Stroke Epidemiology, Patterns of Management, and Outcomes in Fortaleza, Brazil

A Hospital-Based Multicenter Prospective Study

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Background and Purpose—Little information exists on the epidemiology and patterns of treatment of patients admitted to Brazilian hospitals with stroke. Our objective was to describe the frequency of risk factors, patterns of management, and outcome of patients admitted with stroke in Fortaleza, the fifth largest city in Brazil.

Methods—Data were prospectively collected from consecutive patients admitted to 19 hospitals in Fortaleza with a diagnosis of stroke or transient ischemic attack from June 2009 to October 2010.

Results—We evaluated 2407 consecutive patients (mean age, 67.7±14.4 years; 51.8% females). Ischemic stroke was the most frequent subtype (72.9%) followed by intraparenchymal hemorrhage (15.2%), subarachnoid hemorrhage (6.0%), transient ischemic attack (3%), and undetermined stroke (2.9%). The median time from symptoms onset to hospital admission was 12.9 (3.8–32.5) hours. Hypertension was the most common risk factor. Only 1.1% of the patients with ischemic stroke received thrombolysis. The median time from hospital admission to neuroimaging was 3.4 (1.2–26.5) hours. In-hospital mortality was 20.9% and the frequency of modified Rankin Scale score ≥2 at discharge was less than 30%. Older age, prestroke disability, and having a depressed level of consciousness at admission were independent predictors of poor outcome; conversely, male gender was a predictor of good outcome.

Conclusions—The prevalence of stroke risk factors and clinical presentation in our cohort were similar to previous series. Treatment with thrombolysis and functional independency after a stroke admission were infrequent. We also found long delays in hospital admission and in evaluation with neuroimaging and high in-hospital mortality.

See related articles, pages xxx, xxx, xxx, and xxx.

Key Words: Brazil ■ epidemiology ■ South America ■ stroke care

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located in the northeastern region of the country. This is also the largest hospital-based multicenter study of stroke and its risk factors ever done in Brazil.

**Subjects and Methods**

We conducted a prospective cohort study to evaluate consecutive patients admitted with a new stroke in 19 hospitals (6 public, 4 private, and 9 mixed public and private) in Fortaleza, Brazil, from June 2009 to October 2010. Fortaleza has a total of 31 hospitals (11 public, 11 private, and 9 mixed public and private hospitals). To identify which hospitals to include in our study, all certificates of deaths attributed to any of the International Classifications of Diseases, 10th Revision codes related to stroke (I61–I69) in Year 2008 in the city of Fortaleza were obtained from the Brazilian Mortality Information System provided by the National Health Ministry. A review of these death certificates showed that 90% of the patients who died with stroke in 2008 were admitted in 19 hospitals of the region.

We used the methodology suggested by the Stroke Steps modular program of the World Health Organization (Step 1). In the first step (hospitalized cases), trained research coordinators registered daily all new stroke and transient ischemic attack (TIA) cases admitted to the 19 hospitals. We included patients with first-ever stroke and patients with recurrent stroke as long as the current admission was due to a new stroke. We excluded patients admitted with stroke who died within the first 24 hours and had no reliable medical record or neuroimaging studies on patients with epidural or subdural hematomas, or intracerebral hemorrhage secondary to tumors or arteriovenous malformation and those residing outside the city limits.

A dedicated nurse coordinator with special training in stroke reviewed the medical history of all patients. Controversial data were discussed with 2 stroke neurologists. Data collected included demographics, stroke risk factors, stroke subtypes (ischemic or hemorrhagic stroke, subarachnoid hemorrhage, and TIA), clinical presentation, modified Rankin Scale (mRS) scores (prestroke and at discharge), frequency of stroke etiology investigation, patient disposition during hospital admission (intensive care unit, stroke unit, regular ward), length of stay, frequency of treatment with thrombolysis, use of medications (antihypertensives, antplatelets, anticoagulation, and statin), frequency of in-hospital rehabilitation (physical therapy and speech therapy), and frequency of complications (pneumonia and deep venous thrombosis). The patients included in this study were followed until discharge.

The subtypes of stroke were defined using universally accepted criteria: ischemic stroke and intracerebral hemorrhage on the basis of clinical and neuroimaging findings (CT or MRI) and subarachnoid hemorrhage on the basis of clinical, neuroimaging, or cerebrospinal fluid findings. TIA was defined as a transient episode of neurological dysfunction caused by focal brain, spinal cord, or retinal ischemia, without acute infarction, with symptoms usually lasting <24 hours. Patients without neuroimaging studies were classified as having undetermined stroke. Risk factors were considered if described on the patient’s chart or if medications for known risk factors were used before hospital admission or at discharge. Stroke units were defined as an organized in-hospital facility that is entirely dedicated to the care of patients with stroke staffed by a multidisciplinary team with special knowledge in stroke care. All patients with acute stroke (<24 hours from symptom onset) were eligible for stroke unit admission depending on bed availability regardless of age and stroke severity. Patients who required mechanical ventilation were always admitted to intensive care units. The prospective study received Institutional Review Board approval. Informed consent was obtained from all patients or their next of kin.

**Statistical Analysis**

Means and SDs or medians and interquartile intervals were used to describe patients’ characteristics. One-way analysis of variance and Kruskal-Wallis test were used for comparison of continuous parametric and nonparametric variables, respectively, among stroke subtypes. Mann-Whitney with Bonferroni correction was used to compare the different groups of patients against patients with ischemic stroke. Categorical variables were compared with the χ² test. We used multiple logistic regression to investigate the influence of the different epidemiological, clinical, and management characteristics on discharge mRS scores dichotomized at 2 (mRS ≤2 versus ≥3). All variables that showed an association in the univariate analysis with a P≤0.10 were included in the multivariate analysis. A 2-tailed P<0.05 was considered statistically significant. Statistical analysis was performed with SPSS 16.0 software (Chicago, IL).

**Results**

We evaluated 2418 consecutive patients. Eleven patients were excluded from the analysis because the diagnosis of stroke or TIA was not confirmed. In the study period, a total of 3294 patients were admitted to public hospitals with a diagnosis of stroke and an estimated 823 patients to private hospitals in Fortaleza (based on a 20% frequency of the Brazilians with private health insurance). Mean age was 67.7±14.4 years; 51.8% of the patients were females. Ischemic stroke was the most frequent subtype (72.9%) followed by intracerebral hemorrhage (15.2%), subarachnoid hemorrhage (6.0%), TIA (3.0%), and undetermined stroke (2.9%). The median time from symptom onset to hospital admission was 12.9 (3.8–32.5) hours (Table 1). A total of 22% of the patients were admitted within 3 hours from symptom onset, 28.1% within 4.5 hours, and 33.8% within 6 hours from symptom onset. There was a high frequency of prestroke disability (32.6% of the patients had a mRS ≥3). Table 1 shows demographic and clinical characteristics according to stroke subtype.

Stroke risk factors according to stroke subtype are demonstrated in Table 1. Hypertension was the most common risk factor (88% of the patients), and antihypertensive use during hospital stay was frequent (82.1%; Table 2). More than one third (42.9%) of the patients had a previous stroke. Antiplatelets were used in 78.9% of the patients with ischemic stroke or TIA. Less than two thirds of the patients received heparin (including deep venous thrombosis prophylaxis; Table 2). A total of 21 patients (1.1% of the patients with ischemic stroke) were treated with thrombolysis.

Head CT scan was performed in 92.9% of the patients. The median time from hospital admission to first neuroimaging was 3.4 (1.2–26.5) hours (Table 2). Etiologic investigation for ischemic stroke and TIA was infrequently performed: 70.1% of the patients had an echocardiogram, 32.3% had an echocardiogram (transesophageal, transthoracic, or both; the frequency of each examination was not collected), 27% had carotid ultrasonography, 3.5% had a brain MRI, and 2.9%, digital angiography. Considering that a basic etiologic investigation for a patient with ischemic stroke would include at least an echocardiogram, an echocardiogram, and carotid ultrasonography, only 7.2% (42 patients) of the patients were properly investigated. Digital angiography was performed in only 30% of the patients with subarachnoid hemorrhage.

Mortality was higher in patients with intracerebral hemorrhage, undetermined stroke, and subarachnoid hemorrhage when compared with patients with ischemic stroke (Table 2). The frequency of good outcomes (mRs score ≤2) at discharge was low in all stroke subtypes (Table 2). Length of stay was similar among stroke subtypes (Table 2). A total of
### Table 1. Demographics, Clinical Presentation, and Risk Factors Between Stroke Subtypes

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>All Patients (n=2407)</th>
<th>Ischemic Stroke (n=1754)</th>
<th>ICH (n=364)</th>
<th>SAH (n=144)</th>
<th>TIA (n=73)</th>
<th>Undetermined Stroke (n=72)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>67.7±14.4</td>
<td>69.1±13.6</td>
<td>62.7±14.9*</td>
<td>58.3±15.5*</td>
<td>71.4±13.2</td>
<td>71.9±14.7</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Females, %</td>
<td>51.8%</td>
<td>50.1%</td>
<td>47.5%</td>
<td>77.1%*</td>
<td>57.5%</td>
<td>55.6%</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Whites, %</td>
<td>28.7%</td>
<td>26.8%</td>
<td>33.2%*</td>
<td>38.0%</td>
<td>42.6%</td>
<td>28.1%</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Blacks, %</td>
<td>5.5%</td>
<td>4.7%</td>
<td>11.3%*</td>
<td>3.0%</td>
<td>2.1%</td>
<td>3.1%</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Others, %</td>
<td>65.8%</td>
<td>68.5%</td>
<td>55.5%*</td>
<td>59.0%</td>
<td>55.3%</td>
<td>68.8%</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Time, h</td>
<td>12.9 (3.8–32.5)</td>
<td>14.2 (4.4–33.6)</td>
<td>6.6 (1.92–26.5)</td>
<td>16.7 (4.3–39.6)</td>
<td>4.8 (2.3–24.5)</td>
<td>16.0 (3.6–32.9)</td>
<td>0.37</td>
</tr>
<tr>
<td>From symptom onset to hospital admission, median (mean±SD [IQR])</td>
<td>36.2±116.3</td>
<td>38.7±128.33</td>
<td>21.8±39.9</td>
<td>36.1±54.8</td>
<td>48.4±139.6</td>
<td>20.6±21.2</td>
<td></td>
</tr>
<tr>
<td>Prestroke mRS ≤2</td>
<td>67.4%</td>
<td>66.8%</td>
<td>68.8%</td>
<td>67.9%</td>
<td>77.3%</td>
<td>63.2%</td>
<td>0.64</td>
</tr>
<tr>
<td>Family history of stroke</td>
<td>24.5%</td>
<td>46.3%</td>
<td>48.1%</td>
<td>43.2%</td>
<td>62.9%</td>
<td>21.1%</td>
<td>0.06</td>
</tr>
<tr>
<td>Motor symptoms</td>
<td>71.3%</td>
<td>80.7%</td>
<td>72.3%*</td>
<td>33.8%*</td>
<td>68.0%</td>
<td>17.6%</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Sensory symptoms</td>
<td>25.3%</td>
<td>28.6%</td>
<td>25.6%</td>
<td>16.2%*</td>
<td>39.4%</td>
<td>16.8%</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Speech symptoms</td>
<td>62.0%</td>
<td>70.6%</td>
<td>58.5%*</td>
<td>31.1%</td>
<td>79.2%</td>
<td>50.0%*</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Decreased LOC</td>
<td>44.0%</td>
<td>44.1%</td>
<td>55.6%*</td>
<td>63.2%*</td>
<td>36.1%</td>
<td>59.6%</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Headache</td>
<td>27.0%</td>
<td>23.0%</td>
<td>44.5%*</td>
<td>78.7%*</td>
<td>22.5%</td>
<td>9.6%</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Hypertension</td>
<td>88.0%</td>
<td>88.2%</td>
<td>91.3%</td>
<td>80.0%*</td>
<td>81.4%</td>
<td>87.5%</td>
<td>0.03</td>
</tr>
<tr>
<td>Diabetes</td>
<td>46.8%</td>
<td>48.8%</td>
<td>40.2%*</td>
<td>31.7%*</td>
<td>38.7%</td>
<td>65.1%</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>42.5%</td>
<td>43.8%</td>
<td>36.1%</td>
<td>32.1%</td>
<td>60.0%</td>
<td>28.6%</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Smoking</td>
<td>30.6%</td>
<td>31.0%</td>
<td>26.8%</td>
<td>44.4%*</td>
<td>19.3%</td>
<td>20.0%</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Previous stroke</td>
<td>42.9%</td>
<td>46.2%</td>
<td>33.3%*</td>
<td>17.7%*</td>
<td>32.1%</td>
<td>65.6%</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>14.9%</td>
<td>16.6%</td>
<td>7.6%*</td>
<td>5.0%*</td>
<td>27.7%</td>
<td>7.0%</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

ICH indicates intracerebral hemorrhage; SAH, subarachnoid hemorrhage; TIA, transient ischemic attack; IQR, interquartile interval; mRS, modified Rankin Scale; LOC, level of consciousness.

*P<0.0125 when compared with the reference category (ischemic stroke) after adjustment with Bonferroni correction.

Discussion

In our cohort, we found that the prevalence of stroke risk factors was similar to those in series previously reported in Latin America,20,21 Conversely, as compared with other national and international studies, investigation of stroke etiology was less common, time to neuroimaging and time to hospital admission were increased, treatment with thrombolysis was less frequent, and frequency of poststroke disability was higher.4,5,22–27 Our findings of frequent incomplete investigation of stroke etiology and worse stroke outcomes corroborate our hypothesis that the previous studies performed in Brazil on stroke epidemiology and patterns of treatment were not representative of the country as a whole. Overall, epidemiology of stroke, including age, gender, and the prevalence of stroke risk factors, was similar to the other studies published in Latin America. A few discrepancies, however, are worth noting. Our findings, like other Brazilian studies, did not confirm the high frequency of intracerebral hemorrhages found in other stroke series in South America.4,8,28,29 This important difference probably justifies considering Brazilians separate from Hispanics in multicenter trials. Another possibility is that the difference in the frequency of hemorrhages found in our patients reflects a bias of selection of the most severely affected cases in other series neglecting the less severely affected and more difficult to recognize ischemic strokes. Also of remark, like some...
community-based series in Brazil, we showed a higher frequency (>40%) of previous stroke and consequent previous disability than that observed in other countries, probably reflecting genetic, environmental, or sociocultural factors but most likely reflecting poor secondary prophylactic measures.4,6,8,21,30 Prestroke disability (mRS) >3) was also an independent predictor of poor outcome in our series. Measures to assure more efficacious control of risk factors like gratuitous distribution of antihypertensive medications and adequate identification and treatment for patients with atrial fibrillation and carotid stenosis could have a tremendous impact in lowering the risk of stroke recurrence.

The investigation of stroke etiology was frequently suboptimal. Less than 10% of our patients with ischemic stroke were properly evaluated to exclude cardioembolic and large artery atherosclerotic sources. The presence of carotid stenosis and the presence of cardiac or aortic embolic sources were therefore not appropriately excluded in most of our patients. Even simple and inexpensive diagnostic tests like electrocardiograms were not routinely performed. In patients with subarachnoid hemorrhage, the low number of patients investigated with digital angiography was worrisome, because vessel imaging is critical for the diagnosis and correct treatment of the bleeding source.31 This deficiency of appropriate clinical investigation might reflect the lack of training in stroke management by internal medicine doctors in the region studied, because most of our patients were admitted to hospitals underserved by neurologists. This explanation is supported by a study done in a large academic hospital in São Paulo, in which all patients with ischemic stroke had a complete work-up if admitted to the neurology wards, whereas only 33% if admitted to the emergency department.6 Another explanation for the incomplete evaluation of our patients could be the unavailability of diagnostic tests in some of the hospitals studied.

The frequency of undetermined strokes (patients not evaluated with neuroimaging) in our patients was similar to other series.8,21 Undetermined strokes represented a group with peculiar characteristics: a very high prevalence of previous diabetes, less frequent speech and motor symptoms at presentation, and a high in-hospital mortality rate (43.3%). Patients with undetermined strokes received lower standards of care when compared with other groups (less frequent intensive care unit and stroke unit admission; less frequent treatment with antiplatelets, statins, antihypertensives, and deep vein thrombosis prophylaxis). It is possible that those patients had previous comorbidities not captured by our study (eg, terminal diseases) that limited further investigation or that those patients were not investigated simply because of low standards of stroke care.

Length of stay was an average of 15 days for ischemic and hemorrhagic stroke and 6 days for TIs, both longer than that previously described in international and Brazilian series.8,32,33 Higher quality of care during the early phase of stroke was shown to be associated with shorter length of stay.34 Delays in complimentary evaluations is the most feasible explanation for the prolonged admission time in our patients, which not only significantly increases the costs for stroke care, but also increases the risks for infection, deep vein thrombosis, and recurrence in patients with suboptimal treatment and evaluation.32,33 In Brazil, the lack of availability of rehabilitation hospitals also probably plays a role in explaining longer stroke admissions.
The overall thrombolysis rate in our patients was below that of developed countries and much lower than those of reference stroke centers. In Brazil, the percentage of patients who have access to thrombolysis is quite low aside from a few strategic, and mostly private, hospitals located in the southeast and south regions, the wealthiest regions of the country. Most patients with stroke in Brazil are treated in public hospitals, where protocols for the use of thrombolysis are not routinely available. Another obstacle to thrombolysis in Brazil is the lack of lay knowledge, even in individuals with a higher level of education, higher socioeconomic status, and private healthcare coverage, about stroke signs and symptoms leading to delays in hospital admission.

The frequency of poststroke disability was higher in our patients than in previous international and national series. In-hospital mortality was similar to long-term follow-up mortality rates in other Brazilian series. Acute stroke is a heterogeneous disease with respect to prognosis. In fact, the ultimate outcome in patients with stroke depends on several variables, of which important ones are demographic characteristics, the presence of underlying medical disorders, size and location of the lesion, and specific therapies administered. The finding of high in-hospital mortality in our patients could reflect the limited access to hospital care for patients with less severe strokes; due to insufficient number of hospital beds, it is possible that only the more severe strokes were admitted. Alternatively, the high incidence of disability and mortality could reflect low standards of care for patients with acute stroke combined with the admission of more severe cases. The low rates of treatment with thrombolysis, the low frequency of treatment with antiplatelets for patients with ischemic stroke and TIA, the long delays in hospital admission and in evaluation with neuroimaging, and the lower frequency of admission to stroke units suggest that suboptimal care be the most likely explanation.

Our study has some limitations. Our data are restricted to patients hospitalized, and our conclusions, to discharge outcomes because long-term follow-up was not performed. Additionally, we do not have data on stroke severity at admission, which is an important determinant of outcome in series of patients with stroke. Although it is possible that the high in-hospital mortality rate seen in our patients reflects a higher frequency of more severe strokes than in other series, the level of consciousness at admission, as a surrogate for stroke severity, suggests that it was not the case. Finally, ischemic stroke etiologic classification (eg, Trial of ORG 10172 in Acute Stroke Treatment criteria), important to support appropriate treatment decisions, was not available due to the infrequent complementary investigation performed in our patients.

Summary
In conclusion, our study was the largest epidemiological prospective study of stroke done in Brazil and evaluated patients in an underprivileged region of the country. Brazil is known as a country of great disparities. This is also true when we compare the data available for stroke mortality and patterns of care from different parts of the country. Although some regions share the same stroke epidemiology and characteristics of acute care management of developed countries, others urgently need effective health policies to improve acute stroke care.

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Disclosures
None.

References


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SUPPLEMENTAL MATERIAL
Figure 1 (S1): Univariate predictors of poor functional status (modified Rankin scale 3-6) at discharge. mRs: modified Rankin scale
Figure 2 (S2): Factors independently associated with functional outcome (mRS scores 3–6 at 6 discharge) on a multivariate logistic regression model.