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Original article

Post-stroke seizures in a Sub-Saharan tertiary healthcare center

Crises épileptiques post-AVC dans un centre hospitalier tertiaire en Afrique subsaharienne

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Résumé

Introduction : L'AVC est une affection neurologique grave. Les crises épileptiques (CE) sont une complication fréquente de l'AVC. L'objectif de cette étude était de décrire les caractéristiques cliniques des CE post-AVC au Cameroun.

Méthodes : En utilisant le registre AVC de l'Hôpital Général de Douala, nous avons collecté des données des patients admis du 1er janvier 2010 au 31 décembre 2016. Nous avons inclus les patients âgés de plus de 15 ans avec le diagnostic d'AVC confirmé par neuroimagerie. Les CE était défini comme l'apparition d'au moins une CE après l'AVC. L'épilepsie préexistante, les autres causes de crises (infections cérébrales, troubles métaboliques), les tumeurs, les traumatismes crâniens et l'hémorragie sous-arachnoïdienne, ainsi que les dossiers incomplets étaient exclus. Les variables pronostiques étaient la mortalité intra-hospitalière et la mauvaise récupération fonctionnelle évaluée par un score de Rankin modifiée (mRS) > 2 à six mois.

Résultats : Parmi les 913 cas d'AVC, 124 patients ont présenté des CE post-AVC (13,6 %) dont 108 étaient précoces. L'âge moyen des patients était de 61,52 ± 13,20 ans, et 54 % étaient des hommes. Les CE étaient généralisées dans 69,44 % des cas et 8,33 % des patients présentaient un état de mal épileptique. La mortalité hospitalière était de 27,9 % chez les patients AVC avec CE contre 25 % chez les patients AVC sans CE (p = 0,548). À six mois, la récupération fonctionnelle était mauvaise (mRS > 2) chez 39,4 % des patients AVC avec CE contre 31,7 % des patients AVC sans CE (p = 0,642). Après un suivi de 18 mois, moins de 6 % des patients AVC avec CE ont une récidive de crise.

Conclusion : Il n'y a pas de différence significative dans la mortalité hospitalière et la mauvaise récupération fonctionnelle à 6 mois chez les patients

avec et sans CE post-AVC.

Mots-clés : AVC, crises épileptiques, coma, Cameroun.

Abstract

Background: Stroke is a severe neurological condition. Seizures are a common complications of stroke. The aim of this study was to describe the clinical features of post-stroke seizures (PSS) in Cameroon.

Methods: Using the Douala General hospital's stroke registry, we collected data on stroke cases admitted from January 1, 2010, to December 31, 2016. We included patients aged above 15 years diagnosed of stroke using neuroimaging. PSS was defined as the onset of at least one seizure after stroke. Preexisting epilepsy, others causes of seizures (brain infections, metabolic disorders), tumors, brain trauma, and subarachnoid hemorrhage, and incomplete files were excluded. Outcome variables were in-hospital mortality and poor functional recovery with a modified Rankin scale (mRS) > 2 at six months.

Results: Among the 913 cases of stroke, 124 patients presented post-stroke seizures (13.6%) including 108 early onset seizures (< 30 days). The mean age of patients was 61.52 ± 13.20 years, and 54% were male. Seizures were generalized in 69.44%, and 8.33% presented status epilepticus. In hospital mortality was 27.9% in PSS vs. 25% stroke without seizures (SWS) patients (p = 0.548). At six months the functional recovery was poor (mRS > 2) in 39.4% of PSS vs. 31.7% SWS patients (p = 0.642). After a follow up of 18 months, less than 6% of PSS patients have a seizure recurrence.

Conclusion: There is no significant difference in in-hospital mortality and poor functional recovery at 6 months in patients with and without post-stroke seizures.

Keywords: stroke, seizures, coma, Cameroon.

Introduction

Stroke is a clinically defined syndrome of acute, focal neurological deficit attributed to vascular injury (infarction, hemorrhage) of the central nervous system [1]. Stroke is the second leading cause of death in the world, including in the developing world [2]. It is the second leading cause of dementia and the leading cause of motor disabilities in adults [3].

The International League Against Epilepsy (ILAE) has defined epileptic seizure as the transient appearance of signs and/or symptoms due to abnormal or synchronized neural activity in the brain. ILAE defines epilepsy as at least two unprovoked (or reflex) seizures occurring greater than 24 hours apart; one unprovoked (or reflex) seizure and a probability of further seizures similar to the general recurrence risk (at least 60%) after two unprovoked seizures, occurring over the next 10 years; or the diagnosis of an epilepsy syndrome [4].

Stroke is a frequent cause of seizures. Post-stroke seizures (PSS) defined as single or multiple convulsive(s) episode after stroke and thought to be related to reversible or irreversible cerebral damage due to stroke regardless of the time of onset following the stroke [5]. Post-stroke seizures (PSS) occur in approximately 2–14% of ischemic stroke survivors and 10–20% of patients with hemorrhagic stroke. Although the latency to seizure onset is variable, 40–80% of cases develop within the first year after stroke. PSS are associated with increased mortality and morbidity, longer hospital stays, and greater disability at discharge compared to stroke patients without seizures [6].

Experimental and clinical studies show that post-stroke alterations such as reduced regional cerebral blood flow, impaired oxygen metabolism, and increased blood–brain barrier permeability create a pro-epileptogenic environment. Post-stroke seizures are conventionally classified as early or late using a 2-week cutoff: about 5–10% of patients experience early seizures within the first two weeks, while others develop late seizures thereafter. The occurrence of a late seizure is required for the diagnosis of post-stroke epilepsy (PSE). Overall, 3–30% of stroke survivors may develop PSE, which is associated with poorer prognosis and reduced quality of life.

This review outlines current evidence on PSE, including its definition, epidemiology, risk factors, pathophysiology, diagnostic evaluation, and treatment strategies [7]. The prevalence of PSE varies from 5-7 per 1000 at age 65 to 15 per 1000 over age 80 [8]. Patients with hemorrhagic stroke and those with a high NIHSS have a higher risk of developing PSS [9]. Venous stroke, large lesion, cortical location, supratentorial location, hypercoagulable states, and hyperhomocysteinemia are independent predictors [10]. In Cameroon, few data on PSS are available. The aim of this study was to provide clinical data on PSS in a referral hospital in Cameroon.

Methodology

Study design and setting

We retrospectively collected data of patient admitted for stroke from January 1, 2010, to December 31, 2016, in the neurology unit and intensive care unit of the Douala General hospital-stroke registry. Douala General Hospital is the main referral hospital of the economic capital of Cameroon (Douala). It is the only health facility in Cameroon with a stroke unit and a stroke registry.

We carefully reviewed health data of 928 of patients aged ≥ 15 years, admitted for stroke diagnosed using brain imaging (CT scan or MRI). We included patients with PSS based on these definitions: (1) early onset seizures < 30 days after a stroke; (2) late onset of seizures ≥ 30 days after a stroke. We excluded incomplete medical records, previously known epilepsy, sub-arachnoid hemorrhage, cerebral venous thrombosis, hemorrhagic brain tumors (***figure 1***).

Data collection and statistical analysis

Data were socio-demographic characteristics (age, sex), comorbidities and cerebrovascular risk factors (hypertension, diabetes, dyslipidemia, obesity, alcoholism, smoking, etc…), clinical features of PSS cases (GCS, NIHSS, seizure's onset, seizure's types), outcome variables (in-hospital mortality, poor functional recovery at 6 months). We defined the poor functional recovery by a modified Rankin scale (mRS) > 2.

Data were analyzed using SPSS version 20 software. Descriptive statistics were applied to present categorical (n, %) and continuous (mean ± SD) variables. We used the Chi-square test to compare categorical variables. Results were considered statistically significant for a p-value < 0.05.

Ethical considerations

For this study, we applied and obtained ethical approval by institutional ethics committee of the University of Douala (N° CEI-UDo/844/03/2017/T). Written informed consent was not required from individual patients.

Results

Patient characteristics

Among the 913 medical files of stroke patients included in the study, 124 presented at least one seizure (13.58%). The mean age was 61.52 ± 13.2 for PSS patients. Male represented 54% of cases. The main cerebrovascular risk factors were hypertension and diabetes in both PSS and stroke without seizure (SWS) population (table I).

In PSS patients, coma (GCS ≤ 8/15) on admission and initial NIHSS score > 15 were reported in 24 (19.4 %) and 36 (29%) respectively. Early onset seizures occurred in 108 patients (87.1%), with most of these seizures occurring within the first 24 hours after stroke. Generalized seizures were the commonest type of seizure (table II).

Stroke type and etiologies

Ischemic stroke represented 59.5% of stroke type. Early onset seizures were reported in 86.5% of ischemic and 62.5% of hemorrhagic stroke cases. Cardioembolic causes were the most frequent etiologies ischemic stroke. However, 41.5% of ischemic stroke remained of unknown cause. Hypertension was the main cause of hemorrhagic stroke (table III).

Outcome

The in-hospital mortality in PSS population was 27.9% vs 25% in SWS population (p = 0,548). Hemorrhagic stroke represented 67.6% of death. At 6 months poor

functional recovery was observed in 39.4% of PSS vs 31.7% of SWS population (p = 0,642). After 18 months, recurrence of seizure occurred in 5.7% (n = 7) of cases, including 6 patients with late onset seizures.

Table I: Comorbidities and cerebrovascular risk factors among stroke patients with and without seizures

Variable	PSS n (%)	SWS n (%)	p-value
Hypertension	88 (71.0)	562 (69.9)	0.809
Alcohol intake	33 (26.6)	204 (25.4)	0.768
Diabetes mellitus	30 (24.2)	178 (22.1)	0.610
Tobacco smoking	16 (12.9)	102 (12.7)	0.946
Dyslipidemia	7 (5.6)	72 (9.0)	0.219
Sleep apnea syndrome	8 (6.8)	22 (2.9)	0.029
Migraine	5 (4.3)	36 (4.8)	0.843
HIV	4 (3.7)	26 (3.7)	0.993
Cardiopathy	9 (7.8)	74 (9.7)	0.503

HIV: human immunodeficiency virus, PSS: post-stroke seizures, SWS: stroke without seizures.

Table II: Clinical features of stroke patients with seizures

Variable	Category	n (%)
GCS	≤ 8	24 (19.4)
	> 8	100 (80.6)
NIHSS	≤ 15	88 (71)
	> 15	36 (29)
Seizure's onset	Early	108 (87.1)
	Late	16 (12.9)
Seizure's type	Generalized	91 (73.4)
	Focal	16 (12.9)
	Secondary generalized	7 (5.6)
	Status epilepticus	10 (8.1)

GCS: Glasgow coma scale, NIHSS: national institute of stroke scale.

Table III: Stroke nature and etiologies in patients with seizures

Nature	Etiology	n (%)
Ischemic (n=74)	Cardioembolic	23 (31.1)
	Atherothrombotic	16 (21.6)
	Small vessels disease	4 (5.4)
	Unknown source	31 (41.9)
Hemorrhagic (n=50)	Hypertension	31 (62)
	Arteriovenous malformations	2 (4)
	Ruptured aneurism	2 (4)
	Unknown	15 (30)

Discussion

In this study, we described clinical features of PSS among patients in a Sub-Saharan health facility. About 10% of patients with stroke experience seizures from onset to several years after stroke [11]. There is a wide range of variability between studies. About 2 to 67% of patients has been reported at risk of early or late onset seizures after ischemic stroke, while intracerebral and subarachnoid hemorrhages have been associated to 8 to 15% of risk of developing seizures [12]. These disparities could be explained by the difference in the methods and the definition of PSS.

The male predominance found in our study confirms previous data from the literature. Male represented 53.21% and 58% in Croatia and Turkey respectively [13,14]. This male predominance could be related to stroke incidence higher in male than female. This is partly explained by several traditional cardiovascular risk factors more prevalent in male such as higher smoking and alcoholism [15].

Hypertension, diabetes, smoking and alcohol consumption are the commonest modifiable cerebrovascular risk factors [16]. These risk factors are also prevalent in stroke patients presenting seizures according to Labovitz et *al.* [10]. Seizures may be associated with hypertension in two ways. Chronic hypertension is a risk factor for stroke, and predispose for late-onset seizures and epilepsy in the elderly. In addition, acute symptomatic seizure can occur as a clinical manifestation of hypertensive encephalopathy [17]. About one quarter of patients with diabetes mellitus experience different types of seizures. Even if the precise pathogenesis of seizures in the diabetes patient remains undetermined, current hypotheses include microvascular lesions in the brain and brain damage [18].

As found in our study, early onset seizures are the most frequent type reported in literature [5,19,20]. Some studies found relatively low frequency of early onset seizures that have been reported in 2 to 33% of patients by Gutpa et al. and Osvaldo et al. [21, 22]. This variability could be explained by the difference in the definition of early onset seizures. We defined early onset seizures as seizures occurring in the first month after the onset of stroke, while these authors did not include in their definition seizures occurring within two weeks after the onset of stroke [21, 22]. Nevertheless, in our study, the majority of seizures occurred within the 24 hours after the stroke, as reported in other studies [11, 21, 22]. In a study restricted on cerebral infarction, 90% of early onset seizures occurred within 24 hours after stroke [21]. The duration of follow up may also influence the frequency of early and late onset seizures. De Reuck et al. found late-onset seizures in 57.1% of patients on average 8 months after the ICH [23]. Regarding their mechanism, early onset seizures are thought to result from local cellular biochemical dysfunction leading to electrically irritable tissue, while late onset seizures occur when epileptogenesis has occurred and the brain has acquired a sustained predisposition for seizures [24].

As stroke causes a focal structural abnormality in the brain, we were expecting to have prevalent focal seizures. In our study, generalized seizures were the commonest seizures type. Labovitz et *al.* and Osvaldo et *al.* found 24.3% and 32% of generalized seizures respectively [10,22]. De Reuck et *al.* confirm the predominance of focal seizures by reporting 75.7% of ICH patients with seizures [23]. However, in this study, ischemic stroke represented 59.5% of cases. Similar finding was reported in other studies [14]. Ischemic strokes with hemorrhagic transformation have a higher seizure risk compared to ischemic strokes alone [25]. Ischemic stroke accounted for 63.3% of cases in a study of epidemiology of stroke in Douala [26]. Ischemic stroke represents the commonest stroke's type in the general population. The ischemic nature of stroke predominates for both early-onset (59%) and late-onset seizures (62.5%).

More than one-quarter of PSS patients died in hospitalization with higher burden in hemorrhagic stroke cases. Hemorrhagic stroke contributes significantly to mortality in PSS patients [27]. Low- and middle-income countries including Cameroon

share the highest burden of stroke in term of mortality and disabilities. Although we did not observe statistically significant differences in in-hospital mortality or 6-month functional outcome between PSS and SWS patients, this absence of significance should not be interpreted as evidence of equivalence. The number of patients with post-stroke seizures (n=124), and particularly those with late-onset seizures, may have limited the statistical power to detect moderate differences in mortality or disability. A type II error cannot be excluded. Larger multicenter studies would be required to definitively assess the independent impact of post-stroke seizures on mortality and long-term disability in our context.

The management of stroke remain poorly standardized and human resources are still limited. Functional outcome was poor in more than one-third of PSS without statistically difference with SWS patients. Higher mortality has been found among stroke patients with seizures [28]. Although we did not observe statistically significant differences in in-hospital mortality or 6-month functional outcome between PSS and SWS, this absence of significance should not be interpreted as evidence of equivalence. The number of patients with post-stroke seizures (n=124), and particularly those with late-onset seizures, may have limited the statistical power to detect moderate differences in mortality or disability. A type II error cannot be excluded. Arger multicenter studies would be required to definitively assess the independent impact of post-stroke seizures on mortality and long-term disability in our context.

In our cohort, late-onset seizures represented only 12.9% of all post-stroke seizures, and seizure recurrence after 18 months was observed in less than 6% of cases. This low proportion of late seizures should be interpreted with caution. First, the duration of follow-up (18 months) may be insufficient to capture the full burden of post-stroke epilepsy, which may occur several years after the index event. Second, in our setting, long-term follow-u is frequently limited by financial constraints, transportation difficulties, and loss to follow-up, potentially leading to underestimation of late seizures and recurrence rates. Therefore, our findings likely reflect early symptomatic seizures more than the true incidence of post-stroke epilepsy.

Clinical implications in resource-limited settings

In low- and middle-income countries such as Cameroon, where access to continuous EEG monitoring and ling-term neurological follow-up is limited, the management of post-stroke seizures poses specific challenges. Our results suggest that most seizures occur early, frequently within 24 hours. This finding support close clinical monitoring during the acute phase rather than systematic long-term antiseizure treatment in all stroke patients.

Given the low rate of late seizure recurrence observed in our cohort, routine prophylactic antiseizure medication in all stroke patients does not appear justified. However, targeted monitoring could be considered in high-risk patients, particularly those with hemorrhagic stroke, severe neurological deficit (NIHSS > 15), cortical involvement, or status epilepticus.

Systematic EEG for all stroke patients is unlikely to be feasible in our setting. A more pragmatic strategy would be selective EEG use in patients with unexplained alteration of consciousness, suspected non-convulsive seizures, or severe cortical strokes. Further prospective studies are needed to define cost-effective risk stratification strategies adapted to sub-Saharan Africa.

Strengths and limitations

This study benefits from the use of a hospital-based registry in the only structured stroke unit in the country, allowing relatively standardized data collection. However, several limitations must be acknowledged: the retrospective design, possible under-detection of non-convulsive seizures due to limited EEG availability, the relatively short follow-up duration for detecting post-stroke epilepsy, and the limited sample size for late-onset seizures, which may have reduced statistical power for outcome comparisons.

Conclusion

After stroke, more than one patient out of ten may experience a seizure. Seizures occur mainly during the first month after stroke onset. This study did not show any significant differences in term of in-hospital mortality and poor functional recovery. Further studies are needed to identify determinants and long-term outcome of post-stroke seizures.

List of abbreviations:
CT: computed tomography
GCS: Glasgow coma scale
ILAE: International League against Epilepsy
MRI: magnetic resonance imaging
NIHSS: national institute of health stroke scale
PSS: post-stroke seizure
SWS: stroke without seizure

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Authors' contributions:
DGM, YBO, NYM have made substantial contributions to the conception, the study design, the acquisition, analysis, and interpretation of data,
JD, CK, SM, ASM, AMM, CKT have drafted the work or substantively revised it.
All authors have approved the submitted version of the manuscript.
All authors have agreed both to be personally accountable for the author's own contributions and to ensure that questions related to the accuracy or integrity of any part of the work, even ones in which the author was not personally involved, are appropriately investigated, resolved, and the resolution documented in the literature.

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Availability of data and materials:
The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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