Short- and Long-term Survival after Stroke in Hospitalized Patients in Chile: A Nationwide 5-Year Study

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Background: Short- and long-term stroke survival is a key indicator of hospital performance in stroke care. Our aim was to estimate short- and long-term survival rates in discharged patients diagnosed with ischemic stroke in Chile in a 5-year period and identify associated variables. *Materials and Methods:* We included all discharged patients from all hospitals in Chile with main diagnosis of ischemic stroke from 2003 to 2007, which were identified through the National Hospital Discharge Registry. To establish survival, discharges were linked to deaths in the Deaths Registry. Kaplan–Meier survival curves were used to estimate the cumulative 7-day, 30-day, 1-year, and 3-year survival rates. Independent predictors of death (sex, age, geographical regions, and status insurance) were assessed by Cox proportional hazard regression model. *Results:* A total of 51,130 with first-ever ischemic stroke patients were identified. Overall survival rate decreased from 88.9% (95% confidence interval [CI] 88.6-89.2) 7 days after hospital admission to 81.9% (95% CI 81.6-82.3), 69.9% (95% CI 69.5-70.3), and 61.2% (95% CI 60.7-61.6) after 30-day, 1-year, and 3-year, respectively. The multivariable model showed that the elderly patients (>80 years; hazard ratio [HR] 4.07; 95% CI 3.89-4.26) and hospital admission in the North (HR 1.14; 95% CI 1.09-1.20) and South area (HR 1.06; 95% CI 1.03-1.110) were associated with lower survival after stroke. Patients with private health insurance have a higher probability of survival than patients with public insurance (private insurance, HR .53; 95% CI .49-.56). *Conclusions:* Short- and long-term survival after ischemic stroke was heterogeneous by geographic regions and type of health insurance, regardless age and sex were the strongest predictors. This suggests an impact of socioeconomic factors and access to acute management of strokes on survival. **Key Words:** Stroke—brain ischemia—survival—fatal outcome—epidemiology—Chile.

Introduction

Strokes are the third cause of disability-adjusted life years worldwide.[1] Rates of stroke mortality and burden vary greatly among countries, being low- and medium-income countries more affected.[2] In Chile, these events account for 65% of all strokes with an adjusted annual incidence of 97.4 per 100,000 inhabitants,[3] causing 9% of the total number of deaths in the country.[3,4]

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Case fatality after stroke has been used as an indicator of hospital performance for acute stroke care delivery.[5,6] This indicator is usually measured at 7 days, 30 days, and 1 year after the stroke. It has been shown that stroke survival is associated with stroke severity and care provided by the health system. Saposnik[5] reported that the variables associated with higher 7- and 30-day case fatality were stroke severity (measured with the National Institutes of Health Stroke Scale on admission), neurological deterioration during admission, and acute stroke management. In the United States, the probability of in-hospital mortality in patients with ischemic stroke depends on age, history of atrial fibrillation, history of coronary events, and the way patients access emergency medical services.[7] Survival in patients with ischemic stroke also differs according to the pathological subtype. In general, the prognosis for short-term survival is better for patients with small-artery occlusion.[8] In Chile, the population-based study PISCIS (Proyecto de Investigación de Stroke en Chile: Iquique Stroke) study reported that dependency or death at 6 months was highest in cardioembolic strokes (62%) and lowest in small-vessel disease (21%).[9]

Strong evidence has also been found for the association between socioeconomic status and stroke incidence and mortality.[10,11] Low socioeconomic groups also have lower survival and greater stroke severity than high socioeconomic groups, although there is less evidence for this association.[12,13]

In high-income countries, 30-day fatality after ischemic stroke has been reported to range from 13% to 23%,[14] showing a significant decrease in the last 2 or 3 decades.[15-18] In low- or medium-income countries like Chile, these trends have been less studied. The PISCIS study reported a 30-day case–fatality rate of 23.3% in 2000-2002; however, it was performed in a particular region with higher income and low overall stroke mortality rates.[9] Another study performed in public hospitals in the Metropolitan Region of Santiago of Chile found an 8.7% of deaths after ischemic stroke at 30 days.[19]

The purpose of this study was to estimate short-term (7 and 30 days) and long-term (1 and 3 years) survival rates after ischemic stroke and to investigate the prognostic effect of sex, age, geographical region, and type of health insurance in Chile.

Materials and Methods

We performed a retrospective study by linking hospital discharge diagnosis with deaths at a national level. The study population consisted of all patients discharged from Chilean hospitals with a main diagnosis of ischemic stroke between January 2003 and December 2007. We did not exclude patients who died in the first admission. The main outcome measure was 7-day, 30-day, 1-year, and 3-year survival. Patients were selected from the National Hospital Discharge Registry (NHDR) administered by the Ministry of Health. The NHDR is a mandatory and exhaustive registry of discharge to all public and private hospitals in Chile. There are 355 hospitals across the country reporting to the NHDR, where 200 of them are public hospitals and the rest (n = 155) are private. Stroke patients were admitted in acute care facilities including academic and community hospitals and rural and urban facilities from all provinces and territories. A total of 61,507 patients with principal diagnosis of ischemic stroke at discharge according to the *International Classification of Disease, Tenth Revision* (*ICD-10* codes I63 and I64) were identified from all hospitals (Fig 1). Patients with invalid national identification number (n = 2604) were excluded and so were those with an incorrect stroke diagnostic code assigned (n = 139). In cases with multiple discharges for any of these codes, only the first event was included. The first event was identified considering the admissions with stroke code since June 2002 onward.

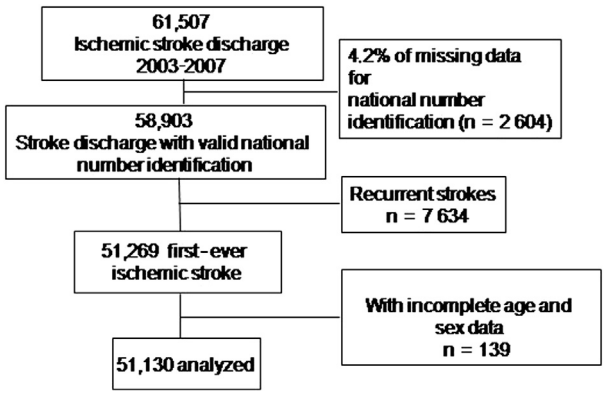

Figure 1. *Flowchart of study population, stroke admission between 2003 and 2007.*

The following variables were selected from the NHDR data set: national identification number, sex, age at event, admitting hospital, and geographical region where the admitting hospital is located. Subsequently, the national identification number, which is a unique and official number for each person living in Chile, was used to link these discharges with deaths reported in the National Death Registry from January 2003 to December 2010 including out-of-hospital deaths up to 3 years after hospital discharge. The codification process is carried out according to the standardized and centralized criteria in the Department of Statistics and Health Information of the Ministry of Health. Codification of the main cause of death and main diagnosis of hospital discharge is based on the *ICD-10*. The exhaustiveness of National Death Registry is optimal, and medical certification for the cause of death was 99.3% in 2007, whereas only 2.9% of deaths were classified as signs, symptoms, and ill-defined causes of deaths (*ICD-10* codes R00-R99), which are usually used as a mortality record quality indicator.[20,21]

The following variables were analyzed: gender, age at first-ever stroke (categorized as ≤60, 61-70, 71-80, and >80), year of admission, geographical area (categorized as North, Center East, Center West, South, and

Extreme South), and type of health insurance. There are significant differences between the private health insurance systems (institutions called Private health insurance companies, PHIC) and the public system managed by the National Health Fund (NHF), for example, while NHF covers 70.4% of the Chilean population, PHICs only cover 16.6%. The members of PHICs, in addition to the compulsory contribution, increase their payments to access higher coverage with an annual average contribution of 6.2 times the NHF contributors.[22] NHF has 4 income based groups: A (indigent), people who do not contribute with their wages and that can only use public health providers; B (low income), those who earn less than a minimum wage; C (middle income), those earning between 1 and 1.5 times the minimum wage; and D (middle-high income), those earning more than 1.5 times the minimum wages. To summarize the profile of income and access to health care in these 2 systems, we arranged the type of health insurance into 3 categories: public health insurance (low income), which includes groups A and B; public health insurance (middle-high income), which includes groups C and D; and private health insurance (high income) including the enrollees of PHICs.

Survival time was calculated from the date of hospital admission for stroke to date of death by any cause. Patients with no record of death were censored at December 31, 2010. Survival curves were generated using the Kaplan–Meier method and were compared by the log-rank test. Cox proportional hazard regression analyses were carried out to evaluate survival differences between sex, age, year of event, geographical area, and type of health insurance. Adjusted and unadjusted hazard ratios and 95% confidence interval (CI) were computed. Possible interaction between age and sex was investigated by constructing interaction terms in the Cox proportional model. All calculations were carried out using the STATA statistical software (version 8.0). All *P* values were 2 sided, and values less than .05 were considered statistically significant.

This study protocol was approved by the Ethics Committee of the Universidad Mayor of Santiago, Chile.

Results

We analyzed 51,130 patients with first-ever ischemic stroke admitted to 272 hospitals across Chile from January 1, 2003, to December 31, 2007 (Fig 1). Of these, 52.1% of the patients were men. The mean age at the event was 69.0 years (SD 12.5) for men and 72.0 years (SD 13.7) for women. A total of 8842 events were registered in 2003 and 12,545 in 2007. For all the years studied, the mean length of hospital stay was 9.8 days (SD 14.2), and 10% of the patients were discharged after 20 or more days.

During follow-up, we identified 23,626 (46.2% of patients) deaths. The median follow-up was 3.3 years (range <1 day to 8.0 years). Causes of death were cerebrovascular disease (37.1%), other cardiovascular disease (30.5%), cancer (7.2%), diabetes (5.9%), and other causes (19.3%). The 7-day, 30-day, 1-year, and 3-year survival rates were 88.9% (95% CI 88.6%-89.2%), 81.9% (95% CI 81.6%-82.3%), 69.9% (95% CI 69.5%-70.3%), and 61.2% (95% CI 60.7%-61.6%), respectively. When we compared patients admitted in each consecutive period from 2003 to 2007, we found that survival gradually improved in all follow-up periods (Table 1). The univariate analysis showed that survival rates were higher in men than women in all follow-ups. Survival rate decreased at advanced ages. Patients discharged from hospitals in the geographic regions of North and South had lower survival rates than those subjects discharged in other geographic regions. The 7-day, 30-day, 1-year, and 3-year survival rates were lower in patients having public health insurance (low income) compared with public health insurance (middle-high income) and private health insurance (high income). Kaplan–Meier survival curves showed significant decrease by age group (*P* value log-rank test <.0001) and by health insurance (*P* value log-rank test <.0001) (Figs 2-4).

Univariate and multivariate analysis are presented in Table 2. The multivariate model showed that there is a progressive and significant improvement in survival across the study period (*P* value for trend <.001). Advanced age was associated with an increased likelihood of unfavorable prognosis (*P* value for trend <.001). Female gender was independently associated with lower survival (hazard ratio [HR] .97; 95% CI .94-.99). Geographical differences were also found to be independently associated with survival—Northern region (HR 1.14; 95% CI 1.09-2.20) and Southern region (HR 1.06; 95% CI 1.03-1.10) show a significant excess risk of deaths compared with the Center-East regions, whereas the Center-West regions had better survival (HR .95; 95% CI .91-.98). Patients with public health insurance belonging to middle-income groups have a lower risk of dying after stroke (HR .76; 95% CI .73-079) than subjects with public health insurance belonging to low-income groups. Also, patients with private health insurance have a lower risk of dying after stroke (HR .53; 95% CI .49-.56). The interaction between age and sex was not significant (data not shown).

Discussion

This is the first study analyzing short- and long-term mortality after ischemic stroke, using a national hospital discharge database in Chile. Three years after stroke, 61.2% of ischemic patients remain alive, whereas 1 year after stroke this percentage rises up to 69.9%. The 30-day case–fatality rate found (18.1%) was within the lower limit values reported for all strokes analyzed in distinct countries.[14] The percentages lie between 17% and 30% in high-income countries and between 18% and 35% in middle-low–income countries. The 30-day case–fatality

Table 1. *Seven-day, 30-day, 1-year, and 3-year survival for ischemic stroke**

Characteristic	N (%)	Overall survival (95% CI) 7 d		30 d		1 y		3 y	
Overall	51.130 (100)	88.9	(88.6-89.2)	81.9	(81.6-82.3)	69.9	(69.5-70.3)	61.2	(60.7-61.6)
Period (y)									
2003	8842 (17.3)	86.7	(85.9-87.4)	78.7	(77.9-79.6)	67.0	(66.0-68.0)	58.3	(57.3-59.3)
2004	9145 (17.9)	87.6	(86.9-88.3)	80.1	(79.3-80.9)	67.6	(66.6-68.5)	59.2	(58.2-60.2)
2005	10,080 (19.7)	88.5	(87.9-89.1)	81.0	(80.2-81.7)	69.4	(68.5-70.3)	60.7	(59.8-61.7)
2006	10,518 (20.6)	90.0	(89.4-90.5)	83.8	(83.1-84.5)	71.9	(71.0-72.7)	63.1	(62.2-64.0)
2007	12,545 (24.5)	90.8	(90.3-91.3)	84.7	(84.1-85.3)	72.6	(71.8-73.3)	63.3	(62.5-64.2)
Sex									
Male	26,645 (52.1)	90.0	(89.6-90.3)	83.4	(83.0-83.9)	71.8	(71.3-72.4)	62.8	(62.2-63.4)
Female	24,485 (47.9)	87.7	(87.3-88.1)	80.3	(79.8-80.8)	67.9	(67.3-68.5)	59.4	(58.8-60.0)
Age (y)									
≤60	10,879 (21.3)	91.8	(91.3-92.3)	88.9	(88.3-89.4)	84.2	(83.5-84.9)	80.7	(79.9-81.4)
61-70	11,959 (23.4)	90.4	(89.9-90.9)	85.5	(84.8-86.1)	77.1	(76.3-77.8)	69.6	(68.8-70.4)
71-80	16,314 (31.9)	88.7	(88.2-89.2)	81.1	(80.5-81.7)	67.6	(66.9-68.3)	57.2	(56.5-58.0)
>80	11,978 (23.4)	85.0	(84.4-85.6)	73.3	(72.5-74.1)	53.1	(52.2-54.0)	40.3	(39.5-41.2)
Geographical area									
Center East	14,725 (28.8)	90.0	(89.5-90.5)	84.1	(83.5-84.7)	71.6	(70.9-72.3)	63.1	(62.3-63.9)
Center West	11,921 (23.3)	89.9	(89.4-90.4)	83.0	(82.3-83.7)	71.5	(70.7-72.3)	62.7	(61.8-63.6)
North	3958 (7.7)	86.5	(85.4-87.5)	78.8	(77.5-80.0)	67.4	(65.9-68.8)	58.9	(57.4-60.4)
South	16,283 (31.8)	87.6	(87.1-88.1)	79.6	(79.0-80.3)	67.7	(67.0-68.4)	58.9	(58.1-59.6)
Extreme South	4243 (8.3)	89.3	(88.3-90.2)	83.3	(82.1-84.4)	70.8	(69.4-72.1)	61.3	(59.8-62.7)
Type of health insurance									
Public (low income)	36,348 (71.1)	87.8	(87.5-88.1)	80.0	(79.5-80.3)	67.0	(66.5-67.4)	58.0	(57.5-58.6)
Public (middle-high income)	7656 (15.0)	91.2	(90.6-91.9)	86.3	(85.5-87.0)	76.1	(75.1-77.0)	68.3	(67.2-69.3)
Private (high income)	3214 (6.3)	94.7	(93.8-95.4)	91.4	(90.4-92.4)	85.4	(84.0-86.4)	77.8	(76.3-79.2)

Abbreviations: CI, confidence interval.
*Results expressed in percentages.

rate in our study is lower than the 23.3% reported in the PISCIS study.[3] It could reflect misclassification of some severe cases in the *ICD-10* codes as nonischemic strokes. The most frequent cause of death in our stroke patients was cerebrovascular disease, as has been show by others.[23]

We found less favorable survival rates for the population assigned to public health insurance in lower and middle-high–income categories, compared with those with private health insurance. The differences in the risk of dying are large and show a gradient effect. We think that the particular socioeconomic segmentation

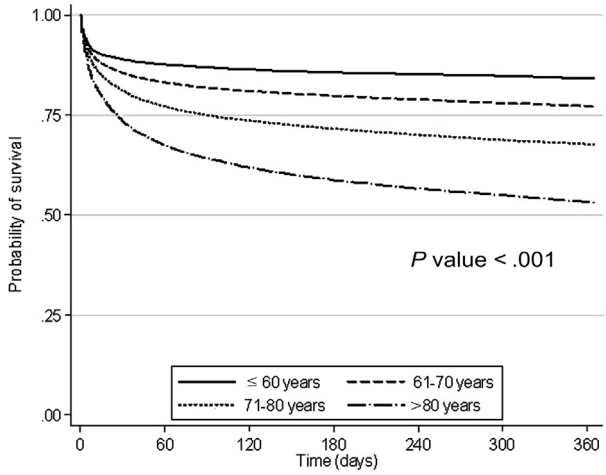

Figure 2. *Kaplan–Meier ischemic stroke survival curves by age groups.*

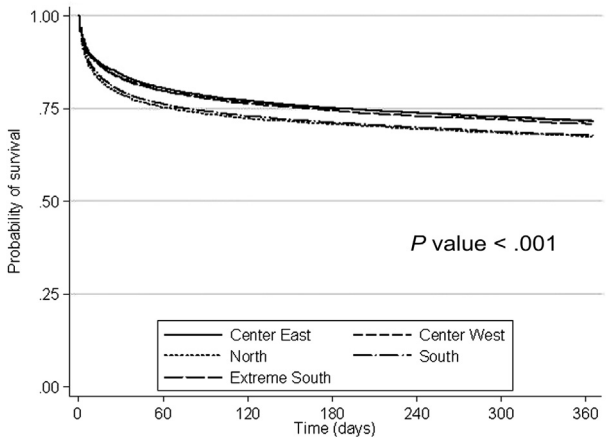

Figure 3. *Kaplan–Meier ischemic stroke survival curves by geographic area.*

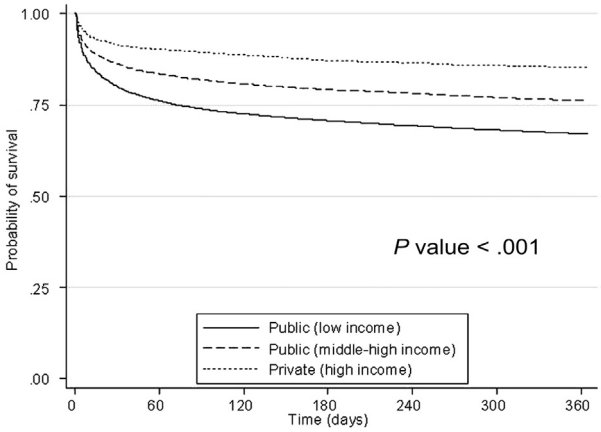

Figure 4. *Kaplan–Meier ischemic stroke survival curves by health insurance.*

health insurance system in Chile captures both the effect of socioeconomic status on survival after stroke and the disparities in access to health services by different types of health insurance. Other authors have reported that socioeconomic status is inversely associated with mortality after stroke and only partially explained by process of care, stroke severity,[24] and other measurable baselines.[25] In Canada, higher income is associated with improvements in some aspects of stroke care delivery. However, the magnitude of the care gap across income quintiles is small, and apparently, it does not explain the differences in survival after stroke,[26] as opposed to what happens in Chile where these socioeconomic gaps are important.[27] Previous studies in Chile have shown that stroke mortality is significantly associated with poverty, region, diabetes, sedentarism, and overweight.[10] Recently, it has been shown that only 7% of patients who were taken care of in a public health region for a cardioembolic infarction were taking prescribed oral anticoagulation after 15 months of the stroke[28]. It is plausible that the higher survival rates of patients with private insurance (higher incomes) are because of better acute stroke care (stroke units, thrombolysis), and more readily access to appropriate preventive health services, such as anticoagulation for patients with atrial fibrillation, decreases risk of larger more severe strokes. In addition, the highest income group have fewer comorbidities and disability[29] and is more likely to seek prompt access to acute stroke care[30]

Table 2. *Crude and adjusted hazard ratios for mortality after ischemic stroke, Cox proportional hazard model*

			Univariate		Multivariate*	
Characteristic	Total	Events	HR	95% CI	HR	95% CI
Period						
2003	8842	4897	1.00	ref.	1.00	ref.
2004	9145	4705	.97	.93-1.01	.95	.91-.99
2005	10,080	4777	.93	.90-.97	.91	.88-.95
2006	10,518	4422	.86	.83-.90	.83	.80-.87
2007	12,545	4825	.84	.81-.88	.81	.78-.85
Sex						
Men	26,645	11,932	1.00	ref.	1.00	ref.
Women	24,485	11,694	1.11	1.08-1.13	.97	.94-.99
Age						
≤60	10,879	2554	1.00	ref.	1.00	ref.
61-70	10,559	3884	1.74	1.66-1.83	1.68	1.60-1.76
71-80	16,258	8174	2.67	2.56-2.79	2.57	2.46-2.68
>80	13,434	9014	4.14	3.96-4.33	4.07	3.89-4.26
Geographical area						
Center East	14,725	6551	1.00	ref.	1.00	ref.
Center West	11,921	5311	1.01	.97-1.05	.95	.91-.98
North	3958	1912	1.14	1.08-1.20	1.14	1.09-1.20
South	16,283	7866	1.14	1.11-1.18	1.06	1.03-1.10
Extreme South	4243	1986	1.06	1.01-1.11	1.01	.96-1.06
Type of health insurance†						
Public (low income)	36,348	17,915	1.00	ref.	1.00	ref.
Public (middle-high income	7656	2975	.72	.69-.74	.76	.73-.79
Private (high income)	3214	943	.48	.45-.52	.53	.49-.56

Abbreviations: CI, confidence interval; HR, hazard ratio; ref., reference.
*Adjusted by all variables included in the table.
†Missing = 3912.

that would improve survival compared with disadvantaged groups.

Our analysis shows geographical differences in survival after stroke in Chile, independent of sex and age distribution. These results may be explained by the number of hospitals with more resources available for the acute management of stroke at each region and by the different degrees of isolation affecting access to these medical services. For instance, Center-West and Center-East regions are located mainly in urban zones with high population density and more hospitals facilities, presenting a higher survival after stroke. Meanwhile, the South area shows higher levels of poverty, lower population density, and less hospital facilities, all of which may contribute to higher stroke mortality rate and risk factors of cerebrovascular diseases.[10] The North area is a desert mining and fishing region with relatively isolated small urban centers and few large cities, showing increased case–fatality rates, which could also be attributed to the effect of environmental toxins such as high arsenic exposure in drinking water as has been found in the city of Antofagasta[31,32] located in these region.

Our findings reveal a decreasing trend of the mortality after stroke. A systematic review of epidemiological studies of case fatality between 1980 and 2005 found a trend toward decreasing rates in high-income countries, with an annual percentage variation of 1.1%, and a lower decreasing trend in middle-low–income countries but with an annual variation of .6%.[14] A population-based study in Brazil showed that the case–fatality rate decreased from 26.6% in 1995 to 19.1% in 2005-2006.[33] According to some authors, the variables associated with this decrease were a lower incidence of severe cases[34] and also a cohort effect[35] as life expectancy in the general population was also improving. Other authors indicate that the decline in case fatality is because of improvements in the acute management of stroke, such as stroke units.[36] However, in Chile, only recently have stroke units begun to be implemented and very few patients are taken care of in these units. Since 2005, through the Regimen of Explicit Guarantees in Health, improved access to hospital admission, CT scanning, access to neurological consultation, and rehabilitation are guaranteed to all the population,[37] and this may be contributing to improve survival.

The analysis showed that survival was lower among women. However, this difference is not observed in the multivariate analysis. Some studies have reported gender differences in mortality after stroke.[38-40] The increased case–fatality rate in women is not associated with the level of care as it is with advanced age, unconsciousness at presentation (severity), depression, and deep vein thrombosis.[41] We have no data on severity, but these differences could be partly explained by the distribution of pathologic subtypes of ischemic strokes between men and women. The PISCIS study reported an increased risk of cardioembolic stroke in women, a pathologic subtype that has a higher case fatality than other subtypes.[9]

As far as we know, this is the largest study evaluating survival in patients with ischemic stroke in Chile. We used an exhaustive national register that covers hospital discharges for ischemic stroke in different facility centers from both networks of public and private health care.

One of the limitations of this study was the inability to ascertain stroke severity, which has been shown to be one of the most important short- and long-term prognostic variables in stroke.[5] Another limitation of this study was that variables reflecting the characteristics of the hospitals or the organization of health services for ischemic stroke care could not be included. However, the geographical dimension allowed us to capture the entire geographical area of Chile and differences in the served population.

In conclusion, we found that geographical area and type of health insurance affect survival of stroke patients in Chile, independently of age, sex, and period. This suggests a major impact of socioeconomic factors and access to acute management of stroke and mortality.

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