

Management of The Acute Serious Strokes in Sub-Saharan Africa: Case of Togo

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ABSTRACT

Introduction: Serious strokes are a particular evolutive form of strokes. They present significant diagnostic and therapeutic challenges.

Objectives: To describe diagnostic and therapeutic aspects of acute serious strokes.

Methods: A prospective cohort study was carried out from January 1st 2015 to December 31st 2016 (2 years) at neurology department of University Hospital Campus. It included patients with acute serious strokes. Clinical features, brain imaging findings, therapeutic measures and outcome were evaluated.

Results: Of the 1964 strokes diagnosed, there were 163 cases of acute serious strokes (8.3%). Among of the latter, it was noted 100 (61.3%) hemorrhages and 63 (38.7%) arterial infarcts. Supra tentorial damage location was predominant (77.3%). Main etiologies of hemorrhages and arterial infarcts were, respectively, hypertension (83.5%) and atherosclerosis of large arteries (84.1%). Rates of patients hospitalized within 4:30 hours (arterial infarcts) and 8:00 hours (hemorrhages) were, respectively, 20.6% and 40%. In the same time ranges, rates of CT scan performing were 4.8 and 6% in patients with arterial infarcts and hemorrhages, respectively. Minimum resuscitation measures and active therapies were implemented in patients. Mortalities in 7 and 15 days were, respectively, 32.5% and 12.3%. Overall mortality (44.8%) was correlated with diagnosis and treatment delay, and active therapy limitations, in addition to the predictive factors of mortality.

Conclusion: Real problems of acute serious strokes management remain in Togo. They have a negative effect on the vital and functional prognosis. Because of that, it is important to strengthen therapeutic management resources and preventive measures.

Keywords

Serious strokes, Diagnosis, Treatment, Sub-Saharan Africa, Togo.

Introduction

Severity of strokes is variable. Serious stroke is defined as a stroke that is life-threatening and/or will cause disabling sequelae [1,2].

Serious strokes have some peculiarities that can justify the admission of patients at the intensive care unit and neurovascular

intensive care unit. Their management requires the use of targeted active therapies, such as thrombolysis/thrombectomy and endovascular treatment, in addition to resuscitation measures [3,4].

Only a small ratio of patients with serious strokes is hospitalized at intensive care unit and neurovascular intensive care unit [3]. Management of targeted active therapies is limited and carried out at neurology departments. This management is often encouraged by parents who take into account unfavourable vital and functional

prognosis. Palliative approach observed in nearly 53% of cases is decided within 24 hours [5].

In sub-Saharan Africa, palliative approach is almost systematic and global, because neuro-diagnostic (CT scan, MRI and angiography) and therapeutic (neurovascular intensive care unit, thrombolysis and/or thrombectomy) resources are limited [6,7]. Because of that, challenges related to acute serious stroke management are numerous.

In sub-Saharan Africa, serious stroke data reported in literature result from search released at intensive care units [6,8]. Those which come from neurology departments without neurovascular intensive care unit are missing.

In this paper, we focus on acute serious stroke management at neurology department of University Hospital Campus of Lomé. Our department has not a neurovascular intensive care unit. The purpose of this study is to describe diagnostic and therapeutic aspects.

Methods

This prospective cohort study focused on patients with acute serious stroke. It was conducted, from January 1st 2015 to December 31st 2016, at neurology department of University Hospital Campus of Lomé.

Serious stroke was defined as a stroke in which:

- National Institute of Health Stroke Score and Glasgow Score were, respectively, higher 17 and lower 9;
- neuroimaging revealed:
 - for the case of hemorrhages, the meningeal hemorrhage classified as stages 3 and 4 according to the Fisher classification, posterior fossa hemorrhage, cerebral hemorrhage with ventricular flood and mass effect/axial involvement;
 - for the case of arterial infarcts, the damage of posterior fossa structures and/or extensive cerebral damage related to the occlusion of large arterial trunks with cardio embolic or atheromatous origin [1,2,9-11].

In addition, serious strokes were grouped into two classes:

- very serious strokes in which ranges of National Institute of Health Stroke Score and Glasgow Score were, respectively, 17–20 and 7–9;
- extremely serious strokes in which National Institute of Health Stroke Score and Glasgow Score were, respectively, higher 20 and lower 7.

Diagnoses of serious strokes were based on neuroimaging and clinical features [1,2]. CT scan was released in all patients in the first position. MRI without axial diffusion sequence owing to low magnetic field (0.5 tesla) was performed in delayed time.

Clinical variables were: clinical history; modifiable cardiovascular risk factors; inaugural symptomatology; depth of loss consciousness; Glasgow Score and National Institute of Health

Stroke Score; arterial pressure and temperature at hospital admission; information from brain imaging. In the case of the variable "information from brain imaging", it was noted:

- in the case of hemorrhages: the anatomical localization (meningeal or parenchymal); the extension in height (cortico-subcortical or to the brainstem if supratentorial location; bulbar, protuberant or peduncular if localization at the brainstem); the possible presence of complications (ventricular contamination or flood, axial involvement, hydrocephalus). Extent of parenchymal lesions was determined using volume and maximum transverse diameter;
- in the case of arterial infarcts, the topography according to the affected arterial territory. Carotid artery infarct was defined as a homolateral occlusion simultaneously present in the middle cerebral artery and anterior cerebral artery.

Inclusion criteria were: age over 18 years old; diagnosis delay lower 8 days; patient's parents who agreed to take part in the study after informed consent.

Not included in the study: patients whose serious stroke diagnosis was not confirmed by brain imaging; patients whose biological examination (blood count; erythrocyte sedimentation rate; plasma activity levels of aspartate aminotransferase and alanine aminotransferase; plasma concentrations of glucose, urea and creatinine, serum creatinine; serological evaluation of human immunodeficiency virus) and first-line check-up were incomplete; subdural hematomas; cerebral venous thromboses; post-traumatic hemorrhages.

Etiological research was performed using MRI and/or cerebral angioscan, cardiac echo-Doppler and supra aortic trunks, coagulation assessment, standard electrocardiogram (ECG) and ECG Holter of 24 hours for patients whose strong suspicion of cardio embolic origin was retained despite the normal standard ECG. Arterial infarct etiologies were grouped according to the Toast classification [11].

For the therapies offered for patients, there were the targeted active therapies, minimum measures of resuscitation (conventional oxygenation, cardiopulmonary resuscitation, anti-edematous, sedatives, hemodynamic balance), decision-making process (transfer to intensive care unit and palliative approach).

In the case of arterial infarcts, active therapies were used according to the protocols established in our department. On account of thrombolysis that is not available in Togo, following therapies were offered for patients: intravenous aspirin at 1 g/day for 5 days, then platelet antiaggregant relay at 250 mg/day if emboligenic heart disease excluded, hospital admission before 5:00 hours, motor deficit and moderate lesion extent, absence of prior arterial infarct, National Institute of Health Stroke Score range of 17–20 and age under 80 years old; heparin with curative dose if emboligenic heart disease and HAS-BLED Score lower 3 for the case of extended arterial infarct; decompressive hemi-craniotomy in the case of extended middle cerebral artery infarct and carotid artery infarct

for patients under 60 years old, hospitalized within 48 hours and having no associated comorbidity.

In the case of hemorrhages, external ventricular drainage or sub-occipital craniotomy was indicated as an active therapy for infra tentorial hematomas and stereotaxis for deep compressive hematomas with or without hydrocephalus and if patients hospitalized within 8:0 hours [4].

Outcome was evaluated by means of mortality in 7 days and mortality in 15 days. SPSS software version 21 was used for statistical analysis. Qualitative and quantitative variables were assessed, respectively, by the frequencies and averages associated with standard deviation. To demonstrate a significant difference between two quantitative variables, Fisher's test was used. Comparison of two groups was released by Pearson correlation test. P value of < 0.05 was considered as statistically significant.

Results

Epidemiological data

Of the 1964 diagnosed strokes, 216 cases of serious strokes were identified. On account of the lack of brain imaging, 53 patients (24.5%) were excluded. Thus, prevalence of serious strokes was 8.3% (95% CI: 7.1 - 9.5%).

Among the 163 serious strokes, there were 63 arterial infarcts (38.7%) and 100 hemorrhages (61.3%). It was also noted 82 men (50.3%) and 81 women (49.7%). Mean age of patients was 55.8 ± 12.9 years old, with limits of 20 and 86 years old.

A history of stroke was noted in 26 patients (16%). Of the latter, 23 patients had initially presented arterial infarct. Among the 23 patients, 18 had sequela with a modified Rankin score ≥ 2 . Mean age of stroke history was 5.15 ± 4.25 years.

The Figure 1 presents medical history and modifiable cardiovascular risk factors.

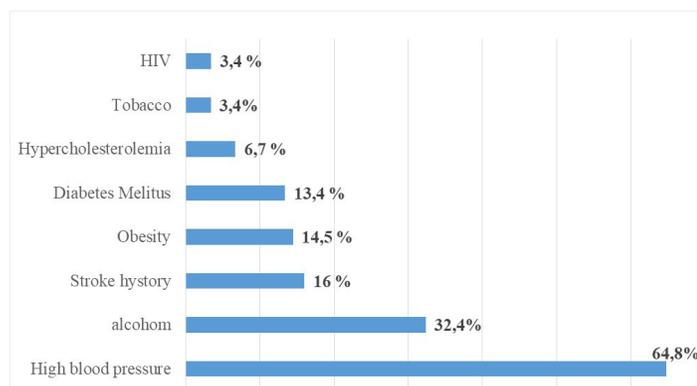


Figure 1: Medical history and modifiable cardiovascular risk factors of serious strokes.

Diagnostic data

Clinical data

Strokes were very serious and extremely serious in 89 (54.6%) and 74 (45.4%) patients, respectively.

Median hospital admission time determined from symptom onset was 82 hours at least, with limits of: 1 and 720 hours. Of the 63 patients with arterial infarct, 13 (20.6%) were hospitalized within 4:30 hours. Among the 100 patients with hemorrhages, 40 (40%) (40/100) were hospitalized within 8:0 hours.

Hospitalization was mainly caused by motor deficit (76.1%), impairment of consciousness (62.6%) and headache (20.9%).

Disease onset was abrupt and in successive shocks sequential during 24 to 48 hours in 156 (96%) and 7 (4%) patients, respectively. There was no particular schedule for symptom onset in all patients.

At hospital admission, patients had a mean temperature of $37 \pm 3^\circ\text{C}$, average arterial pressure of $170.6/170.6 \pm 36/20.6$ mm Hg, average Glasgow Score of 10.03 ± 7.5 and average National Institute of Health Stroke Score of 22.8 ± 8.9 .

Disease onset was correlated with elevated arterial pressure ($p = 0.04$), excessive alcohol consumption ($p = 0.02$), stroke history ($p = 0.004$), obesity ($p = 0.003$) and hypercholesterolemia ($p = 0.008$).

Impairment degree of consciousness was correlated with elevated arterial pressure ($p = 0.01$).

Neuroimaging data.

Median performing time of CT scan determined from symptom onset was 60.21 ± 71.51 hours, with limits of 1 and 720 hours. CT scan was performed within 4:30 and 8:00 hours, respectively, in 3 (4.8%) and 6 (6%) patients with arterial infarct and hemorrhage.

MRI was released in delayed time in 27 patients (16.6%) whose CT scan was not very efficient. It was also performed to search vascular malformation or bleeding tumor in 24 patients and follow-up 2 patients with vertebrobasilar artery infarct ($n = 2$) and 1 patient with extended middle cerebral artery infarct.

Starting point of hemorrhages was meningeal (Figure 2) and parenchymal in 8 and 92 patients, respectively. Mean maximum transverse diameter of hematomas was 43.8 ± 19.6 mm, with hematoma volume of 15–25 ml in 55% of cases, > 25 ml in 37% of cases and < 15 ml in 8% of cases. Diencephalon was starting point for bleeding in 75 (75%) patients with midbrain extension among 7 of them. Brainstem and cerebellum were affected, respectively, in 20 (20%) and 5 (5%) patients. Of the 20 brainstem hematomas, 7 were protuberant, 4 mesencephalic, and 9 extended. The latter were initially protuberant before being extended to the bulb ($n = 2$) or mesencephalon ($n = 7$).

Among the patients with extended hematomas, 76 had encephalic complications: ventricular flood ($n = 38$, 50%), axial involvement ($n = 24$, 31.6%), and hydrocephalus. associated with ventricular flooding ($n = 14$, 18.4%) (Figure 3). The presence of encephalic complications was correlated with hematoma volume (> 15 ml) ($p = 0.0003$), maximum transverse diameter ($p = 0.04$) and elevated

arterial pressure ($p = 0.005$). Table 1 presents arterial territories affected among patients with arterial infarct.



Figure 2: Meningeal hemorrhage classified as stages 4 according to the Fisher classification.

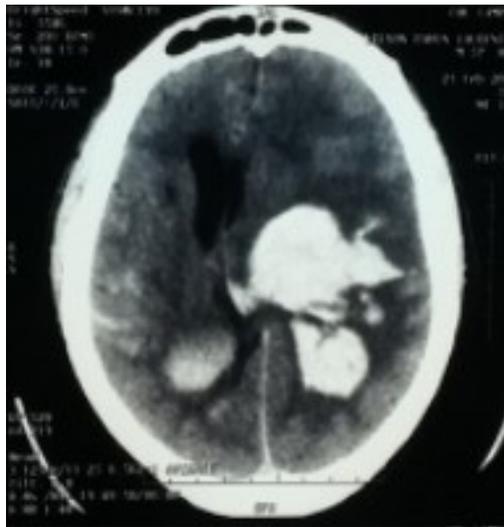


Figure 3: Extended hematomas complicated by ventricular flood, axial involvement and hydrocephalus.

Artery	Number	Percentage
Middle cerebral	48	76,2
Posterior inferior cerebellar	5	7,9
Carotid	3	4,8
Anteroinferior cerebellar	2	3,2
Superior cerebellar	2	3,2
Basilar trunk	1	1,6
Vertebral	1	1,6
Anterior spinal	1	1,6
Total	63	100

Table 1: Arterial territories affected in patients with arterial infarct.

Etiologies of hemorrhages were: presumed hypertensive (81%); aneurysm rupture (9%); acquired disorder of coagulation

(alcoholic cirrhosis) (1%); unknown origin (9%). Arterial infarcts were grouped into 2 classes, according to the Toast classification: atherosclerosis of large arteries (84.1%) (Figure 4) and embolism (15.9%) (Figure 5). Cardiac sources of cerebral embolism were at high risk in 25 (39.7%) patients (atrial fibrillation with left ventricular thrombus) and moderate risk in 38 (60.3%) patients (segmental hypokinesia of the left ventricle with sinus cardiac rhythm).



Figure 4: CT-Scan showing large left pontic infarct by basilar trunk occlusion of atheromatous origin.

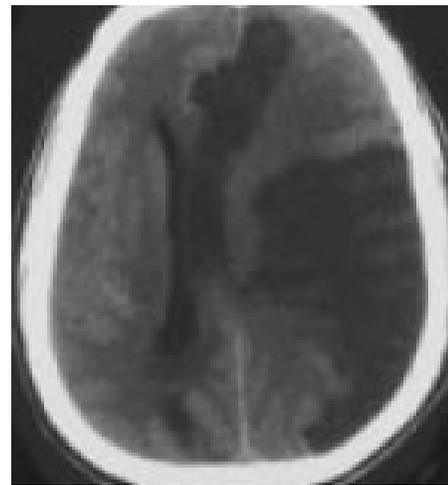


Figure 5: CT-scan showing a left Carotid artery infarct due to a embolism origin.

Therapeutic and outcome measures

Table 2 Indicates minimum resuscitation measures implemented in patients.

Resuscitation measure	Number	Percentage
Conventional oxygenation	148	90.8
Hemodynamic balance	39	23.9
Sedative	25	15.3
Glycemic control	14	8.6

Table 2: Minimum resuscitation measures implanted in patients with serious stroke.

Neurosedation with benzodiazepines or anxiolytics was used to reduce anxiety and treat the patients with agitation. Its effectiveness was noted in 58.2 % of cases.

Following active therapy limitations were decided by the parents: oxygenation stopping (n = 17; 10.4%), no cardiopulmonary resuscitation (n = 2; 1.2%), reduction of complementary examinations (n = 49; 30.1%;) and refusal to transfer the patient from neurology department to intensive care unit (n = 48; 29.5%). The latter was decided by the parents with practitioner advice for 47(28.8%) patients.

Patients with arterial infarct (n = 30) and hemorrhage (n = 60), who presented edema, were treated with hypertonic solutes.

Heparin and platelet aggregation inhibitor were administered in patients whose the origin of arterial infarct was not cardio-embolic (n = 53). Anticoagulation with heparin at curative dose followed by vitamin K antagonists was used to treat the patients whose the origin of arterial infarct was cardio-embolic (n = 5). Patients with occlusion of large vertebrobasilar arterial trunks (n = 5) were treated with aspirin.

Surgical therapies (decompressive hemi-craniotomy, external ventricular derivation, sub-occipital craniotomy and stereotaxis) did not implement in patients.

Mortality during the first 7 days was 32.5% (n = 53). Of the 53 deaths, there are 37 hemorrhages and 16 arterial infarcts. In 15 days, we noted a stabilization of the clinical state in 90 (81.8%) patients and an aggravation with death in 20 (18.2%) patients. Thus, overall mortality was 44.8%.

Overall Mortality was correlated with hematoma volume (p = 0.001), presence of encephalic complications (p = 0.003), high arterial pressure (p = 0.004), deep decrease of consciousness level at hospital admission (p = 0.0001), treatment (minimum resuscitation measures) delay (p = 0.0003) and limitations of therapeutic measures (p = 0).

Discussion

Epidemiology

Prevalence of serious strokes in the present study is lower than those reported in literature (27%) [5]. This low prevalence could be explained by the exclusion of 53 patients who had not confirmation brain imaging, choice of study department, early deaths before admission of patients at neurology department. However, our prevalences of hemorrhages and arterial infarcts are situated in the ranges reported in literature: 46.6-78.7% for hemorrhages and 21.3-44.6% for arterial infarcts [8,12].

Literature data reveal that annual incidence of hemorrhages is higher than that of arterial infarcts [13]. This epidemiological finding is also noted in our study.

The average age of our patients is lower than those reported in

literature (64-65 years old) [6,12]. These results could be explained by the residence in urban areas, work-related or low income-related stress and lifestyle changes that increase the prevalence of modifiable cardiovascular risk factors [7,14-16].

Literature reports that patients who present a serious arterial infarct, notably, an extended middle cerebral artery infarct, have already developed a first ischemic episode [14]. Our results corroborate this epidemiologic finding. Because of that, it is important to strengthen secondary preventive measures in order to prevent serious stroke onset.

Diagnostic aspects

CT scan used as a first-line examination for the positive diagnosis of serious strokes in our study is very efficient. MRI is difficult to access in emergency state because of the limited financial resources of patients or their parents. Thus, it was performed in delayed time in patients with CT scan not efficient. It also used to search vascular malformation or bleeding tumor and follow-up patients with vertebrobasilar artery infarct or extended middle cerebral artery infarct [7,17].

In our study, rate of serious hemorrhages related to aneurysms and unspecified origin could result from the inadequate technical resources. Insufficiency of the latter does not allow carrying out a complete and appropriate etiological search.

Origin of serious arterial infarcts is most often cardioembolic [18]. In our study, origin is poorly represented. This result could be explained by:

- the difficulty in confirming origin owing the coexistence of atherosclerosis [11];
- the performing of 24-hour ECG only in patients strongly suspected of having a cardio-embolic arterial infarct, despite the variable embolic risk of some patients. For this purpose, a long-term ECG (average time: 3 days) and transesophageal echocardiography must be carried out in all patients with serious arterial infarcts. The optimization of diagnosis of paroxysmic atrial fibrillation, as well as the visualization of various cardiac abnormalities in absence of cardiac history (thrombus of left atrium, foramen oval and/or atrial septal aneurysm, aortic plaques) in a patient with sinus rhythm, would be guaranteed [7].

Therapeutic aspects

Elevated median times of hospital admission and radiological examination implicate a treatment delay, as well as a great variability in the therapeutic management. This delay could be explained by the absence of mobile emergency units [17], serious state of patients which requires a stabilization, distance between the department of medical imaging and that of neurology in University Hospital Campus of Lomé, limited financial resources of patients.

Use of minimum resuscitation measures in patients with serious strokes is open to discussion. Artificial ventilation with intubation is more effective than conventional oxygenation [3]. Because of

that, conventional oxygenation would be only performed in 5-8 % of cases [19]. In our study, conventional oxygenation is greatly used (Table 2) because of the lack of neurovascular intensive care unit and/or decision of parents to limit active therapies that is caused by the low yield of intensive resuscitation [3,6].

Neurosedation reduces the sympathetic response and extent of ischemic damage. It can also damage the self-regulation of cerebral blood flow and make brain more vulnerable [20]. In our study, its effectiveness is higher than those reported in literature (16.2–24 %) [8,12]. This practice would be justified by the volume of cerebral lesions and alcohol withdrawal syndrome [12].

Anti-thrombotic treatment and anticoagulation implemented in our patients are in accordance with recommendations reported in literature [21-24]. Intravenous aspirin administration in patients with arterial infarct is an alternative therapy to thrombolysis. The latter is not available in most countries in sub-Saharan Africa [7].

Active therapy limitations are essentially passive in sub-Saharan Africa, as compared with data reported in literature [12]. They could be justified by the neurological severity and limited financial resources of patients or their parents, associated with inadequate technical resources. Rate of no resuscitation guidelines, noted in our study, is lower than those reported in literature (10–30%) [12,25]. This difference could be explained by the absence of a law relating to patients' rights and life end, as well as education of the populations.

Our mortality is higher than that reported in literature (33%) [6,8,12,26]. This mortality is related to the size of lesion, severity of coma, presence of encephalic complications, factors related to stroke management (diagnosis and treatment delay, active therapy limitations and lack of inadequate technical resources) [7,12,27].

Strengths and weakness of study

This exhaustive collection of patients during two years allows us evaluating primary and secondary management measures already implemented. The other strengths of this study are the use of first-line CT scan for the positive diagnosis of serious strokes with high efficiency, description of decision-making process for acute serious stroke management, intravenous administration of aspirin in patients with arterial infarct, in whom thrombolysis was indicated.

The weakness of our study which do not allow us carrying acute serious strokes management through are the limited financial resources of patients or their parents, delaying the performing of radiological explorations and treatment, and insufficient therapeutic resources (neurovascular unit, rtPA for thrombolysis, intubation equipment, electric syringes, external ventricular drainage, sub-occipital craniotomy, stereotaxis).

Conclusion

These results suggest that serious strokes management is mainly confronted with diagnosis and treatment delay, insufficient

therapeutic resources and limited financial resources of patients or their parents. These problems have a negative effect on the vital and functional prognosis. Because of that, it is important to strengthen therapeutic and preventive measures.

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