An Epidemiological Study of Stroke Hospitalizations in Maputo, Mozambique

A High Burden of Disease in a Resource-Poor Country

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Background and Purpose—Already a major cause of death and disability in high-income countries, the burden of stroke in sub-Saharan Africa is also expected to be high. However, specific stroke data are scarce from resource-poor countries. We studied the incidence, characteristics, and short-term consequences of hospitalizations for stroke in Maputo, Mozambique.

Methods—Over 12 months, comprehensive data from all local patients admitted to any hospital in Maputo with a new stroke event were prospectively captured according to the World Health Organization’s STEPwise approach to stroke surveillance program. Disability levels (pre- and posthospital discharge) and short-term case-fatality (in-hospital and 28 days) were also studied.

Results—Overall, 651 new stroke events (mean age 59.1 ± 13.2 years and 53% men) were captured by the registry with 601 confirmed by CT scan (83.4%) or necropsy (8.9%). Crude and adjusted (world reference population) annual incidence rates of stroke were 148.7 per 100 000 and 260.1 per 100 000 aged ≥25 years, respectively. Of these, 531 (81.6%) represented a first-ever stroke event comprising 254 ischemic (42.0%) and 217 (36.1%) an intracerebral hemorrhage. Before admission, 561 patients (86.2%) had hypertension and 271 (41.6%) had symptoms for >24 hours. In-hospital and 28-day case-fatality were 33.3% and 49.6% (72.3% for hemorrhagic stroke), respectively. From almost no preadmission disability, 64.4% of 370 survivors at 28 days had moderate-to-severe disability.

Conclusions—The burden of disease associated with stroke is high in Maputo, emphasizing the importance of primary prevention and improvement of the standards of care in a developing country under epidemiological transition. (Stroke. 2010;41:2463-2469.)

Key Words: Mozambique ■ population surveillance ■ stroke

The global incidence of stroke is estimated to be approximately 15 million new acute strokes per year, two thirds of which occur in low- and middle-income countries. Its impact tends to grow along with the potential for prolonged life expectancy and increasing exposure to major stroke risk factors, namely hypertension, obesity, diabetes, and smoking. Stroke is a major cause of death and disability with motor and cognitive impairment leading to important losses in the patient’s quality of life. Ranking as the second leading cause of death worldwide, with 5.8 million fatal cases per year, stroke is now recognized as an important cause of death also in sub-Saharan Africa. Low standards of care, limited access to health services and pharmacological treatment, and delay in hospitalization enhance the impact of stroke in African countries.

In Mozambique, one third of the adult population is hypertensive, among whom only 7.7% are under pharmacological treatment. The prevalence of obesity is 4.8%, and approximately one third of the population consumes tobacco. In 1994, cerebrovascular diseases were already the sixth cause of death in individuals aged 15 to 59 years and the first among those >60 years in Maputo. Stroke surveillance is essential to plan future resources that are needed to meet the increasing health service needs.

This study used the World Health Organization’s (WHO) STEPwise approach to Stroke surveillance (STEPS Stroke)
methodology to estimate the incidence of stroke hospitalization, the epidemiological features of stroke events, and the 28-day case-fatality rate and disability status in Maputo, Mozambique.

Methods
The present investigation follows the STEPS Stroke protocol, Step 1 (registration of hospitalized patients) and followed the manual Version 2.0. A published pilot study allowed training of the research team and the testing of the translated version of the STEPS Stroke questionnaire.

During a 12-month period (August 1, 2005, to July 31, 2006), all patients admitted to any governmental or private hospital in Maputo (the Maputo Central Hospital, 3 general public hospitals, the Military Hospital, and 6 private clinics), living in town for >12 months, and suspected of having an incident stroke event were registered. To improve data capture, cases could also be identified retrospectively either by information obtained from their attending physician or by autopsy, but most stroke events (97%) were identified prospectively.

Case Definition
Stroke was defined according to the World Health Organization clinical definition: “a focal (or at times global) neurological impairment of sudden onset, and lasting more than 24 hours (or leading to death), and of presumed vascular origin.” The study aimed to register only incident stroke events (symptoms onset within the time period of the study). Both first-ever and recurrent stroke events were registered. New symptoms were counted as a recurrent stroke event, when occurring in the same arterial distribution >29 days previously, or occurring unequivocally in a different arterial territory from an earlier one occurring in the previous 28 days. Events occurring before the onset of the study period were not considered in the analyses and are described as old strokes. Events were confirmed clinically and, in 92.3% of the cases, either by CT scan or by necropsy, which allowed categorization regarding type of stroke: ischemic, intracerebral hemorrhage, or subarachnoid hemorrhage. HIV infection status was assessed only when stroke-like presentations likely to be related with HIV were suspected. All stroke events were accounted for regardless of the patients’ HIV infection status.

Data Collection
When the patient reached a health care facility, the STEPS Stroke questionnaire was administered. Trained interviewers were permanently stationed at the emergency department of the Maputo Central Hospital and were responsible for data collection. In other emergency departments, 1 trained nurse in each shift was in charge of collecting information on suspected stroke events. Questionnaires were usually administered in the presence of a next of kin. In each medical ward, 1 trained physician with clinical experience in cerebrovascular diseases was responsible for admitted patients with stroke.

Disability before stroke was evaluated using the modified Rankin Scale. Determination of a first-time or a recurrent stroke event was based on self-report, a review of medical records, and by checking current CT scan images or necropsy reports for evidence of previous stroke. Assessment and pharmacological treatment during admission, prescribed treatment at discharge, biochemical tests, and complications during the hospital stay were recorded. At discharge, the patient’s destination was determined and modified Rankin Scale calculated.

Hypertension and diabetes were considered present when reported by the patients or their next of kin or when pharmacological treatment was prescribed on an inpatient or postdischarge basis. The presence of dyslipidemia was defined based on questionnaire evaluation. Atrial fibrillation was assessed through an electrocardiogram performed at baseline or during the in-hospital stay.

All in-hospital deaths were registered and surviving patients’ survival status established at 28 days (including date of any subsequent death). In surviving patients, vital and disability status (using the modified Rankin Scale) was established at Day 28 during a prescheduled outpatient visit or by phone call.

Statistical Analysis
Stroke incidence rates were computed for the Maputo City population aged ≥25 years according to the 2007 Census and age-standardized incidence rates were computed by the direct method using the World Health Organization world population as a reference.

Patients with stroke were described and compared according to gender and stroke subtype using the χ² or the Fisher exact test, as appropriate, for proportions, and the Kruskal-Wallis test for quantitative variables. The small number of events in nonblack subjects precluded stratified analyses by race. In-hospital mortality was calculated as a cumulative incidence. With loss to follow-up of 22 patients, the 28-day case-fatality rate was quantified through Nelson-Aalen estimates of the cumulative hazard function. All analyses were conducted using STATA, Version 9.2 (Stata Corporation, College Station, Texas).

Ethics
The study protocol was approved by the National Mozambican Ethics Committee and written informed consent was obtained for all participants.

Results
During the 12-month study period, 825 patients were suspected of having a stroke. Of these, 174 (21.1%) were excluded, mostly because they corresponded to old stroke events (23.0%) or transient ischemic attacks (22.4%) or were due to HIV-related cerebral infections (15.5%). Therefore, 651 incident cases were identified, corresponding to an incidence rate of 148.7 per 100 000 person-years and an age-standardized incidence rate of 260.1 per 100 000 person-years in subjects aged ≥25 years.

Among incident cases, 531 patients (81.6%) were classified as having a first-ever stroke and the remainder (n=120) as “recurrent” events due to evidence of their surviving at least 1 previous stroke. Very few patients (n=50 [7.7%]) were diagnosed without a confirmatory imaging technique or necropsy. Overall, 601 cases (92.3%) were confirmed either by CT scan (83.4%) or necropsy (8.9%). From these, 351 (58.4%) ischemic, 242 (40.3%) hemorrhagic, and 8 (1.3%) subarachnoid hemorrhages were identified (Figure 1). The frequency of ischemic events increased continuously with age with higher rates among men aged 45 to 64 years. The incidence of hemorrhagic stroke rose more modestly and only up to 74 years (declining thereafter). In subjects aged >54 years, men had the highest observed rates (Figure 2).

Nearly 15% of the stroke events occurred in subjects aged <45 years and approximately one fourth in those aged 45 to 54 years. Almost 60% of patients arrived to the hospital on the same day of symptom onset; only 57% arrived >7 days thereafter. From the 543 patients with stroke confirmed by CT scan, 21.2% were scanned within 24 hours of symptom onset, 68.3% between 24 hours and 7 days, and 10.5% >1 week after stroke.

Patients with hemorrhagic stroke were significantly younger than those with an ischemic event overall: mean difference of 6 to 7 years for first-ever and recurrent cases, respectively, with the latter 3 to 4 years older overall (P<0.001 for all comparisons). However, there were few differences according to gender, race, or education level.

The
proportion of patients arriving to the hospital on the same day as symptom onset was markedly higher for hemorrhagic events, particularly in first-ever strokes (22% absolute difference; \(P < 0.001\)) compared with recurrent cases (11% absolute difference; \(P = 0.540\)). The most prevalent risk factor was hypertension (86.6% to 96.0% of patients with stroke) being present in almost every hemorrhagic case presentation. Atrial fibrillation was more frequent among ischemic event patients (Table 1).

Overall in-hospital mortality was 33.3% and more than double for those presenting with a hemorrhagic event. Subsequently, 254 patients (101 ischemic and 133 hemorrhagic stroke events) died during 28-day follow-up, estimated case-fatality rates of 32.9%, 47.7%, and 49.6%, respectively at the 7th, 14th, and 28th days. The median in-hospital stay was 6 days for the whole sample, 3 days for inpatient case-fatalities and 7 days for those discharged alive. Hemorrhagic events were associated with 2- to 3-fold higher case-fatalities, but there were no meaningful gender differences in survival (Table 2; Figure 3).

Less than 1% of the patients with a first event and 7% with a recurrent stroke had moderate to severe (scored 4 on the modified Rankin Scale) or severe disability (scored 5 on the modified Rankin Scale) before the current event (Table 1). In the 432 patients evaluated at discharge, moderate disability (score 3 on the modified Rankin Scale) was observed in 20.6% (20.1% ischemic versus 21.8% hemorrhagic cases), moderate to severe disability in 49.3% (46.5% versus 56.4%), and 12.7% (11.6% versus 15.3%) were severely disabled. Among the 370 patients alive at 28 days, 27.8% (27.4% ischemic versus 28.0% hemorrhagic cases), 27.6% (28.6% versus 26.2%), and 9% (7.7% versus 12.2%) had moderate, moderate to severe, and severe disability, respectively. Most patients (97.9%) were discharged home.
Discussion

These unique data show the burden of disease associated with stroke is high in Maputo. In 1 year, 148.7 per 100,000 inhabitants sought medical care for incident stroke. In-hospital mortality and 28-day case-fatality were 50% and 70%, respectively, for hemorrhagic events, representing one third of all cases. More than one third of survivors had moderate to severe or severe disability at follow-up.

This study successfully followed STEPS Stroke for standardized data collection, benefited from the training of the
Mozambican research team and interviewers during the pilot study, and a large number of collaborators in the public and private hospitals in Maputo were involved to ensure data capture on any suspected stroke. Regarding the confirmation of stroke subtype through CT scan or necropsy evaluation, the survey had the expected yielding for a low-income country and it also showed the feasibility of a 28-day follow-up in this setting. These data do, of course, have their limitations.

Step 1 of STEPS Stroke is hospital-based and our study can only provide a lower estimate range for the overall incidence of stroke in Maputo. Conversely, it is likely to overrepresent more severe events. The extent to which our estimates are biased depends on the access of the population to medical care and in particular the likelihood of eligible patients with stroke being admitted to an institution involved in this study.

In Mozambique, a small in-hospital stay fee is due, but people with scarce resources do not pay. Patient transportation to hospital facilities, however, is problematic, although this is expected to be less important in the capital than in the rest of the country.

Only subjects living in Maputo ≥12 months were eligible, and therefore stroke events among recent immigrants and long-term emigrants were not considered, minimizing biases introduced by internal and external migrations. The seeking of health care in hospitals outside Maputo is unlikely, because in the adjacent province, there are no central hospitals and only 2 small regional hospitals with no emergency medicine available to serve a population 10% larger and spreading over an area 87-fold larger than Maputo City. In the African culture, stroke is attributed to a supernatural force requiring intervention by a traditional healer (at least in the first days of symptom onset), although individuals with severe symptoms are expected to seek medical care regardless of their cultural beliefs or ability to recognize the stroke event. These local customs may bias our sample, to an extent that is difficult to predict, toward the underestimation of less severe ischemic and overestimation of the most severe hemorrhagic strokes.

In the absence of routine mortality statistics, the limitations of this hospital-based approach could be partially overcome by analysis of death certificates as previously accomplished to estimate the burden of disease in Maputo City, although suboptimal completeness and the veracity of attributed cause of death remain a concern.

Population-based surveys conducted in low-resource settings yielded overall adjusted incidence rates ranging from 68 first-ever strokes per 100 000 inhabitants in Zimbabwe (world standard population; ages ≥20 years) to 151 per 100 000 inhabitants in Maputo.

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Table 2. Stroke-Related, Short-Term Case-Fatality According to Case Presentation

<table>
<thead>
<tr>
<th></th>
<th>First-Ever Events*</th>
<th>Recurrent Events*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All Events (n=651)</td>
<td>Ischemic (n=264)</td>
</tr>
<tr>
<td>Intra-hospital mortality</td>
<td>33.3 (29.7 to 37.1)</td>
<td>17.4 (13.0 to 22.5)</td>
</tr>
<tr>
<td>7-day case-fatality‡</td>
<td>32.9 (28.4 to 38.0)</td>
<td>16.2 (11.9 to 22.2)</td>
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<tr>
<td>14-day case-fatality‡</td>
<td>47.7 (42.1 to 54.1)</td>
<td>26.0 (20.2 to 33.4)</td>
</tr>
<tr>
<td>28-day case-fatality‡</td>
<td>49.6 (43.8 to 56.2)</td>
<td>27.4 (21.4 to 35.1)</td>
</tr>
</tbody>
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*Includes those subjects with available information regarding the stroke subtype (ischemic or intracerebral hemorrhagic event). †Data are presented as percentage (95% CI).
‡Nelson-Aalen cumulative hazard estimates.

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Figure 3. Cumulative hazard of death estimates by main stroke subtype and gender.
100 000 in Martinique\textsuperscript{15} (European standard population; all ages). In Maputo, the incidence of stroke hospitalization is in the upper range of these estimates from other non-African developing settings. Severe hypertension\textsuperscript{18} and related end-organ damage, alcohol consumption,\textsuperscript{7} and HIV-related vascular inflammation\textsuperscript{19} are prevalent in young individuals and add to the pyramid-shaped age distribution of the Mozambican population,\textsuperscript{11} contributing to the low mean age at stroke diagnosis in Maputo. This is 10 to 15 years lower than in high-income settings\textsuperscript{20} in accordance with that observed in other low-income countries.\textsuperscript{4,21} The differences in age-specific incidence rates of hemorrhagic and ischemic strokes are in accordance with previous observations\textsuperscript{17} and reflect etiologic differences between these nosological entities, survival bias, and the hospital-based nature of the present survey. The high prevalence of HIV infection in Mozambique (16\% in 2007\textsuperscript{22}) contributes to a high frequency of ischemic strokes at young ages.\textsuperscript{19} Hemorrhagic stroke is more strongly associated with hypertension\textsuperscript{18} and subjects with severe hypertension are at a higher risk of both stroke and early death, which contributes to the peak of hemorrhagic stroke incidence at 65 to 74 years and its subsequent decline. On the other hand, these estimates reflect the incidence of stroke events reaching the hospitals, and hemorrhagic strokes, more disabling and lethal,\textsuperscript{2} are more likely to be missed by a hospital registry, especially those occurring in older subjects. This is also reflected in the smaller delay from symptom onset to hospitalization observed in our study for these cases. Small hemorrhages may have been missed in patients scanned long after the stroke, but the proportion of CT scans performed >7 days after stroke was relatively low and is unlikely to meaningfully influence our estimates. A higher proportion of intracranial hemorrhages has been observed in hospital-based studies, ranging from 19\% to 60\%,\textsuperscript{23} whereas that reported in population-based surveys was <15\%,\textsuperscript{15,16,24} Our investigation yielded a proportion twice higher than observed in the recent STEPS Stroke multicenter survey (including 2 African centers),\textsuperscript{4} and both the high stroke incidence rate and the high proportion of hemorrhagic stroke events in Maputo are largely justified by the high prevalence of hypertension in Mozambique along with the low awareness and poor compliance with antihypertensive therapies.\textsuperscript{3} In accordance to our data, a recent South African study based in a single hospital yielded a 27\% proportion of hemorrhagic events and mean age of 51 years among black patients.\textsuperscript{21}

The early stroke case-fatality is similar to that observed in other African hospital-based studies (1 week: 35\% in South Africa\textsuperscript{2}; 1 month: 54\% in Gambia,\textsuperscript{25} 33.6\% in Nigeria\textsuperscript{26}), reflecting the scarce human, technical, and pharmacological resources. Patients are cared for in a general medical ward and not in stroke units, and thrombolyis is not available for acute management of stroke in Maputo. Only 1 CT scan device is available for 1 000 000 inhabitants, which is reflected in the lack of imaging confirmation in nearly one fifth of the patients and the delay in the evaluation of the remaining. Moreover, our results highlight important gaps in secondary prevention due to insufficient access to pharmacological treatment and poor monitoring of health conditions after diagnosis. Poor access to tertiary prevention and palliative care is also a concern, because in Maputo, there are no institutions to care for disabled poststroke patients, and virtually all return home after discharge. Physical rehabilitation therapy is free of charge, but transportation needs to be assured by the patient, which limits the access to those with higher socioeconomic status. Overall, these results are in accordance with Mozambique being among the countries with higher risk of adult mortality.\textsuperscript{27}

Summary

Our systematic surveillance approach showed a high burden of stroke morbidity and mortality in a developing country still struggling with the burden of infectious diseases. Specifically, it provides invaluable information about the antecedents and dismal consequences of stroke in Maputo. The country’s economical deprivation and resource limitations clearly impact on our ability to apply effective stroke prevention, acute management, and subsequent management/prevention. Overall, stroke represents a significant and increasing burden resulting from epidemiological transition in Mozambique.

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Disclosures

A.D. received grants and is consultant/advisor of the African Regional office of the World Health Organization.

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