Survival After Ischemic and Hemorrhagic Stroke: A 4-Year Follow-Up at a Mexican Hospital

Copytzy Cruz-Cruz, DSc,* Hortensia Moreno-Macías, DSc,† María del Socorro Parra-Cabrera, DSc,‡ Carlos Hernández-Girón, DSc,‡ and Juan Manuel Calleja-Castillo, MD$

Background: Overall, 75.2% of deaths from stroke occur in low- and middle-income countries. Mexico is a middle-income country with little information about the prognosis of early and late postischemic and hemorrhagic stroke. *Objective:* To evaluate the factors associated with post-stroke survival in the Mexican population. *Methods:* Observational study of consecutive stroke cases involving a first-ever hemorrhagic or ischemic stroke, with patients who received care at the National Institute of Neurology and Neurosurgery, in Mexico City, between 2009 and 2012. Patients were followed for up to 4 years after the index event. Exploratory analysis of survival was carried out with Kaplan-Meier and log-rank tests. Factors associated with survival time were determined using Cox models. *Results:* A total of 300 out of 544 (55.15%) patients had a hemorrhagic stroke, 135 of 544 (24.82%) patients died during the entire follow-up period, and 56 of 544 (10.29%) died in the first 30 days post-stroke (early mortality). Early mortality after stroke was associated with age ≥ 65 years (Adjusted Hazard Ratio − AHR = 2.07, $P = .02$) and ≥ 2 in-hospital medical complications (AHR = 46.13, $P < .01$). Late mortality was associated with age ≥ 65 years (AHR = 3.43, $P < .01$), ≥2 in-hospital medical complications (AHR = 2.55, $P < .01$), high comorbidity (AHR = 5.43, $P < .01$), and recurrence (AHR = 1.90, $P = .01$). *Conclusions:* Patients with hemorrhagic and ischemic stroke who presented in-hospital medical complications, high comorbidity, and were over 65 years old had higher rates of early and late mortality.

Key Words: Ischemic stroke—hemorrhagic stroke—survival analysis—México

Introduction

Stroke is one of the leading causes of death and disability, particularly in developing countries.[1] According to the 2013 Global Burden of Disease *(GBD-2013)* study, the burden of stroke between 1990 and 2013 was 3 times greater in middle- and low-income countries (4.85 million deaths in 2013) than in high-income countries (1.6 million deaths).[2] In 2012, the mortality rate in Mexico was 3.92 per 100,000 inhabitants for ischemic stroke, 2.10 per 100,000 for subarachnoid hemorrhage (SAH), and 7.62 per 100,000 for intracerebral hemorrhage (ICH).[3] The study of the long-term prognosis for patients with a first-ever stroke is helpful for planning by public health care services.[4-7]

Various countries have studied long-term post-stroke mortality rates and associated prognostic factors. Cumulative mortality ranges from 13.6% to 34.2% at 1 year, and 29.1% to 41.7% at 5 years.[8-12] The main prognostic factors that are known to be associated with long-term mortality after stroke are type of stroke, age, sex, comorbidities, and characteristics related to in-hospital medical care.[7-12] In developed countries, "organized stroke unit care" has reduced early post-stroke mortality by providing acute care and preventing medical complications.[13] However, it is necessary to know which prognostic factors modify the

From the *School of Public Health of Mexico, National Institute of Public Health of Mexico, Cuernavaca, México; †Division of Social Sciences and Humanities, Department of Economy, Metropolitan Autonomous University-Iztapalapa, Mexico City, Mexico; ‡Chronic Disease Division, Center for Population Health Research, National Institute of Public Health of Mexico, Cuernavaca, México; and $Stroke Clinic, National Institute of Neurology and Neurosurgery Manuel Velasco Suarez, México City, Mexico.

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Address correspondence to Juan Manuel Calleja-Castillo, MD, Stroke Clinic, National Institute of Neurology and Neurosurgery Manuel Velasco Suarez, Insurgentes Sur 3877 Del. Tlalpan, Col. La Fama, México City C.P.14269, Mexico. E-mail: juancalleja@me.com.

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long-term post-stroke prognosis in developed and developing countries.

The stroke registry of the National Institute of Neurology and Neurosurgery (INNN)[14] and the National Mexican Record of Cerebrovascular Disease[15] reported 24.5% and 21.2% mortality at 30 days post-stroke, respectively, while First Mexican Record of Cerebral Ischemia (PREMIER) reported 30% mortality at 1-year post-stroke.[16,17] However, no information exists about the prognostic factors that modify long-term mortality after stroke. We evaluated factors that are associated with post-stroke survival prognosis in Mexican patients.

Methods

Design

An observational, analytical study of consecutive stroke cases was performed with patients that had been diagnosed with an ischemic or hemorrhagic stroke and who were treated at the INNN in Mexico City, with follow-up for up to 4 years. Collection of information about mortality and recurrence was planned and obtained prospectively, whereas the collection of clinical and sociodemographic patient characteristics were unplanned.

Participants and setting

This study included patients with a first-ever stroke who were over 18 years old, were residing in Mexico, and were treated at INNN between 2009 and 2012. Patients whose final diagnosis was a transient ischemic attack, traumatic brain injury, tumor, or subdural hematoma were excluded. Cases whose clinical records had incomplete information were eliminated.

Baseline and Follow-Up Information

Clinical and sociodemographic information was obtained from the patients' clinical records using a standardized data extraction form. The information that was extracted from the clinical records was generated by neurologists and reviewed by a stroke expert. Stroke patients and their relatives were contacted and interviewed by phone up to 4 years after the first event in order to register their clinical status, recurrence status, or death. The semi-structured phone interview was administered by trained personnel. Stroke was defined according to guidelines by the World Health Organization (WHO).[18,19]

Variables

The main outcome of this study was survival time, or time to death after incident stroke, examined at 30 days and for up to 4 years after the event. Cases that were alive as of the last contact were treated as censored cases. Information about fatal events and classification of cause of death were obtained from death certificates and clinical records. The cause of death was categorized according to the classification scheme presented by the Oxford Stroke Study.[19] The information about stroke type, that is, ischemic (cerebral infarction) and hemorrhagic (SAH and ICH), was obtained from the clinical records, and was diagnosed by stroke experts in accordance with international guidelines.

Covariables and Confounders

The sociodemographic variables explored in this study were age (<65 years and ≥65 years), sex, and educational level (4 classes). Monthly family income, in Mexican pesos, was classified by tertiles. Comorbidity was evaluated with the Charlson-Deyo comorbidity index (CCI), calculated based on the presence or absence of 17 medical conditions.[20,21] The CCI for each patient included 16 diseases, with the exception of stroke, which was the study's objective.[21] CCI was categorized as no-comorbidity (0), low to moderate comorbidity (1-2), and high comorbidity greater than 3.[20,21]

The Glasgow Coma Scale (GCS) was used to evaluate the stroke severity because National Institutes of Health Stroke Scale data were not available for all patients, baseline stroke severity was determined based on the GCS obtained within 48 hours of the event.[22] The GCS was classified as low (13-15 points), moderate (9-12 points), and high severity (3-8 points).[22] In-hospital medical complications were classified as none, 1 complication, and 2 or more. Timely rehabilitation after hospital discharge was defined as reported participation in a physical or psychological rehabilitation program. Recurrence was defined as a new focal neurological deficit after the first event and lasting for >24 h.[23,24] A cluster analysis was used to determine the sequelae level, which was classified as severe or not severe, and included hemiplegia, alterations in urinary-fecal control, dysphagia, seizures, depression, anxiety, cognitive deterioration, dementia, and sensory, visual, and language alterations.[25] In an effort to reduce potential sources of bias, we used the best criteria for diagnosing hemorrhagic and ischemic stroke. We used a standardized instrument to collect the information from the clinical records and to reduce the measurement error. To confirm deaths, we included information from death certificates, which are reliable sources of this information.

Statistical Analysis

Sociodemographic and clinical characteristics, and those related to in-hospital medical care were reported as medians and proportions. Differences between ischemic and hemorrhagic groups were evaluated with the Mann-Whitney test and tests of proportion or Pearson's chi-square.

Early survival (0 to 30 days), late survival (30 days to 4 years), and survival during the entire follow-up period (0 to 4 years) were explored with the Kaplan-Meier method and the log-rank test. Adjusted Cox regression models were used to evaluate the association between stroke type (ischemic or hemorrhagic) and survival time over the entire follow-up period (0 to 4 years) and the early (0 to 30 days) and late stage (30 days to 4 years). A P value of

≤ .05 was considered statistically significant. The Schoenfeld residuals method was used to evaluate the adjustment and fulfillment of the statistical requirements inherent to each model.[26] The statistical analyses were carried out using the STATA 13 statistical package. This study was approved by the INNN IRB (Internal Review Board). Participants provided verbal informed consent, and a close relative provided consent in cases where the patient was not able.

Results

Sociodemographic and Clinical Characteristics

Between 2009 and 2012, 761 stroke cases were admitted to the INNN, 196 cases did not meet the inclusion criteria, and another 21 were eliminated from this study. The study sample included 544 cases of incident stroke, 300 of which (55.15%) were hemorrhagic. Of the 300 cases of hemorrhagic stroke, 114 were ICH and 186 were SAH. The follow-up period was between 2 and 4 years for 86.50% of cases. With regard to the censored individuals, follow-up time did not differ between stroke type (main exposure variable).

Table 1 shows the sociodemographic, clinical, and medical care characteristics. The median age of the patients was 53 years, and ischemic patients were older than hemorrhagic cases (57 versus 51 years $P < .01$). A total of 58.6% of patients were female, 69.6% of stroke cases had a primary educational level, and 24.1% of the 544 cases had high comorbidity. Ischemic cases had a higher comorbidity than hemorrhagic cases (32.8% versus. 17.0%, $P < .01$). No difference in the prevalence of hypertension was found between ischemic and hemorrhagic cases. In addition, 8.3% of stroke cases presented a high stroke severity, and a larger proportion of hemorrhagic cases presented high stroke severity (12.0% hemorrhagic versus 3.7% ischemic, $P = .01$). During hospitalization, 37.4% of stroke cases developed 2 or more medical complications, and hemorrhagic cases had more medical complications than ischemic cases (70.7% versus 46.5%, $P < .01$). A total of 20.9% of patients presented severe sequelae at hospital discharge, which did not differ by stroke type.

Outcomes After Stroke

Table 2 shows recurrence and survival outcomes after stroke. Recurrence was 20.2% during the post-stroke follow-up period. Cases of hemorrhagic stroke had a higher post-stroke recurrence than ischemic cases (17.3% versus 9.8%, respectively) in the early phase (30 days post-stroke). During the 4-year follow-up, 135/544 (24.8%) of patients died, 70/244 patients had ischemic stroke (28.7%), and 65/300 had hemorrhagic stroke. A total of 56 out of 544 patients (10.3%) died during the first 30 days post-event (7.8% ischemic, 12.3% hemorrhagic stroke). With regard to survival at 30 days, 79 subjects died during the 4-year follow-up, and ischemic patients had a higher mortality rate than hemorrhagic patients (22.7% versus 10.7%, $P < .01$).

Survival After Stroke

The 544 stroke patients represented 495,130 person-days at risk of death, and 409 survived up to 4 years post-stroke (75.2%). Table 3 shows the factors that are associated with survival during the entire follow-up period. Age ≥65 years (AHR = 5.58, $P < .01$), high comorbidity (AHR = 5.15, $P < .01$), and severe sequelae (AHR = 2.00, $P = .03$) were significantly associated with higher mortality. Lastly, timely rehabilitation upon hospital discharge was associated with a 61.5% lower long-term risk of death ($P < .01$). The variation explained by the model was 0.75.

Factors associated with early and late survival

Table 4 shows the factors associated with early (30 days) and late (31 days to 4 years) survival after stroke with the adjusted model. The variation explained by the early survival model was 0.78, and 0.81 for late survival model. At 30 days after incident stroke, the AHR for death was higher for cases ≥ 65 years (AHR = 2.07, $P = .02$) and cases with more than 2 in-hospital complications (AHR = 46.13, $P < .01$), adjusted by stroke type, comorbidity, sex, educational level, stroke severity, and recurrence. With regard to survivors at 30 days after stroke, age ≥ 65 years (AHR = 3.43, $P < .01$), high comorbidity (AHR = 5.43, $P < .01$), high stroke severity (AHR = 1.09-1.91, $P = .02$), more than 2 hospital complications (AHR = 2.54, $P < .01$), and recurrence (AHR = 1.90, $P = .01$) were associated with a high risk of death, adjusted by sex and educational level.

Discussion

This study evaluated the factors associated with post-stroke survival (early, late, and the entire follow-up period) among Mexican patients with ischemic and hemorrhagic stroke. Overall survival was 75.2%, which was higher than findings reported by other studies with similar follow-up periods (46.4% to 73.4%). Differences found by the present work could be attributed to sample characteristics (hospital-based study, exclusion of recurrent cases, inclusion year of patients, newer cohorts having lower mortality due to overall advances in medical practice as well as in specific treatments for stroke, i.e., thrombolysis).[4,5,7,9,10] Survival at 4 years was better for hemorrhagic cases than for ischemic stroke cases (78.3% versus 71.3%, respectively). This finding differs from the study by Cabral et al, who reported 46.48% survival for hemorrhagic and 73% for ischemic stroke cases in Brazil.[12] Sun et al reported 55.4% survival for hemorrhagic and 59.2% for ischemic stroke cases.[9] And Kim et al found 70.1% survival for hemorrhagic cases and 71.4% for ischemic stroke cases.[27] Differences may be explained by the characteristics of the samples, the referral bias implicit in studies of hospital cases, and the effect of variables related to medical care.

The Cox regression model confirmed that stroke cases ≥ 65 years had a greater risk of dying than those <65 years, which is similar to what has been reported in

Table 1. *Characteristics of patients, by stroke type*

	Ischemic (n=244)	Hemorrhagic (n=300)	*P*	Total (n=544)
Sociodemographics				
Age, years, median (IQR)	57.0(46.0-69.0)	51.0(37.5-60.0)	0.00[a]	53.0(41.0-64.0)
Sex Female, n (%)	129(52.9)	190(63.3)	0.01[b]	319(58.6)
Educational level, n (%)				
No primary education	16(6.6)	28(9.3)	0.24[c]	44(8.1)
Primary school	148(60.9)	186(62.0)	0.79[c]	334(61.5)
High school	46(18.9)	55(18.3)	0.85[c]	101(18.6)
Bachelor degree	33(13.6)	31(10.3)	0.24[c]	64(11.8)
Income level, n (%)				
Low (320-2080)	57(25.3)	113(39.8)	0.00[c]	170(33.4)
Medium (2100-4000)	91(40.4)	114(40.1)	0.94[c]	205(40.3)
High (more than 4000)	77(34.2)	57(20.1)	0.00[c]	134(26.3)
Clinical				
Comorbidity n (%)				
None	55(22.5)	148(49.3)	0.00[c]	203(37.3)
Low to medium	109(44.7)	101(33.7)	0.01[c]	210(38.6)
High	80(32.8)	51(17.0)	0.00[c]	131(24.1)
Hypertension, n (%)	154(63.1)	191(63.7)	0.89[a]	345(63.4)
Atrial fibrillation, n (%)	39(15.9)	10(3.3)	0.00[a]	49(9.0)
Stroke severity, n (%)				
Low	178(72.9)	214(71.6)	0.72[c]	392(72.2)
Moderate	57(23.4)	49(16.4)	0.04[c]	106(19.5)
High	9(3.7)	36(12.0)	0.01[c]	45(8.3)
Hospital care				
In-hospital medical complications, n (%)				
None	130(53.5)	88(29.3)	0.00[c]	218(40.2)
One	44(18.1)	78(26.0)	0.02[c]	122(22.5)
Two or more	69(28.4)	134(44.7)	0.00[c]	203(37.4)
Sequelae, n (%)				
Severe	52(23.0)	49(19.1)	0.29[a]	101(20.9)

Abbreviations: IQR, Interquartile range
[a]*P*-value from Mann-Whitney test
[b]*P*-value from Pearson test
[c]*P*-value from proportion test

the literature, that is, age is a consistent predictor of post-stroke mortality. Sex did not contribute significantly to survival, as has been shown by other works.[8,9,10,27,28] Other studies have evaluated the effect of in-hospital medical complications on late stroke survival, and a possible explanation is a delay in the patient's recovery due to complications such as infections, rebleeding, edema, vasospasm, and hydrocephalus.[5,8,24] The present study found that the development of more than 2 complications during the subacute phase results in a greater risk of death. Although each type of stroke presented different complications, designing medical care mechanisms to handle each one should be a priority so as to improve the prognosis for this population. Furthermore, comorbidity

Table 2. *Outcomes after stroke, by type*

	Stroke type			
Variable	Ischemic	Hemorrhagic	*P*	Total
Died, n (%)				
0-1460 days	70/244(28.7)	65/300(21.7)	.05[a]	135/544(24.8)
0-30 days	19/244(7.8)	37/300(12.3)	.08[a]	56/544(10.3)
31-1460 days	51/225(22.7)	28/263(10.7)	.00[a]	79/488(16.2)
Recurrence, n (%)				
0-30 days	24/244(9.8)	52/300(17.3)	.01[a]	76/544(13.9)
0-1460 days	47/244(19.3)	63/300(21.0)	.62[a]	110/544(20.2)

[a]*P* value from Pearson test.

Table 3. *Factors associated with 4-year survival (n = 544)*

Variable	AHR	95% CI		*P*
Stroke (Ischemic)	1			
Hemorrhagic	.55	.29	1.02	.06
Age (<65 years)	1			
≥ 65 years	5.58	3.01	10.07	<.01
Comorbidity Without	1			
High	5.15	2.08	12.76	<.01
In-hospital medical complications without	1			
1	1.31	.64	2.66	.46
≥ 2	1.73	.92	3.22	.09
Sequelae (not severe)	1			
Severe	2.04	1.07	3.89	.03
Timely rehabilitation (No)	1			
Yes	.39	.22	.68	.00

Abbreviations: AHR, adjusted hazard ratio; CI, confidence interval Cox model adjusted by sex, educational level, hypertension, stroke severity, and recurrence.

was associated with a greater risk of late mortality, which was also reported by Kapral (2002) and Chen (2014), and was explained by the effect of comorbidities on the decline of patient health.[6,10]

Recent publications on post-stroke prognosis have not evaluated the effect of sequelae on late survival. Only the effect of aphasia and functionality has been assessed, with the Rankin scale, both of which were associated with a higher risk of death.[29,30] The present study analyzed the effect of both severe and nonsevere sequelae on survival, and found that patients with severe sequelae had a higher long-term risk of dying. This could be explained by the delay in patient recovery due to severe sequelae, which results in immobility and feeding deficiencies, thereby increasing mortality rates. In addition, participation in rehabilitation programs upon discharge and for 2 months after stroke was found to have a protective effect on late survival. This finding should be explored and a timely rehabilitation program should be implemented for stroke survivors. Lastly, with the adjusted models, the prognostic factors for early and late survival after stroke were age and in-hospital medical complications, which increased the risk of death for both periods. High comorbidity and recurrence increased the risk of late death but not the risk of early death. These findings indicate the need to develop timely follow-up programs for stroke patients, with adequate handling of comorbidities to prevent recurrence for these at-risk patients.

An extended follow-up period for ischemic and hemorrhagic stroke cases is one of the strengths of this analysis. In addition, the data was collected from a highly specialized institution with personnel trained in the care of stroke patients. The internal validity of this work is high, and the cases were well identified (clinically and radiologically). However, the external validity of this study is limited, and there is a slight selection bias since the sample only included people who were treated at this third-level hospital, and patients who died before reaching the

Table 4. *Prognostic factors for early (less to 30 days) and late (between 30 days and 1460 days) survival after stroke*

	30 days survival				30 to 1460 days survival			
Variable	AHR	95% CI		*P*	AHR	95% CI		*P*
Ischemic	1				1			
Hemorrhagic	1.01	.55	1.87	.97	.66	.39	1.11	.11
Age (<65 years)	1				1			
≥ 65 años	2.07	1.11	3.85	.02	3.43	2.10	5.61	<.01
Comorbidity None	1				1			
Low to medium	.49	.26	.95	.04	1.35	.62	2.96	.44
High	.49	.25	.99	.05	5.43	2.64	11.19	<.01
In hospital medical complications None	1				1			
1	5.36	.55	51.99	.15	1.18	.59	2.36	.64
≥ 2	46.13	6.17	344.97	≤.01	2.55	1.44	4.53	<.01
Recurrence (No)	*	*	*	*	1			
Yes	*	*	*	*	1.90	1.16	3.12	.01

Cox model adjusted by sex, educational level, and stroke severity.

hospital were not included. The retrolective nature of the information collected could also result in a possible bias in our results. We used the GCS to adjust the prognostic models by stroke severity, since the National Institutes of Health Stroke Scale was not available for all the patients. Another limitation of this study was the number of autopsies performed in the cases of death, and in Mexico, those procedures are not always conclusive. Nonetheless, the information obtained regarding deaths involved a review of clinical records and death certificates, which are reliable sources. In conclusion, the factors associated with a higher risk of death were age ≥ 65-years, high comorbidity, 2 or more in-hospital medical complications, and the presence of severe sequelae upon hospital discharge. Meanwhile, early participation in rehabilitation therapy was found to reduce the long-term risk of death.

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Declaration of Conflicting Interests

The authors declare that there are no conflicts of interest.

References

1. Norving B, Kissela B. The global burden of stroke and need for a continuum of care. Neurology 2013;80:S5-S12.
2. Feigin VL, Krishnamurthi RV, Parmar P, et al. Update on the Global burden of ischemic and hemorrhagic stroke in 1990−2013: The GBD 2013 Study. Neuroepidemiology 2015;45:161-176.
3. Cruz-Cruz C, Campuzano-Rincón JC, Calleja-Castillo JM, et al. Temporal trends in mortality from ischemic and hemorrhagic stroke in Mexico, 1980-2012. J Stroke Cerebrovasc Dis 2017;26:725-732.
4. Hankey GJ. Secondary stroke prevention. Lancet Neurol 2014;13:178-194.
5. Andersen K, Olsen T. Body mass index and stroke: overweight and obesity less often associated with stroke recurrence. J Stroke Cerebrovasc Dis 2013;22:e576-e581.
6. Pennlert J, Eriksson M, Carlberg B, et al. Long-term risk and predictors of recurrent stroke beyond the acute phase. Stroke 2014;45:1839-1841.
7. Kapral M, Wang H, Mamdani M, et al. Effect of socioeconomic status on treatment and mortality after stroke. Stroke 2002;33:268-273.
8. De Wit L, Putman K, Devos H, et al. Five-year mortality and related prognostic factors after inpatient stroke rehabilitation: a European multi-center study. J Rehabil Med 2012;44:547-552.
9. Jones S, Sen S, Lakshminarayan K, et al. Poststroke outcomes vary by pathogenic stroke subtype in the Atherosclerosis Risk in Communities Study. Stroke 2013;44:2307-2310.
10. Sun Y, Lee S, Heng H, et al. 5-year survival and rehospitalization due to stroke recurrence among patients with hemorrhagic or ischemic strokes in Singapore. BMC Neurol 2013;13:133.
11. Chen H, Li C, Lee S, et al. Improving the one-year mortality of stroke patients: an 18-year observation in a teaching hospital. Tohoku J Exp Med 2014;232:47-54.
12. Cabral N, Muller M, Franco S, et al. Three-year survival and recurrence after first-ever stroke: the Joinville stroke registry. BMC Neurol 2015;1:70.
13. Towfighi A, Saver JL. Stroke declines from third to fourth leading cause of death in the United States: historical perspective and challenges ahead. Stroke 2011;42:2351-2355.
14. Arauz A, Marquez JM, Artigas C, et al. The Mexican Institute of Neurology stroke registry: vascular risk factors, subtypes and long-term prognosis in 4,491 consecutive patients. Cerebrovasc Dis 2010;29(Suppl. 2):197-198.
15. Cantú BC, Ruiz SJ, Chiquete E, et al. Factores de riesgo, causas y pronóstico de los tipos de enfermedad vascular cerebral en México: Estudio RENAMESVAC. Revista Mexicana de Neurociencia 2011;12:224-234.
16. Cantú BC, Ruiz SJL, Murillo BM, et al. The first Mexican multicenter register on ischaemic stroke (The PREMIER Study): demographics, risk factors, and outcome. Int J Stroke 2011;6:90-94.
17. Marquez RJ, Arauz A, Góngora RF, et al. The burden of stroke in México. Int J Stroke 2015;10:251-252.
18. World Health Organization. Stroke, Cerebrovasc accident, (2013), www.who.int/topics/cerebrovascular_accident/en/ (Accessed December 10, 2017).
19. Dennis MS, Burn JP, Sandercock PA, et al. Long-term survival after first-ever stroke: The Oxfordshire Community Stroke Project. Stroke 1993;24:796-800.
20. Bar B, Hemphill C. Charlson comorbidity index adjustment in intracerebral hemorrhage. Stroke 2011;42:2944-2946.
21. Boogaarts HD, Duarte CM, Janssen E, et al. The value of the Charlson Co-morbidity Index in aneurysmal subarachnoid hemorrhage. Acta Neurochir 2014;156:1663-1667.
22. Canadian Partnership for Stroke Recovery. Glasgow coma scale (GCS), (2017) www.strokengine.ca/indepth/gcs_indepth/ (Accessed January 21, 2017).
23. Boysen G, Truelsen T. Prevention of recurrent stroke. Neurol Sci 2000;21:67-72.
24. Mohan KM, Wolfe CD, Rudd AG, et al. Risk and cumulative risk of stroke recurrence. A systematic review and meta-analysis. Stroke 2011;42:1489-1494.
25. Kaufman L, Rousseeuw PJ. Finding Groups in Data: An Introduction to Cluster Analysis. New York: Wiley; 1990.
26. Kleinbaum DG, Klein M. Survival Analysis. A Self-Learning Text. 3rd ed USA: Springer Science and Business Media; 2012.
27. Kim HC, Choi DP, Ahn SV, et al. Six-year survival and causes of death among stroke patients in Korea. Neuroepidemiology 2009;32:94-100.
28. Lee BC, Hwang SH, Jung S, et al. The Hallym stroke registry: a web-based stroke data bank with an analysis of 1,654 consecutive patients with acute stroke. Eur Neurol 2005;54:81-87.
29. Tsouli S, Kyritsis AP, Tsagalis G, et al. Significance of aphasia after first-ever acute stroke: impact on early and late outcomes. Neuroepidemiology 2009;33:96-102.
30. Chiu HT, Wang YH, Jeng JS, et al. Effect of functional status on survival in patients with stroke: is independent ambulation a key determinant. Arch Phys Med Rehabil 2012;93:527-531.