence of underlying diseases, including DM, HTN, high blood cholesterol, atrial fibrillation (AF), IHD, the past or present history of stroke, and surgical interventions. The time interval between referring to the hospital and death was determined by the researcher based on the exact time of referral and the death recorded in patient records. The information required was provided by the researcher using the checklist developed to determine the frequency of in-hospital stroke deaths by the type of stroke [ischemic, intracranial hemorrhage (ICH), or subarachnoid hemorrhage (SAH)], the location of the lesion in the brain, the size of the lesion by brain imaging (CT scans or MRI scans), as well as the help of a neurologist. The location of the lesion in the brain in ischemic stroke was classified into anterior and posterior circulations. In ICH, it was classified into thalamus, basal ganglia, the cerebellum, the pons, and lobar hemorrhage. The size of the lesion in ischemia was classified into lacunar, minor, as well as major, and in hemorrhage, it was classified into extensive and non-extensive (19). Access to the patients' CT scans or MRI scans was possible using the Hospital Information System based on the patients' file numbers. The causes of death or deadly complications following a stroke were determined by an investigator and a physician based on the evidence in the patients' files, a CT scan, or a brain MRI. Death in stroke patients could have been caused by one or more cases of stroke complications, including neurological complications, cardiac complications, infections, renal failure, venous thromboembolism, or other complications. In this study, neurological complications being the causes of death were divided into the three groups of cerebral edema, intracranial HTN, as well as herniation and hemorrhagic transformation, which were grouped together. In addition, SAH and brainstem stroke, both of which are fatal, were grouped separately. In addition, the fatal complications of cardiovascular diseases were classified into the four categories of myocardial infarction, congestive heart failure, fatal cardiac arrhythmias, and sudden cardiac death. Post-stroke fatal infections included pneumonia, sepsis, meningitis following surgical intervention, thromboembolisms, including pulmonary embolism, as well as other complications, such as multiple organ dysfunction and disseminated intravascular coagulation. In cases where patient death was not justified by either evidence in the file or brain imaging and where none of the subsequent stroke complications could be considered as the cause of patient death, the cause of patient's death would be considered to be sudden cardiac arrest. Incomplete files were excluded from the study. In addition, some samples including non-diagnostic stroke (2 samples), non-acute stroke (2 samples) because of the passing of more than 72 hours from the onset of the symptoms, being younger than 18 years (1 sample), and incomplete file information (1 sample) were excluded from the study.

Statistical Analysis

After recording the information on risk factors by checking the patients' files in the checklist, the data were entered into

SPSS 20 Software and analyzed. Frequency tables, graphs, as well as mean and standard deviation indices were used to describe the data. A p value less than 0.5 was considered significant.

Results

Out of the total 2,199 stroke patients admitted to Ali-Ibn-Abi Talib Hospital of Rafsanjan from March 2012 to March 2017, 85.58% (1,882 cases) had ischemia and 14.42% (317 cases) had bleeding. In-hospital mortality rates in ischemic stroke and in cerebral hemorrhage were 7.54% (142 cases) and 17.98% (57 cases), respectively. In addition, a total of 9.04% (199 cases) died during hospitalization. The mean age of dead patients was 75.28±14.83 years. In addition, 78.4% of the patients (156 patients) were older than 65 years. Out of 199 cases of death following stroke, 57.8% (115 deaths) and 42.2% (84 deaths) were female and male, respectively. In addition, smoking history accounted for 15.1% (30 cases), and the major underlying disease in stroke patients who died was HTN at 68.3% (n=136) followed by stroke history and DM at 36.2% (n=72) and 35.7% (n=71), respectively. The highest frequency of mortality based on the stroke size was 56.34% (n=78) in major ischemia, 70.2% (n=33) in extensive intracerebral hemorrhage, and 100% in severe SAH (n=10). The minimum and maximum time intervals between referral and death in the study population was 1 day and 97 days, respectively, with the mean and standard deviation of 53.13±24.12. In addition, 50.3% and 90.5% of the deaths occurred during the first week and the first month after stroke, respectively. In other words, the frequency of the deaths was higher in the first week but gradually decreased. In addition, 12.1% of the patients who died due to stroke (n=24) had undergone brain surgery interventions. There was no significant difference in the type of stroke between the males and females and between the positive and negative cases in the variables of smoking, DM, HTN, and hypercholesterolemia. The most common complications leading to death in patients were neurological complications (48.7%, n=97) followed by infections (23.1%, n=46), cardiac complications (18.1%, n=36), and thromboembolism (5.5%). There was a statistically significant difference between the ischemic and hemorrhagic AF groups (p=0.001), with AF having been present in 31.7% of ischemic cases, while only 7% of hemorrhage cases had a history of AF. There was a history of IHD in 35.9% and 21.1% of ischemic cases and hemorrhage cases, respectively. In addition, there was a statistically significant difference between ischemic stroke and hemorrhage in terms of IHD (p=0.04). A history of stroke was also present in 40.8% and 24.6% of ischemic cases and hemorrhagic cases, respectively. In the ischemic group, the number of patients over the age of 65 years was significantly higher than the hemorrhagic group (86.6% vs 57.9%, p=0.0001). The results are presented in Table 1. All patients with neurological complications (100%) died within less

Table 1. Comparison frequency of age group, sex, smoking and underlying diseases according to the type of stroke in the study population

Variable		Ischemic- stroke		Hemorrhagic stroke		Total		p value
		n	%	n	%	n	%	
Age group	<65 yrs	19	13.4	24	42.1	43	21.6	<0.001
	>65 yrs	123	86.6	33	57.9	156	78.4	
Sex	Male	60	42.3	24	42.1	84	42.2	0.98
	Female	82	57.7	33	57.9	115	57.9	
Smoking history	Positive	20	14.1	10	17.5	30	15.1	0.53
	Negative	122	85.9	47	82.5	169	84.9	
Diabetes	Positive	52	36.6	19	33.3	71	35.7	0.66
	Negative	90	63.4	38	66.7	128	64.3	
HTN	Positive	98	69	38	66.7	136	68.3	0.74
	Negative	44	31	19	33.3	63	31.7	
High cholesterol	Positive	30	21.1	7	12.3	37	18.6	0.14
	Negative	112	78.9	50	87.7	162	81.4	
AF	Positive	45	31.7	4	7	49	24.6	<0.001
	Negative	97	68.3	53	93	150	75.4	
IHD	Positive	51	35.9	12	21.1	63	31.7	0.04
	Negative	91	64.1	45	78.9	136	68.3	
History of CVA	Positive	58	40.8	14	24.6	72	36.2	0.03
	Negative	84	59.2	43	75.4	127	63.8	

Yrs: Years, HTN: Hypertension, AF: Atrial fibrillation, IHD: Ischemic heart diseases

than 30 days, while 81.4% of the patients with non- neurological complications died within less than 30 days. Thus, there was a statistically significant difference (p=0.001) between the two groups of neurological and non-neurological complications in this respect. The frequency of death in less than 30 days in ischemic stroke cases and in hemorrhage cases was 89.4% and 93%, respectively, which indicated no significant difference between the two groups. In addition, there were no significant differences between the major and extensive groups with the minor and lacunar groups, as well as between the two age groups (Table 2). In addition, 69.8% of the patients over the age of 65 years and 42.9% of patients below the age of 65 years had neurological complications, and there was a significant difference between the two age groups (p=0.01). Neurological complications occurred in 77.2% of hemorrhagic stroke patients, yet these complications occurred in only 37.3% of the patients with ischemic stroke; thus, there was a significant difference between the ischemic and hemorrhagic groups (p=0/000). There was also a significant difference between the two stroke size groups (p=0.001), with 62.8% of the major and extensive strokes having had neurological complications and 27.6% of the patients with minor, lacunar, and non-major strokes having had neurological complications.

Discussion

In the present study, among 2,199 stroke patients admitted to Ali-Ibn-Abi Talib Hospital of Rafsanjan from March 2012 to March 2017, 199 patients died during hospitalization, and the frequency of in-hospital mortality among stroke patients during the mentioned period was 9.04%, which was consistent with past studies (20-26). The percentage is higher in developing countries than in developed ones, indicating that middle- and low-income countries, including Iran, need to improve the treatment and care of stroke patients. In addition, this percentage is lower than that of other studies conducted in Iran or in underdeveloped countries, which is possibly due to the early diagnosis of stroke in patients or because of recent advances in stroke treatment and care at Ali-Ibn-Abi Talib Hospital of Rafsanjan (27). In this study, 85.58% of the patients had ischemic stroke, and 14.42% of them had hemorrhage. This finding is in line with the results of the study conducted by Firoozabadi et al. (21), who reported ischemia at 85.4% as well as with the statistics in major neurological sources that accounted for 90% of ischemic and 10% of hemorrhagic stroke (1). In the present study, the in-hospital mortality rate of stroke in ischemia and in hemorrhage was 7.54% and 17.98%, respectively. In many studies, including those of Khatri et al. (28), Oveisgharan et al. (29), Collins et al. (30), and Farhoudi et al. (22), the rate was significantly higher in hemorrhage. Therefore, the fatality rate of bleeding is higher in hemorrhage than in ischemia. According to the findings of the present study, the highest frequency of in-hospital mortality was 78.4% for patients over the age of 65 years and 57.8% for females. In addition, the mean age of the dead patients was 75.28 years. Although the mortality rate in this study was relatively high, the mean age of dead patients was higher than in most of other studies. For instance, the mean age of dead patients was 64.3 years in Borhani-Haghighi's (20) study, 67 years in Shah et al.'s (23) study, 69.9 years in Farhoudi et al.'s (22) study, 74.12 years in Ong et al.'s (31) study, and 79.9 years in Roquer et al.'s (32) study. The frequency of mortality in the age group over 65 years in these studies was 10-19% lower than that of the present study, as it was 60% in Borhani-Haghighi's (20) study, 69.9% in Farhoudi et al.'s (22), 70.69% in Shah et al.'s (23) study, and 67.5% in Ong et al.'s (31) study. The frequency of mortality was higher in men than in women in the studies of Borhani-Haghighi (20), Farhoudi et al. (22), Roquer et al. (32), and Shah et al. (23); in contrast, in Ong et al.'s (31) study, similar to the present study, the mortality rate was higher in women than in men due to the more common AF and more severe stroke in women. According

Table 2. Comparison the frequency of time leading to death in stroke patients according to type of complication, stroke type, size of stroke and age group

Variable		≤30 days		>30 days		Total		p value
		n	%	n	%	n	%	
Complication (leading to death)	Neurologic	97	100	0	0	97	100	<0.001
	Non-neurologic	83	81.4	19	18.6	102	100	
Type of stroke	Ischemic	127	89.4	15	10.6	142	100	0.44
	Hemorrhagic	53	93	4	7	57	100	
Size of stroke	Non-major Non-extensive	67	88.2	9	11.8	76	100	0.40
	Major Extensive	111	91.7	10	8.3	121	100	
Age group	<65 yrs	40	93	3	7	43	100	0.51
	>65 yrs	140	89.7	16	10.3	156	100	

Yrs: Years

to past studies on stroke patients at Ali-Ibn-Abi Talib Hospital of Rafsanjan, stroke was more prevalent in women than in men, and this could have been the cause of the higher mortality rate in women who participated in the present study (33). Among the underlying diseases, the highest frequency of the in-hospital mortality of stroke for HTN was 68.3%. The order of frequencies of other underlying diseases in this study included the history of stroke (36.2%), DM (35.7%), IHD (31.7%), AF (24.6%), and hypercholesterolemia (18.6%), respectively. Only 15.1% of dead patients were smokers. In the studies of Shah et al. (23), Doğan et al. (34), and Ong et al. (31), HTN had the highest mortality rates of 60%, 85.4%, and 82.5% among the underlying diseases, respectively. However, the mortality rate was higher among smokers at about 35.8%, 34.4%, and 66.2%, respectively, which was higher than that of the present study, which could have been due to the different form of registration of positive cases of smoking in the files of the present study (23). Cardiovascular risk factors, including DM, HTN, IHD, AF, hypercholesterolemia, the history of stroke, and smoking are among the risk factors for post-stroke complications, and some of them increase the risk of mortality (13). Hence, identifying these factors in patients with acute stroke as well as adopting accurate treatment and care procedures in these patients could be effective in reducing the complications or risks of death. According to the results of the present study, the most frequent mortality according to the size of the stroke in all three types of stroke was for large lesions (major and extensive), which accounted for 56.34% of the cases in the ischemic type, 70.2% in ICH, and 100% in SAH. In addition, the highest incidence rate of death in ischemic stroke was within the anterior circulation range (78.17%) and in ICH, followed by the basal ganglia and lobar hemorrhage (42.6% each) as well as thalamic hemorrhage (17%). Hofmeijer et al. (35) have found out that the brain infarct size is a major determinant of fatal brain edema, and the larger the brain infarct size is, the greater the risk of fatal brain edema will be. In Ong et al.'s (31) study, the mortality rate was higher in the anterior circulation than in the posterior circulation, and large anterior circulation infarcts were associated with high mortality rates. In the present study, the most common complications leading to the death of patients were neurological complications (48.7%) followed by infections (23.1%), cardiac complications (18.1%), and pulmonary embolism (5.5%). In the same vein, Prosser et al.'s (14) study showed that the most common complications leading to death were neurological complications followed by cardiac complications, infections, and other complications. In Mogensen et al.'s (36) study, neurological complications were the most common cause of death within the first month after stroke. Zhang et al. (37) and Balami et al. (38) have concluded that a reduction in the incidence of post-stroke fatalities, which mainly include pneumonia, cardiovascular complications, and arterial embolism according to clinical evidence, reduces post-stroke mortality rates. In addition, improving the diagnosis and treatment of neurological complications in the acute post-stroke phase could improve patient survival and reduce the burden of stroke. Therefore, identifying the risk factors of these complications is necessary because many of such complications are preventable, and early diagnosis and treatment could be effective in reducing them. In the present study, the average time interval between the patients' referral and death was 12.24 days, which is approximately similar to that of Heuschmann et al.'s (25) study (10.6 days), but it is different from the studies of Farhoudi et al. (22) (25.8 days) and Doğan et al. (34) (8 days). In Farhoudi et al.'s (22) study, the longer time interval between referring to the hospital and death could have been due to better stroke care and the younger age of the patients died. In the present study, 50.3% of the deaths occurred in the first week, and 90.5% of them occurred in the first month after stroke. Mortality rates in the first week after stroke were reported to be 57.4% and 66% in Farhoudi et al.'s (22) study and in Heuschmann et al.'s (25) study, respectively (25). The study of Prossor et al. (14) showed that mortality rates were very high in the first week after stroke and gradually decreased afterwards. Mortality rates of less than 30 days and more than 30 days of admission in the two groups showed a significant difference ($p<0.001$) between neurological complications and non-neurological complications; accordingly, all patients with neurological complications died in less than 30 days. Numerous studies have shown that neurological complications occur earlier than other stroke complications and are associated with premature death following direct brain injuries (11,12,15,39). According to the findings of the present study, there was no significant difference between ischemic and hemorrhagic groups in terms of gender, smoking, DM, HTN, and hypercholesterolemia; however, the positive history of stroke, AF, IHD, as well as being older than 65 years were more significantly prevalent in ischemia than in hemorrhage. The main difference between other studies and the present one in analyzing different types of stroke in terms of risk factors is that none of them has investigated the types of stroke in the group of dead patients. Roquer et al. (32) have found out that DM, HTN, AF, and IHD increase the severity of stroke and the risk of in-hospital mortality in acute ischemic stroke. According to the findings of the present study, the prevalence of neurological complications is significantly higher than that of non-neurological complications in ischemia compared to hemorrhage, in major and extensive stroke compared to minor, lacunar, and non-extensive strokes, as well as in patients younger than 65 years compared to those older than 65 years. However, there has been no significant difference in the frequency of death-related complications between males and females as well as between positive and negative cases in terms of smoking and underlying disease variables. The results of the studies of Chen et al. (40) and Jaramillo et al. (41) showed that younger patients were more prone to fatal brain edema than older ones, which was attributed to brain atrophy and the presence of more space

around the brain of the elderly in Hacke et al.'s (42) study. In addition, Hofmeijer et al. (35) have found out that the brain infarct size is a major determinant of fatal brain edema.

One of our major limitation was the retrospective type of study, in which we could not follow the patients precisely during their admission. Another limitation was the incompleteness of some cases' documents that made them excluded from our study. The third limitation was the unknown cause of death in some cases' hospital files. The absence of a control group may be a problem for us. On the other hand, a sufficient number of cases in our study was one of our strength points. The second strength of the study was long-term duration and the existence of a treatment center for stroke patients. As a result, it is possible to generalize the results to the total population of stroke patients.

Conclusion

According to our study, neurologic complication, infections, cardiac complications, and thromboembolism are the most frequent causes of death in stroke patients. The future of stroke care and the rate of mortality depend on our early management of complications and controlling of risk factors. It is recommended that subsequent prospective studies be conducted to have full access to patient information. In addition, designing a control group makes the comparison of different risk factors in dead stroke patients and living ones.

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Ethics

Ethics Committee Approval: The study was approved by the Ethics Committee under the code: (IR.RUMS.REC.1395.145), in accordance with the Helsinki Criteria (protocol number: 31/20/4, date: 31.01.2017).

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: A.V., S.A., Design: A.V., S.A., Data Collection or Processing: Z.K., S.A., A.M.A., N.J., Analysis or Interpretation: Z.K., Literature Search: A.V., S.A., A.M.A., Writing: A.V., Z.K.

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