

## The influence of the day of the week of hospital admission on the prognosis of stroke patients

O dia da semana de admissão hospitalar influenciando o prognóstico de pacientes com acidente vascular cerebral

Influencia del día de la semana de admisión hospitalaria en el pronóstico de pacientes con accidente vascular cerebral

Juliana B. Barros <sup>1</sup>  
Alessandra Carvalho Goulart <sup>1</sup>  
Airlane P. Alencar <sup>1</sup>  
Paulo A. Lotufo <sup>1</sup>  
Isabela M. Bensenor <sup>1</sup>

### Abstract

*This study aimed to evaluate the weekday and weekend distribution of stroke case hospital admissions and their respective prognosis based on a sample from the Estudo de Mortalidade e Morbidade do Acidente Vascular Cerebral (EMMA), a cohort of stroke patients admitted to a community hospital in the city of São Paulo, Brazil. We ascertained all consecutive cases of first-time strokes between April 2006 and December 2008 and performed a subsequent one-year follow-up. No association was found between frequency of hospital admissions due to ischemic and hemorrhagic strokes and the specific day of the week on which the admission occurred. However, ten-day and twelve-month case-fatality was higher in hemorrhagic stroke patients admitted at the weekend. We also found that intracerebral hemorrhage patients admitted on weekends had a worse survival rate (50%) compared with those admitted during weekdays (25.6%,  $P$  log-rank = 0.03). We found a multivariate hazard ratio of 2.49 (95%CI: 1.10-5.81,  $P$  trend = 0.03) for risk of death at the weekend compared to weekdays for intracerebral hemorrhage cases. No difference in survival was observed with respect to the overall sample of stroke or ischemic stroke patients.*

Stroke; Survival; Patient Admission

### Resumo

*O estudo avaliou a distribuição de casos incidentes de acidente vascular cerebral (AVC) que procuraram hospital de 2ª a 6ª feira ou nos finais de semana no Estudo de Mortalidade e Morbidade do AVC (EMMA). O EMMA é uma coorte de pacientes com AVC em hospital comunitário da cidade de São Paulo, Brasil. Casos consecutivos de primeiro episódio de AVC internados entre abril de 2006 e dezembro de 2008 foram seguidos prospectivamente por um ano. Não houve diferença na frequência das internações por AVC isquêmico ou hemorrágico pelos dias da semana. Entretanto, a letalidade em dez dias e após um ano estava aumentada no AVC hemorrágico. Na análise da sobrevivência de um ano, pacientes admitidos nos finais de semana por hemorragia intraparenquimatosa apresentaram menor sobrevivência (50%) quando comparados aos admitidos de 2ª a 6ª (22%) ( $p$  log-rank = 0.03). Encontrou-se uma razão de risco multivariada de 2,49 (IC95%: 1,10-5,81,  $p$  tendência = 0,03) de morrer nos fins de semana em comparação ao período de 2ª a 6ª feira para hemorragia intracerebral. Não houve diferença na sobrevivência para amostra total de AVC nem para AVC isquêmico.*

Acidente Vascular Cerebral; Sobrevivência; Admissão do Paciente

<sup>1</sup> Hospital das Clínicas, Faculdade de Medicina, Universidade de São Paulo, São Paulo, Brasil.

#### Correspondence

A. C. Goulart  
Hospital das Clínicas, Faculdade de Medicina, Universidade de São Paulo, Av. Lineu Prestes 2565, Hospital Universitário, 3º andar, São Paulo, SP 05508-000, Brasil.  
alecgoulart@yahoo.com.br

## Introduction

Strokes are one of the most common causes of death worldwide. Despite the fact that 87% of stroke-related deaths occur in low-and middle-income countries <sup>1</sup>, reliable data on cerebrovascular mortality in Latin America is scarce, and most studies have concentrated on cases in small towns <sup>2,3,4,5</sup>. Stroke mortality rates in Brazil are the highest in the Americas <sup>2</sup>. Despite this fact, few studies have evaluated incidence, case fatality and stroke prevalence rates <sup>4,5,6,7</sup>.

Research in different countries has detected a variation in stroke occurrence according to the day of week on which the patient is admitted to hospital, with most studies showing that the onset of stroke is more common on Mondays <sup>8,9,10</sup>. In contrast to this data, other studies report a peak of stroke onset on Tuesdays <sup>11,12</sup> and Wednesdays <sup>13</sup>, or a mixed pattern of occurrence between Saturday and Tuesday <sup>14</sup> or Sunday and Monday <sup>15</sup>. Other studies report an increase in frequency of stroke onset on weekends among young women <sup>16</sup>. On the other hand, other studies did not observe any weekly pattern with regard to stroke onset <sup>17,18</sup>. Some studies show that different patterns occur between men and women; Wang et al. <sup>19</sup>, for example, found that frequency of stroke and cerebral infarct in men was greater on Mondays, while in women the frequency of cerebral hemorrhage was greater on Mondays and the frequency of cerebral infarction was greater on Thursdays and Fridays. In some cases, weekday variations in frequency of stroke onset according to gender occurred only in specific age groups or were associated with low socioeconomic status <sup>15</sup>. Research carried out by Manfredini et al. <sup>20</sup> using a large sample showed no differences in frequency between men and women.

Previous epidemiological studies show that risk of death is higher in stroke patients admitted to hospital on weekends than in those admitted on weekdays <sup>21,22,23,24</sup>. This phenomenon has also been observed for other diseases and has been defined by some authors as the “weekend effect”. However, the evidence supporting the weekend effect related to stroke cases is inconsistent and a number of studies confirm that no such association exists for stroke cases or for other diseases <sup>25,26</sup>.

This study aimed to evaluate the daily distribution (weekdays or weekends) and prognosis of cases of the main stroke subtypes (ischemic and hemorrhagic) using data from the EMMA (*Estudo de Mortalidade e Morbidade do Acidente Vascular Cerebral*), a cohort of stroke patients admitted to a community hospital in the city of

São Paulo, Brazil that adopts the STEPS Stroke WHO protocol <sup>6,27</sup>.

## Methods

The sample consisted of patients participating in the EMMA, a stroke assessment study conducted in the Butantan region that encompasses six districts of the city of São Paulo. This sample is representative of a local community with varying social characteristics and has been described in detail in other studies <sup>6,27</sup>.

The present study analyzes 430 stroke patients aged 35 years and over admitted to the University of São Paulo Hospital that participated in the EMMA. This study only uses data obtained in STEP 1 of the WHO protocol that consists of a hospital assessment that analyzes the risk factors associated with stroke cases and survival after 10, 28, 180 days and 12 months. First-time stroke cases (ischemic stroke and intracerebral hemorrhage) occurring between April 2006 and December 2008 were analyzed and subject to a one year follow-up conducted by the neurological liaison team. Since the number of subarachnoid hemorrhage cases was minimal this subtype was excluded from the analysis. All potential stroke patients were informed about the questionnaire, follow-up and risks of blood sample collection and medical records review to check clinically relevant information. Information, including vital status during follow-up, was updated through telephone contact, medical registers and death certificates with the collaboration of the municipal and state health offices. All participating patients signed and received a copy of a written informed consent form.

This study was approved by the hospital's Ethics Research Committee.

## Statistical analysis

Categorical variables were compared using the chi-square or Fisher exact test as necessary. Mean values were compared using ANOVA. Stroke case fatality after 10, 28, 180 days and 12 months was calculated separately for ischemic and hemorrhagic stroke cases according to the specific day of the week on which the patient was admitted to hospital. Survival was evaluated by stroke subtype (ischemic and hemorrhagic) and the specific day of the week on which the patient was admitted to hospital using a Kaplan-Meier analysis. Data was compared using the log-rank test. Age-adjusted and multivariate regressions were performed considering all other variables and significant effects on univariate analysis at the  $p \leq 0.2$  level

using the Cox proportional hazards model. All tests were two-sided, and  $p < 0.05$  was considered as statistically significant. Statistical analysis was carried out using the SPSS software version 16.0 (SPSS Inc., Chicago, USA) and the free software R (The R Foundation for Statistical Computing, Vienna, Austria; <http://www.r-project.org>).

## Results

Table 1 shows the general characteristics of the study sample by the specific day of the week on which the patient was admitted to hospital. A total of 430 first-time stroke patients aged 35 years and over admitted between April 2006 and December 2008 were included in our analysis. No variation in frequency was found between weekday and weekend admissions. Figure 1 shows stroke cases by the specific day of the week of admission. The highest frequency of stroke onset was on Tuesday (18.1%) and Thursday (16.7%) for ischemic

stroke, and Monday (20%), Thursday (20%) and Tuesday (18.5%) for intracerebral hemorrhage. No statistically significant differences in frequency of stroke subtypes across specific days of the week of admission (Monday to Sunday) ( $p = 0.59$ ) were found. Frequency of ischemic strokes was higher on weekends and frequency of hemorrhagic strokes was higher on weekdays (Monday to Friday); however these differences were not statistically significant ( $p = 0.11$ ). No statistically significant differences were found between genders. With regard to case fatality after 10, 28, 180 days and 12 months, no statistically significant difference in the number of deaths across specific days of the week of admission was found with regard to ischemic stroke. However, a statistically significant difference in case fatality after 10 days and 12 months was found with respect to hemorrhagic stroke (Table 2).

With regard to one-year survival, we found that patients admitted on weekends had a lower survival rate than those admitted on weekdays

Table 1

Baseline characteristics of 430 first-time stroke patients from the EMMA by the specific day of the week of admission to hospital.

Characteristics	Monday to Friday (n = 315)	Weekend (n = 115)	Total (n = 430)	p-value
Mean age, years ( $\pm$ SD)	67.5 (13.2)	69.5 (13.0)	68 (13.2)	0.17
Gender (%)				
Men	167 (53.0)	61 (53.0)	228 (53.0)	0.54
Race/Ethnicity (%)				
White	216 (68.8)	79 (68.7)	295 (68.6)	0.93
Afro-descendant	79 (29.0)	29 (31.2)	107 (24.9)	
Asian	7 (2.2)	2 (1.7)	9 (2.1)	
Years of education (%)				
None	61 (19.9)	23 (20.5)	84 (20.1)	0.48
1-7	155 (55.7)	48 (42.9)	203 (48.6)	
8-10	53 (17.3)	23 (20.5)	76 (18.2)	
$\geq 11$	37 (12.1)	18 (16.1)	55 (13.2)	
Hypertension (%)				
Yes	260 (82.5)	96 (83.5)	356 (82.8)	0.47
Diabetes				
Yes	88 (27.9)	26 (22.6)	114 (26.5)	0.16
Current alcohol consumption (%)				
Yes	46 (14.6)	22 (19.1)	68 (15.8)	0.16
Current smoker (%)				
Yes	116 (36.8)	47 (40.9)	163 (37.9)	0.26

Note: hypertension is defined as previous history of high blood pressure, or current treatment for hypertension; diabetes was defined as previous history of diabetes or current treatment for diabetes.

Figure 1

Ischemic and parenchymal hemorrhagic stroke cases by the specific day of the week of admission to hospital.

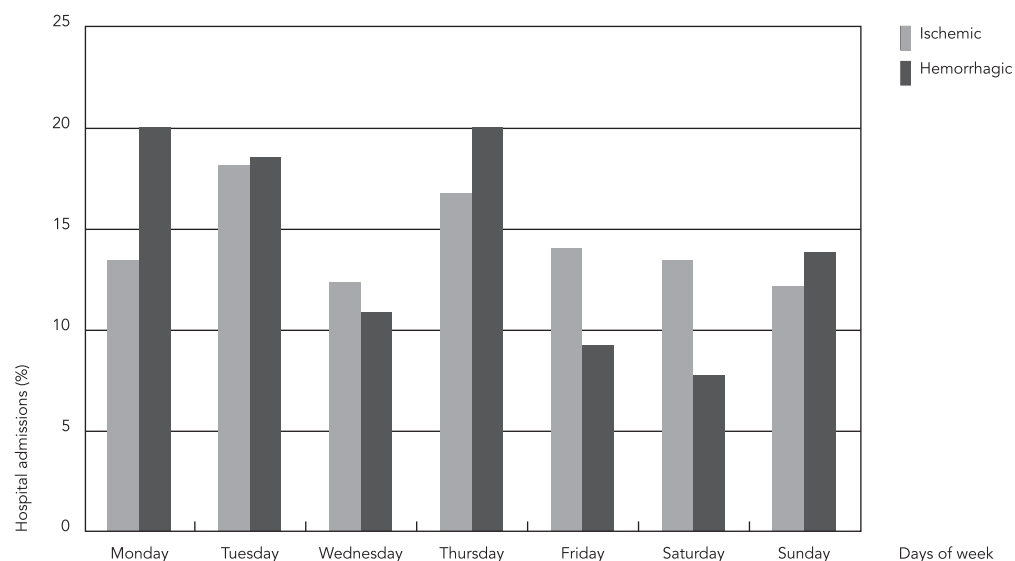


Table 2

Case-fatality after 10, 28, 180 days and the one-year follow-up in in-hospital admissions for stroke by stroke subtype (ischemic and hemorrhagic).

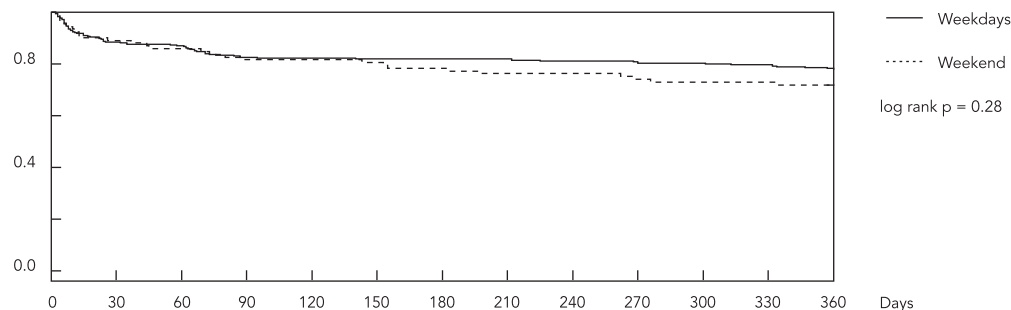
	Monday to Friday n (%)	Weekends n (%)	p-value
Ischemic			
Time of follow-up			
10 days	19 (7.0)	6 (6.5)	0.86
28 days	31 (11.4)	10 (10.8)	0.87
180 days	50 (18.4)	20 (21.5)	0.51
One-year	60 (22.1)	26 (28.0)	0.25
Hemorrhagic			
Time of follow-up			
10 days	5 (11.6)	7 (31.8)	0.047
28 days	7 (16.3)	7 (31.8)	0.15
180 days	10 (23.3)	10 (45.5)	0.07
One-year	11 (25.6)	11 (50.0)	0.049

( $p = 0.039$ ). The analysis of survival by stroke subtypes showed no statistically significant difference with regard to ischemic stroke patients (Figure 2). However, with respect to intracerebral hemorrhage, a significant difference in survival

rates was found between patients admitted on the weekend (50%, 11/22) and those admitted on weekdays (25.6%, 11/43),  $p$  log-rank = 0.03; intracerebral hemorrhage patients admitted at the weekend also had a worse prognosis than those

Figure 2

Kaplan-Meier curves showing deaths after first-ever stroke with one-year follow-up by specific day of the week of admission to hospital of ischemic stroke patients participating in the EMMA.



admitted on weekdays (Figure 3). The results of the Cox analyses demonstrate a similar pattern (Table 3) with an increased risk of death on weekends among intracerebral hemorrhage patients (multivariate hazard ratio of 2.49; 95%CI: 1.10-5.81,  $p$  trend = 0.03).

## Discussion

The frequency of ischemic strokes was highest on Tuesdays and Thursdays, while hemorrhagic strokes were more common on Mondays, Tuesdays and Thursdays. No statistically significant difference in the weekday patterns was observed between the ischemic and hemorrhagic stroke subtypes. However, risk of death from hemorrhagic stroke after 10 days and 12 months was greater for patients admitted on weekends and chance of survival from intracerebral hemorrhage was lower in patients admitted on weekends. No difference in survival was found among ischemic stroke patients.

Most studies show that the frequency of stroke onset is higher in the beginning of the week<sup>8,9,10,11,12,13</sup>. However, a number of studies show that frequency of stroke onset is higher on the weekend<sup>18,19</sup> or that a mixed pattern of frequency occurs beginning on the weekend and continuing into the beginning of the week until Monday<sup>14</sup> or Tuesday<sup>15</sup>. Our analysis showed that the frequency of strokes was lower at weekends followed by higher frequencies on Mondays, Tuesdays and Thursdays; however, these differences are small and statistically insignificant. Several authors have questioned whether

frequency is really higher in the beginning of the week or lower on the weekend<sup>11,15</sup>. The only study that observed higher frequency at the end of the week (Thursdays and Fridays) analyzed frequencies by gender and stroke subtype, finding that frequency of ischemic stroke onset on Thursdays and Fridays was highest in women<sup>19</sup>. Our study showed no statistically significant differences in frequency of the different stroke subtypes between men and women. It should be noted however that the present study may lack power of analysis when it comes to gender.

In Brazil, the only retrospective study to evaluate cardiovascular deaths (International Classification of Diseases – ICD 9; codes 390 to 459) by the day of the week of occurrence, carried out in Ribeirão Preto, State of São Paulo, showed that incidence peaked on Mondays. However, this study does not provide separate information for stroke cases<sup>21</sup>. The weekly pattern of occurrence of coronary heart disease has been widely studied and results suggest that onset frequency is highest on Mondays. However, there is no consensus on this possibility, even in the case myocardial infarction. The reasons for a possible pattern of increased stroke onset on Mondays are not clear, but may include stress associated with the beginning of weekly activities, higher blood pressure or an inadequate profile of lifestyle risk factors on Monday after weekends<sup>28</sup>. The profile of cardiovascular risk factors between the two groups in this study was very similar and the reasons for this pattern remain unclear.

The majority of studies that evaluated stroke mortality by day of week of occurrence only evaluated in-hospital mortality<sup>24,26</sup> or case-

Figure 3

Kaplan-Meier curves showing deaths after first-ever stroke with one-year follow-up by specific day of the week of admission to hospital of intracerebral hemorrhage patients participating in the EMMA.

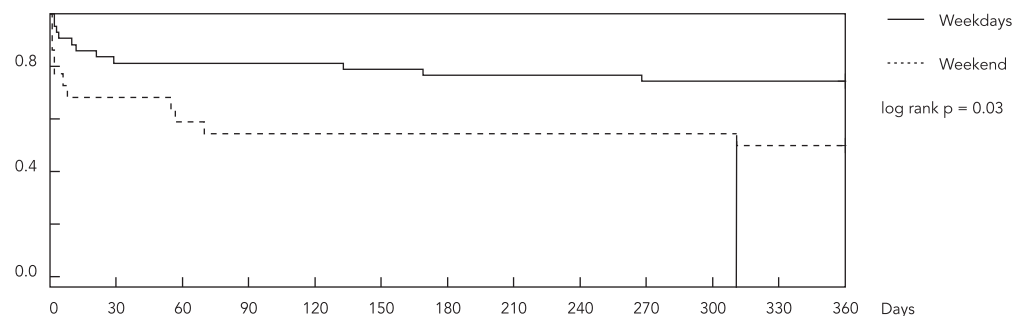


Table 3

Adjusted hazard ratios (95%CI) for fatal stroke cases by the specific day of the week of admission to hospital in the EMMA during one-year of follow-up.

Stroke (deaths/events)	Day of the week (deaths/events)		p-trend
	Monday to Friday	Weekend	
All stroke (108/430)	(71/315)	(37/115)	
Age-adjusted	Reference (1.00)	1.42 (0.95-2.11)	0.09
Cardiovascular risk factors adjusted	Reference (1.00)	1.44 (0.97-2.15)	0.07
Ischemic stroke (86/365)	(60/272)	(26/93)	
Age-adjusted	Reference (1.00)	1.18 (0.78-1.87)	0.48
Cardiovascular risk factors adjusted	Reference (1.0)	1.20 (0.75-1.90)	0.45
Intracerebral hemorrhage (22/65)	(11/43)	(11/22)	
Age-adjusted	Reference (1.00)	2.47 (1.07-5.73)	0.04
Cardiovascular risk factors adjusted	Reference (1.00)	2.49 (1.10-5.81)	0.03

Note: cardiovascular risk factors model included adjustments by age, history of diabetes, alcohol consumption and smoking status.

fatality after seven days<sup>22,23</sup>. One study carried out in a stroke center that evaluated mortality at a three-month follow-up showed no significant differences for cases that occurred during normal office hours and out of office hours<sup>25</sup>. Most studies show higher mortality among patients admitted at weekends<sup>22,23,24,26</sup>. One study concluded that weekends represent a period of increased risk of death for ischemic stroke patients, but that this increased risk appears to represent an exacerbation of underlying night-time risk present during weekdays<sup>26</sup>. Another study showed no differences in stroke mortality by day of week

of occurrence<sup>25</sup>. Our results suggest a higher ten-day and 12-month case-fatality among hemorrhagic stroke patients admitted at the weekend.

It is important to note that only one study evaluated late case fatality. A study by Albright et al.<sup>25</sup> that evaluated in-hospital and 90-day case-fatality found no differences in mortality according to day of admission by stroke subtypes (ischemic and hemorrhagic). Furthermore, most studies have only addressed ischemic stroke cases and provide no information regarding hemorrhagic strokes<sup>22,26</sup>. These studies showed that in-hospital mortality was higher in ischemic stroke

patients admitted at the weekend. One study found that mortality was higher on the weekend and showed that certain types of hospital care, such as brain scans, were less available on these days and this could explain the higher risk of mortality at weekends<sup>29</sup>. In contrast, with regard to ischemic stroke, no difference was found between in-hospital mortality rates and day of admission. However, the rate of ten-day and twelve-month case-fatality was higher among hemorrhagic stroke patients.

We found a high rate of mortality after twelve months among the intracerebral hemorrhage patients in our sample. The only study that evaluated late case-fatality (after 90 days) was that of Albright et al.<sup>25</sup>. One important difference is that they evaluated stroke fatality in a stroke unit as opposed to a community hospital and therefore differences in patient profile could explain any differences. It is possible to speculate that certain factors related to the hospital stay could be associated with the survival rates observed at the one-year follow-up. However, the effect of these factors is very small and unclear due to the small number of stroke deaths at one-year follow-up.

The weekend effect is not restricted to stroke patients and several possible explanations for this phenomenon have been given for a number of different conditions worldwide. One of the most plausible explanations is the reduced number of hospital staff and lack of availability of certain invasive procedures at weekends. Furthermore, the weekend effect may exist due to differences in the profiles of weekend and weekday stroke patients; however, this was not the case in our study because the cardiovascular risk factors and sociodemographic characteristics of the two groups were very similar. Manfredini et al.<sup>20</sup>

also suggests that patients with multiple comorbidities and more severe stroke cases are more likely to arrive at hospital at the weekend as is the case with more severe cases of acute myocardial infarction (with ST segment elevation). In our analysis, a multivariate adjustment for age and certain cardiovascular risk factors did not affect the results. However, the EMMA adopts the original protocol of WHO protocol and information regarding other cardiovascular risk factors, such as diet and physical activity, that may also influence the results and could help to explain the higher mortality from hemorrhagic strokes at the weekend, were not available.

Our study has the following advantages: it was performed at a community hospital that accounts for approximately 80% of all hospitalizations in the study region; the diagnosis of the stroke subtype was performed by a neurological liaison team using CT-scan; the present study evaluated survival after a one-year follow-up as opposed to most studies that evaluated only in-hospital mortality or seven-day case-fatality. Limitations of this study include: the exclusion of outpatients, which might be considered as a bias due to the exclusion of mild cases that do not seek medical care or more severe cases that died before being admitted to hospital; the sample size may not provide for certain stratified analyses; since this was an observational study losses (66 individuals or 15.3%) occurred during the twelve-month follow-up. Despite the latter limitation, additional missing data analysis found no significant changes to the findings described here.

Our findings show a poor twelve-month survival rate among intracerebral hemorrhage patients admitted at the weekend. This difference cannot be explained by the risk factor profile of patients that was similar in both groups.

## Resumen

*El estudio evaluó la distribución de casos incidentes de accidente vascular cerebral (AVC) que fueron al hospital de lunes a viernes o durante los fines de semana en el Estudio de Mortalidad y Morbilidad del AVC (EMMA). El EMMA es una cohorte de pacientes con AVC en un hospital comunitario de la ciudad de São Paulo, Brasil. Casos consecutivos de primer episodio de AVC internados, entre abril de 2006 y diciembre de 2008, fueron seguidos prospectivamente durante un año. No hubo diferencia en la frecuencia de las internaciones por AVC isquémico o hemorrágico durante los días de la semana. Sin embargo, la letalidad en 10 días y tras un año había aumentado en el AVC hemorrágico. En el análisis de supervivencia de un año, pacientes admitidos los fines de semana por hemorragia intraparenquimatosa presentaron menor supervivencia (50%), comparados con los admitidos de Lunes hasta Viernes (22%,  $p$  log-rank = 0.03). Se encontró una razón de riesgo multivariada de un 2,49 (IC95%: 1,10-5,81;  $p$  tendencia = 0,03) de morir los fines de semana en comparación con los lunes y viernes para la hemorragia intracerebral. No hubo diferencia en la supervivencia para la muestra total de AVC ni para el AVC isquémico.*

*Accidente Cerebrovascular; Supervivencia; Admisión del Paciente*

## Contributors

J. B. Barros performed statistical analysis, wrote the first draft of this manuscript and reformulated subsequent versions. A. C. Goulart participated in study design, performed statistical analysis and revised the final version of this manuscript. A. P. Alencar performed statistical analysis and revised the final version of this manuscript. P. A. Lotufo participated in study design, performed statistical analysis and revised the final version of this manuscript. I. M. Bensenor participated in study design, performed statistical analysis and revised the final version of this manuscript.

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