Early stroke case-fatality rates in three hospital registries in the Northeast and Southeast of Brazil

Taxas de letalidade precoce por acidente vascular cerebral em três registros hospitalares no nordeste e sudeste do Brasil

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ABSTRACT

Few studies have addressed early cerebrovascular lethality in Brazil. **Objective:** To evaluate 10 and 28-day stroke case-fatality rates in three hospitals in three Brazilian cities. **Methods:** We described the stroke registries in São Paulo, João Pessoa, and Natal. **Results:** Out of a total of 962 first-ever events (mean age, 68.1 years-old; 53% men), 83.6% (804 cases) were classified as ischemic and 16.4% (158) as hemorrhagic stroke. Overall, the case-fatality rates and 95% confidence intervals (95%CI) for hemorrhagic stroke events were higher than for ischemic events, both at 10 (12.3%; 95%CI 7.2–17.4 *versus* 7.0%; 95%CI 5.3–8.8) and at 28 days (19.8%; 95%CI 13.6–26.0 *versus* 11.1%; 95%CI 8.9–13.3). **Conclusions:** We did not find any substantial differences in early case-fatality rates according to stroke subtypes, when comparing the three centers.

Key words: stroke, lethality, hemorrhagic stroke, ischemic stroke.

RESUMO

Poucos estudos abordaram a letalidade cerebrovascular precoce no Brasil. **Objetivo:** Avaliar taxas de letalidade por acidente vascular cerebral (AVC) em 10 e 28 dias após evento em três hospitais em três cidades brasileiras. **Métodos:** Foram descritos os registros de AVC em São Paulo, João Pessoa e Natal. **Resultados:** De um total de 962 primeiros eventos (idade média de 68,1 anos; 53% homens), 83,6% (804 casos) foram classificados como AVC isquêmico e 16,4% (158) como hemorrágico. As taxas de letalidade e intervalos de confiança de 95% (IC95%) para eventos de AVC hemorrágico foram maiores que para os isquêmicos em: 10 (12,3%; IC95% 7,2–17,4 *versus* 7,0%; IC95% 5,3–8,8) e 28 dias (19,8%; IC95% 13,6–26,0 *versus* 11,1%; IC95% 8,9–13,3). **Conclusões:** Não foram encontradas diferenças substanciais nas taxas de letalidade precoce por subtipo de AVC ao comparar os três centros estudados.

Palavras-Chave: acidente vascular cerebral, letalidade, acidente vascular hemorrágico, acidente vascular cerebral isquêmico.

Despite declining stroke mortality over recent years, Brazil has one of the highest stroke mortality rates in the Americas for both genders, with a higher proportion of deaths among the poorest states in the country[1-3]. To explain the higher burden of cerebrovascular deaths, it is important to ascertain both the incidence and case-fatality rates among Brazilian macroregions. Two Brazilian population-based studies estimated the incidence and case-fatality rates for first-ever stroke in the cities of Joinville, Santa Catarina State[4], and Matão, São Paulo State[5]. In Matão, incidence rates per 100,000 inhabitants for ischemic stroke and intracerebral hemorrhage of 91.9 and 14.7, respectively, were reported. The

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30-day case-fatality rate was 18.5% and the one-year case-fatality rate was 30.9%[5]. In the study carried out in Joinville, the 30-day case-fatality for all stroke subtypes was 19.1%[4].

In our previous hospital-based registry analysis (April 2006 to December 2008) performed in the city of São Paulo[6], we found stroke subtype proportions (84.9% ischemic stroke, 15.1% intracerebral hemorrhage) that were similar to those in the studies performed in Matão and Joinville. Our results were also similar to other hospital-based registries in the Northeastern region of Brazil, in the cities of Natal, Rio Grande do Norte[7], and Fortaleza, Ceará[8]. However, the overall stroke 30-day case-fatality rate was lower (12.8%, first-ever and recurrent) than in Matão (18.5%), Joinville (19.1%) and Fortaleza (20.9%), and similar to that in Natal (10.4%)[9].

Our aim was to investigate regional differences in 10 and 28-day stroke case-fatality rates by comparing data from two public hospitals located in the Northeastern region and one in the Southeastern region of Brazil, based on the standardized World Health Organization (WHO) stepwise approach to stroke surveillance[9].

METHODS

Design and population study

The study subjects were the participants in two registries of stroke: in São Paulo, the EMMA study (Stroke Mortality and Morbidity Study); and in Natal/João Pessoa, the PRODIAVC (Diagnosis and Intervention Program in Stroke). The first of these is an ongoing prospective stroke cohort at the University Hospital of the University of São Paulo (HU-USP). Details of the EMMA cohort have been previously described elsewhere[10]. The second of these is a study involving the Monsenhor Walfredo Gurgel Hospital (HMWG) in Natal, and the Senador Humberto Lucena Emergency and Trauma Hospital (HETSHL) in João Pessoa, in the states of Rio Grande do Norte and Paraíba, respectively. All of these hospitals are public services that are free on demand.

HU-USP is a community-based teaching hospital (260 beds) in Butantã (São Paulo), a neighborhood on the west side of the city with 424,377 inhabitants (2009). This hospital provides the sole support for emergencies coming from primary care units and for paramedic ambulances in the area. Neurological referrals from this community facility are made to Hospital das Clínicas, a tertiary-care hospital located 8 km away.

HMWG is the main tertiary-care public hospital in the city of Natal. It is also a teaching hospital with 264 beds. HETSHL is a reference center for orthopedic and neurological trauma in the city of João Pessoa and has 187 beds. Among the three hospitals, this is the only one with neurosurgery service. There is no stroke unit in any of these hospitals, but all of them have intensive care units that admit stroke patients.

We gathered data on individuals over the age of 35 years with a first-ever stroke. They all had a medically confirmed diagnosis of ischemic stroke or intracerebral hemorrhage and were admitted during the following periods: from April 2006 to December 2010 in São Paulo; from January 2009 to December 2009 in Natal; and from May 2009 to October 2010 in João Pessoa.

Data gathering

The data gathering for this study was based on the WHO manual of steps for stroke surveillance, hospital phase (step 1)[9]. The baseline information included sociodemographic data such as age, gender, race (according to self-reported skin color, i.e., white, mixed or black), years of education (none or less than year, 1-7 years and 8 or more years), along with the patients' history of stroke and preexisting comorbidities, such as high blood pressure and diabetes. All the data gathered were based on self-reported information from patients or caregivers, or came from the hospital records. Furthermore, acute stroke characteristics (stroke subtype and date, and time of initial symptoms) and information on acute hospital care (delayed hospitalization and length of hospital stay) were also evaluated by trained interviewers. Vital status during follow-up (at 10 and 28 days) was updated for all participants by means of telephone interviews, medical registries, and death certificates provided by local health statistics departments.

The written informed consent was obtained from all potential stroke patients admitted to the hospitals who agreed to participate in each study center. The research protocols had previously been approved by the institutional review boards of all the centers.

Definition of stroke

Stroke was defined in accordance with the WHO criteria as "rapidly developing symptoms and/or signs of focal (or at times global) neurological alterations, and lasting longer than 24 hours (or leading to death), and of presumed vascular origin". This definition excluded transient ischemic attack and recurrent stroke. Each event was classified as being the patient's first-ever-in-a-lifetime clinically evident stroke, and it was confirmed through noncontrast computed tomography (CT) findings and a neurological evaluation during hospitalization. The stroke diagnosis was validated by physicians, who classified stroke subtypes based on the International Classification of Diseases 10th revision as ischemic stroke (ICD-10: I-63) or intracerebral hemorrhage (ICD-10: I-61). Because there were only a few cases of subarachnoid hemorrhage, these cases were not included in this analysis.

Statistical analysis

Categorical and continuous variables were compared according to the study center, using the χ^2 test and ANOVA, respectively. Age was analyzed as a continuous variable or according to age strata (35–59 years-old, 60–79 years-old

and ≥80 years-old). Age standardization was applied to the 10 and 28-day case-fatality rates using the sampling distribution of São Paulo as the default, by means of the direct method. No adjustments for sex were made, because there were no differences regarding sex distribution among the centers. Stratified analyses according to the main stroke subtypes (ischemic and hemorrhagic) were performed among the study centers. Age-adjusted logistic regression was performed to estimate the risks of death (odds ratio – OR) at 10 and 28 days, according to sociodemographic and cardiovascular factors for ischemic and hemorrhagic stroke, separately. All the tests were two-tailed, and a p-value <0.05 was considered significant with 95% confidence intervals (95%CI). The Statistical Package for the Social Sciences (SPSS) software, version 16.0, was used for the statistical analyses.

RESULTS

The total number of participants with stroke who fulfilled the inclusion criteria at baseline in the three sites was 962. The mean age at baseline was 68.1 years (standard deviation ±13.8) and 52.3% of the participants were men, independently of the originating center. Approximately 58% of the participants were white and 30%, illiterate. The highest percentages of black people and individuals with no education were reported in the city of João Pessoa, followed by Natal and then São Paulo (Table 1).

Previous disease

Most of the patients had a history of previous high blood pressure. Other preclinical conditions presented included diabetes and heart disease, accounting for approximately one quarter of the total, with no differences among the cities. Out of the 962 individuals classified as first-ever stroke cases, 98.6% had their diagnosis confirmed by CT scan and the other 1.4% had their diagnoses of stroke and stroke subtype confirmed only through clinical criteria, stated by a neurologist after a complete clinical and neurological evaluation (Table 1).

Case-fatality and risk factors associated

Table 2 shows the 10- and 28-day age-standardized case-fatality rates for total and main stroke subtypes according to the study center. Overall, hemorrhagic stroke death rates were higher than ischemic ones both at 10 and 28 days. Other than advanced age, the risk factors for ischemic stroke case-fatality at 28 days were diabetes (OR=1.69; 95%CI 1.06–2.68) and previous heart disease (OR=1.86; 95%CI 1.17–2.96) after adjustment for age. No other risk factors had a statistically significant influence on early stroke case-fatality rates according to the stroke subtype (data not shown).

Table 1. Baseline characteristics of stroke patients according to location of the study.

Characteristics	João Pessoa (n=45)	Natal (n=288)	São Paulo (n=629)	Total (n=962)	p-value*
Mean age – years (±SD)	70.1 (12.1)	67.3 (15.1)	68.3 (13.2)	68.1 (13.8)	0.357
Age strata (%)					
≤59	10 (22.2)	87 (30.2)	168 (26.7)	265 (27.5)	0.514
60–79	25 (55.6)	130 (45.1)	318 (50.6)	473 (49.2)	
>80	10 (22.2)	71 (24.7)	143 (22.7)	224 (23.3)	
Sex (%)					0.157
Male	25 (55.6)	137 (47.6)	341 (54.2)	503 (52.3)	
Race					
White	17 (38.6)	119 (41.3)	414 (67.0)	550 (57.9)	<0.001
Mixed	17 (38.6)	140 (48.6)	172 (27.8)	329 (34.6)	
Black	10 (22.8)	29 (10.1)	32 (5.2)	71 (7.5)	
Years of education (%)					
None	26 (57.8)	125 (43.4)	127 (20.6)	278 (29.3)	<0.001
1–7 years	13 (28.9)	81 (28.1)	290 (47.0)	384 (40.4)	
8 or more years	6 (13.3)	82 (28.5)	200 (32.4)	288 (30.3)	
Self-reported pre-stroke conditions (%)					
High blood pressure	35 (77.8)	240 (83.3)	503 (80.0)	778 (80.7)	0.419
Diabetes	12 (26.7)	94 (32.6)	171 (27.2)	277 (28.8)	0.227
Heart disease	10 (22.2)	66 (22.9)	154 (24.5)	230 (23.9)	0.844
Stroke diagnosis confirmed by brain CT (%)	45 (100.0)	287 (99.7)	617 (98.1)	949 (98.6)	0.199
Stroke subtype (%)					
Ischemic	33 (73.3)	247 (85.8)	524 (83.3)	804 (83.6)	0.107
Intracerebral hemorrhage	12 (26.7)	41 (14.2)	105 (16.7)	158 (16.4)	

*p-values were obtained from ANOVA for continuous variables and χ² for categorical ones. Some proportions might not add up to 100% because of rounding. CT: computed tomography; SD: standard deviation.

DISCUSSION

We found no differences in age-adjusted early case-fatality rates according to stroke subtype among the three study centers. Through analyzing stroke case-fatality according to stroke subtypes, we found that hemorrhagic stroke mortality rates were higher than ischemic ones at 10 and 28 days in almost all places, except for João Pessoa. The proportions of stroke subtypes observed in our study were quite similar to those reported in a systematic review (1970 to 2008), which was conducted in population-based studies including European countries and the USA[11].

According to this review, the prevalence rates for cerebral infarction were around 67.8 to 80.5% and for intracerebral hemorrhage, 6.5 to 19.6%. Early case-fatality rates for all strokes ranged from 17 to 30% for high-income countries and from 18 to 35% for low to middle-income countries during the period of 2000 to 2008[11]. Similar to our findings, higher proportions of ischemic than of hemorrhagic stroke events were reported from the two-population stroke registries in the cities of Joinville and Matão. However, their 30-day fatality rate estimates for all strokes were higher than those in our study (19.1 and 18.5% *versus* 12.5%)[4,5]. Moreover, the 30-day case-fatality rates for hemorrhagic stroke were much higher than our findings (41.4 and 45% *versus* 19.8%)[4,5]. These differences observed might be explained by the exclusion of hemorrhagic cases of greater severity with death before hospital admission, and by the age adjustment that was done in the case-fatality analysis of this study.

Two hospital-based studies in the Northeastern region estimated their case-fatality rates including recurrent cases, for all stroke types. In the study performed in Natal, a similar 30-day case-fatality rate for all stroke types of 10.4% was reported[7]. Another prospective survey conducted among stroke patients admitted to 19 hospitals in the city of Fortaleza estimated an in-hospital mortality rate of 20.9%[8]. Although some of our findings are similar to the registries from the Northeastern region,

some methodological differences, such as the inclusion of all stroke subtypes and of recurrent events, particularly in the Fortaleza study, make comparisons more difficult. Our high 28-day case-fatality rate for hemorrhagic stroke found in João Pessoa (24.3%) also located in the Northeastern region might be due to under-notification of mild events. Because the hospital in this city is the only one among the three studied that has a neurosurgery service, it is likely to admit more severe cases. Moreover, the small sample in this center could introduce some kind of bias into the analysis.

Most early case-fatality risk factors for hemorrhagic and ischemic stroke are well-described in the literature[6,12]. Overall, we found that advanced age, diabetes and previous heart disease were associated with a high case-fatality rate at 28 days for the ischemic subtype. However, we were not able to show any statistical differences in the distribution of risk factors according to stroke subtypes among the centers.

Even considering the methodological differences related to population-based or hospital-based studies, we found a trend of relatively low early death rates due to stroke, particularly in São Paulo and Natal. Moreover, the low early case-fatality rates found in more developed regions in Brazil might explain the hypothesis of high mortality due to high incidence rates[13] rather than high lethality[6].

Our study had some limitations. We only investigated stroke cases among people aged 35 years or over. The number of stroke cases in João Pessoa at 10 days of follow-up was very small, which may have introduced some kind of bias into the analysis. However, it is important to note that regarding the data from stroke cases in João Pessoa, the differences in the case-fatality rate were not statistically significant. In addition, we only included data from three cities in Brazil. Contrasting with this, the present study has some strength because it is the first paper to compare case-fatality rates among hospitals located in different cities in Brazil.

In conclusion, despite the sociodemographic and modifiable risk factor differences observed in our study sample, we did

Table 2. 10- and 28-day case-fatality age-adjusted* rates according to study location and stroke subtype.

10-day						
Place	Ischemic		Hemorrhagic		All	
	Death	Rate (95%CI)	Death	Rate (95%CI)	Death	Rate (95%CI)
João Pessoa	5	14.1 (2.2–26.0)	1	6.0 (-7.4–19.4)	6	13.4 (3.4–23.3)
Natal	12	4.9 (2.2–7.6)	3	8.8 (0.2–17.5)	15	5.4 (2.8–8.0)
São Paulo	40	7.5 (5.3–9.8)	15	14.4 (7.7–21.1)	55	8.7 (6.5–10.9)
Total	57	7.0 (5.3–8.8)	19	12.3 (7.2–17.4)	76	7.9 (6.2–9.7)
28-day						
Place	Ischemic		Hemorrhagic		All	
	Death	Rate (95%CI)	Death	Rate (95%CI)	Death	Rate (95%CI)
João Pessoa	7	19.8 (6.2–33.4)	4	24.9 (0.4–49.3)	11	24.3 (11.8–36.8)
Natal	20	8.2 (4.8–11.7)	3	8.8 (0.2–17.5)	23	8.4 (5.2–11.6)
São Paulo	63	11.9 (9.1–14.7)	22	22.4 (14.4–30.3)	85	13.5 (10.8–16.2)
Total	90	11.1 (8.9–13.3)	29	19.8 (13.6–26.0)	119	12.5 (10.4–14.5)

*Age-adjusted according to the population of São Paulo.

not find any substantial differences in early case-fatality rates according to stroke subtypes, when comparing three cities in Brazil. Overall, we found higher hemorrhagic stroke case-fatality rates than ischemic ones up to 28 days. Population-based studies with larger sample sizes, including different ethnic groups, should be conducted to further confirm these results.

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