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Research Article

One-Month Mortality of Acute Cerebral Infarctions and its Predictive Factors in African Low-Income Country: Case of Ouagadougou in Burkina Faso

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Abstract

Introduction: Early mortality rates of cerebral infarctions remain high in low-income countries, especially in Sub-Saharan Africa due to delays in admission and management of patients, absence of Stroke Units and fibrinolysis in hospitals, testifying to dysfunctions and gaps in African health systems. The aim of our study were to assess the one-month mortality of cerebral infarctions and to identify his predictive factors.

Patients and Methods: This was a prospective, descriptive and analytical study of patients hospitalized for cerebral infarction, from March 2015 to February 2016, at the University Hospital Centre of Tingandogo, in Ouagadougou (Burkina Faso). The socio-demographic, risk factors, comorbidities, clinical, and paraclinical characteristics of patients present at admission were analyzed, as well as intra-hospital and extra-hospital mortality at one-month of brain infarct. Univariate analysis, then multivariate analysis according to the Cox regression model, between the independent variables (general characteristics of the patients on admission) and the dependent variable (one-month mortality) identified the independent predictive factors of mortality at one-month post infarction.

Results: In all 151 patients were collected, with a male predominance (59.6%), an average age of 63.4 years. 30 days after the occurrence of the infarction, thirty patients died (19.9%). The independent predictive factors of mortality at one-month were ≥ 65 years of age (OR: 2.67), NIHSS score ≥ 17 (OR: 6.41), co-morbidity (3,06).

Conclusion: Short-term mortality remains high due to shortcomings in our health systems. An improvement in the quality of care, including fibrinolysis, early admission to stroke units, optimisation of management, including elderly and comorbidities, will contribute to the significant reduction in early mortality of cerebral infarctions.

Keywords: *Cerebral Infarction; Mortality; Predictors*

Introduction

Stroke is emerging today as one of the leading causes of preventable death and disability worldwide and 85% of the deaths attributable to it occur in developing countries [1,2]. Numerous more or less recent studies based on hospital series in sub-Saharan Africa (SSA) report overall high mortality rates at one month ranging from 20.4% in Cameroon [3] to 38% in Senegal [4]. On the other hand, in the developed

countries and certain emerging countries, notably the Organisation for Economic Co-operation and Development (OECD), as of 2013, the 30-day mortality rate, from cerebral infarction, was 10.1%, due to improved access quality care for stroke management, including timely patient transportation, evidence-based medical interventions such as thrombolysis, and high quality specialized facilities such as stroke units (SUs) [5]. In contrast, in SSA, the high rates of early or short-term mortality observed would result from long delays in patient admission and management, the absence of SUs and fibrinolysis, due to dysfunctions and gaps in African health systems. The 30-day mortality assessment of brain infarction is an excellent tool for measuring the performance and quality of hospital care. A better understanding of the predictors of early or short-term brain infarction mortality is helpful in identifying and implementing specific therapies and effective strategies for the management of high-risk patients in an limited resources like ours. According to some estimates and projections, Burkina Faso, like other countries in SSA, has apparently experienced an increase in age-adjusted cerebral infarction mortality rates between 1990 and 2010, about + 95% [6]. However to this day, to our knowledge, no study has yet been conducted in this country on the earlier or short-term mortality of cerebral infarctions or its predictors. In order to fill this gap and to contribute to the reduction of the mortality of cerebral infarctions, we realized the present study. The purpose of this study was to evaluate the one-month mortality of patients initially hospitalized for acute cerebral infarction and to identify its predictors of occurrence.

Patients and Methods

It was a prospective, observational, cross-sectional, descriptive and analytical study conducted at Tingandogo University Hospital Center in Ouagadougou, Burkina Faso. It is one of four tertiary hospitals in the city of Ouagadougou. Our study took place in the department of neurology, housed in the department of medicine and medical specialties, which has 34 beds in 12 rooms. Our study was conducted over 12 months, from May 1, 2016 to April 31, 2017. Included in the study were all patients 16 years of age or older, of any gender, who were consecutively hospitalized in the neurology department, during the study period, for cerebral infarction, confirmed by neuroimaging (CT or brain MRI), within 72 hours of hospitalization, having given their informed consent.

Patients who had been hospitalized for intracerebral hemorrhage, subarachnoid haemorrhage, cerebral venous thrombosis or transient ischemic attack during the study period were not included in the study. Similarly, patients who were unable to perform brain imaging, or those for whom informed consent could not be obtained (refusal or comatose or aphasic or confused patient with no legal representative), or those who were hospitalized for other neurological conditions were not included in this study. Patients were prospectively enrolled as they were admitted to hospital by three senior neurologists. Informed consent was obtained by senior neurologists at the time of admission or during the hospitalization of patients, once the diagnosis of cerebral infarction has been made and the therapies instituted. For patients unable to give informed consent, including patients with impaired consciousness, confusion or aphasia, consent was obtained from a legal representative of each patient.

For any patient, upon admission, measurement of vital constants, initial neurological and general clinical evaluation by a senior neurologist, standard ECG, CT and/or brain MRI interpreted by a radiologist, standard initial blood test results, including lipid status, were performed. Transthoracic echocardiography and the 24-hour ECG holter were also performed, if necessary. The standard chest x-ray was performed if there was suspicion of bronchopulmonary infection, some biological examinations for monitoring metabolic disorders, venous doppler and thoracic CT angiography, respectively in case of suspicion of limb venous thrombosis or pulmonary embolism ; thick blood, cytobacteriological examination of urine, blood cultures, respectively in case of suspected access to malaria, urinary tract infection, sepsis. Cerebral CT scan was not systematic; it was performed in case of neurological deterioration or headache. At discharge from hospital, patients were subdivided according to discharge status, surviving patients or deceased patients. In the event of death occurring during hospitalization, the immediate causes of death were determined in staff of senior neurologists. Each patient was followed up for 30 days (or one month) from the date of stroke, including a hospital phase and possibly a post-hospital phase for patients discharged alive from hospitalization. These were scheduled for an outpatient neurological clinical assessment that was to coincide with the 30th day post

stroke. Prior to this examination date, patients were called weekly to assess their general clinical condition. For patients who died in the post-hospital phase during the 30 days following stroke, the date and immediate cause of death were obtained from the family of patients by telephone. Those unable to attend the hospital were assessed at home.

Patient management was done according to the recommendations of the European Stroke Organization (ESO 2008). The neurology department does not yet have a SU, and intravenous fibrinolysis is not yet performed.

Study variables included socio-demographic characteristics, vascular risk factors (VRF), diabetes mellitus, smoking, dyslipidemia (total cholesterol, HDL cholesterol (High Density Lipoprotein), LDL cholesterol (Low Density Lipoprotein), triglycerides))), alcohol consumption (> 3 drinks per day), physical inactivity (patients whose physical activity did not exceed 30 minutes during most days of the week), obesity (BMI > 30 kg/m^2), history of stroke, coronary artery disease, atherosclerosis of supra-aortic trunks, atrial fibrillation, heart failure, peripheral arterial occlusive disease, migraine, sickle cell disease, hormonal contraception], pre-existing co-morbidities, time to hospital admission and performing brain CT, the initial clinical examination at admission [PA, temperature, Glasgow Coma Scale (GCS), neurological according to National Institute of Health Stroke Scale (NIHSS), the radiological features of cerebral infarction at admission, qualitative biological data at admission, status at 30 days post-infarction (alive or deceased), and if possible, the immediate causes of death. A GCS ≤ 8 defined a coma. An NIHSS score ≥ 17 defined a severe neurological deficit.

Outcome measures were: intra-hospital mortality and one-month mortality of cerebral infarction.

The consent of patients or their legal representatives, as well as the anonymity of the investigation, were guaranteed prior to recruitment. The protocol of the study was approved by the national ethics committee of Burkina Faso, then authorized by the General Direction of the University Hospital of Tingandogo.

Statistical analyzes were performed using SPSS12 software. Student's t-test was used to compare the means and Pearson's Chi-square test to compare percentages; the value of $p \leq 0.05$ was considered as a threshold of statistical significance. Univariate analyzes between the independent variables (general characteristics of the patients on admission) and the dependent variable (one-month mortality) allowed to select the variables significantly associated with mortality at one month. Finally, we proceeded by a multiple logistic regression analysis (with odds ratios calculation) according to the proportional hazards model of Cox, to identify the independent predictive factors of deaths at one month. Only variables with a $p < 0.20$ value in univariate analysis were taken into account for multivariate analysis.

Results

Descriptive study

During the study period, 204 patients were consecutively hospitalized for cerebral infarction, of which, 151 patients (74,0%) met the inclusion criteria. The mean of age was 63.4 years (range 26 - 99 years); there was a male predominance (59.6% versus 40.4%). The mean admission time was 24 hours (range 2 - 72 hours), only 28 patients (18.5%) of patients were admitted within ≤ 3 hours. The average time to perform CT scan from admission to the emergency room was 16.8 hours (1-161 hours). HTA (70.2%), alcohol (15.9%), history of stroke (11.9%), diabetes (11.3%) and sedentary lifestyle (11.3%) were the main LIFs. Comorbidities were present in 25.8%. The demographic characteristics and risk factors of the patients are presented in table 1 below.

At admission, the mean NIHSS was 14 (range 0 - 45), neurological deficit was severe in 48 patients (31.8%), 13 patients were in coma (8.6%) and 8 patient (5.8%) had epileptic seizures; hyperglycemia (38.4%), leukocytosis (23.8%) and anemia (16.5%) were the main biological abnormalities. The infarction of middle cerebral artery (88.5%) was the most frequent territory. Cerebral edema (39.7%) and mass effect (35.1%) were the most common early neuroradiologic complications. Cervico-cephalic atherosclerosis (28.5%) and emboligenic heart disease (17.9%) were the main etiologies identified. The clinical, biological neuroradiological features present at admission and etiological characteristics of patients are presented in tables 2-5.

Characteristics	Number (n= 151)	Frequencies (%)
Average age : 63.4 ±15.10 (26 to 99 years)		
Age groups		
≤ 64 years	89	58,9
≥ 65 years	62	41,1
Gender		
Male	90	59,6
Female	61	40,4
Residence		
Urban	100	66,2
Rural	51	33,8
Average time of admission: 24h (range 2 - 72h)		
Average time to perform cerebral CT: 16.8h (range 1 - 161h)		
Vascular risk factors		
HBP	106	70.2
Alcohol	24	15.9
History of stroke	18	11.9
Diabetes	17	11.3
Physical inactivity	17	11.3
Smoking	16	10.6
Hypercholestérolemia	12	7.9
Obesity	10	6.6
Cervical atherosclerosis	2	1.3
Anticoagulants/antiplatelet	2	1.3
Other	8	5.4
Comorbidities	39	25.8

Table 1: *The demographic characteristics and risk factors of the 151 patients.*

Clinical characteristics at admission	Number (n = 151)	Frequencies (%)
Mean initial NIHSS: 14 ± 6 (range 0-45)		
NIHSS ≥ 17	48	31.8
Mean initial GCS initial: 13.4 ± 2,8 (extrêmes 1-15)		
Categories of GCS		
GCS ≤ 8	13	8.6
GCS [14-9]	42	27.8
GCS 15	96	63.6
Admission epileptic seizures	8	5.3
Fever at admission	21	13.9

Table 2: *Clinical characteristics of 151 patients at admission.*

Biological examinations at admission		
Hyperglycemia	58	38.4
Leucocytosis	36	23.8
Elevated creatinine	28	18.5
Hypokaliemia	29	19.2
Anemia	25	16.5
Hyponatremia	23	15.2
Hypo proteinemia	23	15.2
Hypernatremia	13	8.6
Hyperkaliemia	9	6

Table 3: *Biological characteristics of 151 patients at admission.*

Neuroradiological characteristics at admission		
Early signs of cerebral ischemia	16	10.6
Cerebral vascular territories		
Anterior choroidal artery	8	5.30
Anterior cerebral artery	17	11.4
Midle cérébral artery	100	66.2
Vertebro-basilar	30	19.9
Junctional	2	1.3
Neuroradiological complications present upon admission		
Brain swelling	60	39.7
Mass effect	53	35.1
Cerebral herniation	18	11.9
Sylvian malignant infarction	18	11.9
Haemorrhagic transformation	23	15.2

Table 4: *Neuroradiological characteristics of 151 patients at admission.*

Etiologies		
Cervicocephalic atherosclerosis	43	28.5%
Embolic heart diseases	32	17.9
Cerebral microangiopathy	19	12.6
Associated causes	14	9.3
Undetermined causes	60	39.7
Carotid dissection	1	0.7

Table 5: *Etiologies of cerebral infarction in 151 patients.*

The duration of hospitalization was on average 13.4 days ± 9.1 (range 3 to 57 days). In all, 27 patients died during hospitalization, giving an intra-hospital mortality rate of 17.9%. During the post-hospital period, three additional deaths were recorded, bringing the number to 30, giving a 30-day post-cerebral infarction death rate of 19.9%. The main immediate causes of death were neurological (brain damage directly related to infarction), 11 patients (36.7%), infectious (respiratory infections and/or fatal sepsis), 10 patients (33.3%), cardiac fatalities (congestive heart failure, extended myocardial infarction, sudden death), 6 patients (20%) and others (metabolic, multi-systemic failure, massive pulmonary embolism), 3 patients (10%).

Analytical study

After a univariate analysis, age ≥ 65 years (p = 0.027), > admission time > 24 hours (p = 0.078), history of diabetes (p = 0,0204), co-morbidity (p=0.0036), score of NIHSS ≥ 17 (p = 0.001), leukocytosis (p = 0,000), anemia (p = 0.04), hyperglycemia (p = 0.003), and neuroradiological anomalies, in particular, cerebral edema (p = 0,024), mass effect (p = 0.033), cerebral herniation (p = 0.007), hemorrhagic transformation (p = 0.000), and sylvian malignant infarction (p = 0.003) were significantly associated with one-month mortality of cerebral infarctions.

After multivariate analysis, according to the Cox proportional risk model, age ≥ 65 years (OR 2.67; 95% CI [1.04 - 7,63]; p = 0,048), comorbidities (OR 3.06; 95% CI [1.17 - 8,01]; p = 0.0225) and NIHSS ≥ 17 (OR 6.41; 95% CI [2,49 - 16,47]; p = 0.0001), were the independent predictive factors of mortality at one-month of cerebral infarctions. Table 6 below presents the results of the univariate and multivariate analysis on the associations between patient characteristics of admission and mortality at one-month.

Patient characteristics	Univariate analysis			Multivariate analysis	
	Deaths n (%)		p	OR [95% IC]	P
	Yes	No			
Age ≥ 65 years	23 (25.8)	66 (74.2)	0,027	2.67 [1.04-7.63]	0.048
Educated patients	10 (16.4)	51 (83.6)	0.378	-	-
Urban residence	20 (20.0)	80 (80.0)	0.954	-	-
Admission delay ≤24 hours	10 (13.9)	62 (86.1)	0.078	2.30 [0.87-6.08]	0.092
HBP	20 (18.9)	86 (81.1)	0.590	-	-
Smocking	2 (12.5)	14 (87.5)	0.338	-	-
Hypercholesterolemia	2 (16.7)	10 (83.3)	0.555	-	-
Diabetes	7 (41.2)	10 (58.8)	0.0204	-	-
Prior stroke	2 (11.1)	16 (88.9)	0.254	-	-
Obesity	3 (30.0)	7 (70.0)	0.320	-	-
Sedentary lifestyle	6 (35.3)	11 (64.7)	0.094		
Alcohol	23 (95.8)	1 (4.2)	*0.023*	0.21 [0.02 - 1.87]	0.1653
Comorbidities	14 (35.9)	25 (64.1)	0.0036	3.06 [1.17 - 8.01]	0.0225
NIHSS ≥ 17	20 (41.7)	28 (58.3)	<0.001	6.41 [2.49 - 16.47]	0.0001
GCS ≤ 8	2 (15.4)	11 (84.4)	0.501	-	-
Fever at admission	5 (23.8)	16 (76.2)	0.222	-	-
Seizures at admission	3 (37.5)	5 (62.5)	0.222	-	-
Hyperglycemia	18 (31.0)	40 (69.0)	0.003	-	-
Kidney failure	13 (46.4)	15 (53.6)	0.000	-	-

Anemia	21 (17.6)	98 (82.4)	0.040	-	-
Leucocytosis	15 (41.7)	21 (58.3)	0.000	-	-
Hyponatremia	2 (8.7)	21 (91.3)	0.277	-	-
Hyper natremia	5 (38.5)	8 (61.5)	0.082		
Early signs of cerebral ischemia	7 (43.8)	9 (56.3)	0.015	-	-
Vertebro-basilar territory	2 (40.0)	3 (60.0)	0.273	-	-
Internal carotid territory	20 (17.5)	94 (82.5)	0,111	-	-
Cerebral edema	18 (30.0)	42 (70.0)	0.021	-	-
Mass effect	16 (30.2)	37 (69.8)	0.033	-	-
Cerebral herniation	8 (44.4)	10 (55.6)	0.007	-	-
Hemorrhagic transformation	11 (47.8)	12 (52.2)	0.000	-	-
Sylvian malignant infarction	10 (55.6)	8 (44.4)	0.000	-	-

Table 6: *Results of bivariate and multivariate analysis on associations between patient characteristics at admission and mortality at one-month of cerebral infarctions.*

Discussion

The 1-month mortality rate of 19.9% found in this study is comparable to the results of recent SSA hospital studies. Indeed, these series report high rates of mortality at one month ranging from 20.4% to 38%, or 20.4% in Cameroon [3], 23.8% in Kenya [7], 26.1% in Uganda [8], 27.4% in Mozambique [9] and finally 38% in Senegal [4].

In developed countries (Western Europe, USA, Canada, Australia, Japan, South Korea) and some emerging countries (South America), between 2003 and 2013, the rates of early death of cerebral infarction decreased sharply from 12.7% to 10.1% for mortality at 30 days [5]. In Scandinavian countries such as Denmark, 30-day mortality of cerebral infarctions was significantly reduced by about 45% between 1994 and 2011, from 17.2% in 1994 - 1998 to 10.6% in 2009 - 2011, independently of the continuing burden of comorbidities. However, the burden of comorbidities remained a powerful independent predictor of short-and long-term mortality [10]. These encouraging results in this part of the world have been reported to the improvement of access to quality care for stroke management, including patient-time transport, medical interventions based on data evidence such as the thrombolysis of acute cerebral ischemia and high quality specialized facilities such as SUs [5]. Conversely, in SSA, the high rates of early mortality observed would result from delays in admission and management of stroke patients, the absence of SUs or fibrinolysis, yet only therapeutic strategies proven efficiency [11,12]. These dysfunctions could be explained by the weakness of the African health systems, marked among other things by the deficiency in primary prevention of stroke, causing the occurrence of serious catastrophic strokes, frequently described In Africa [2], the low availability and/or low accessibility of medical equipments, the lack of human resources [13]. Indeed, this region has the lowest neurologist/population ratio (1/1000 000 people versus 1/100 000 people in high-income countries). Given the high proportion of people living below the poverty line, the rare means of taking care of the available strokes are not accessible to the majority of the population who have to pay for their pockets [14].

Several studies have reported coma or alteration of consciousness at admission and the initial clinical severity of cerebral infarction (NIHSS ≥ 17) at admission as powerful independent predictors of early or short-term mortality [8,15-18]. In fact, initial clinical severity directly reflects the extent and severity of neurological damage induced by infarction [8,17,18]. Only the initial clinical severity of stroke was identified as a predictive mortality factor of 30 days in our series. Admission coma has not been identified as a predictor of mortality, probably due to the weakness of our study population.

In the literature, as in our series, advanced age, most often ≥ 65 years and pre-existing comorbidities to stroke, have been identified as independent predictors of short-term mortality of cerebral infarctions [19-24]. According to Schmidt M., et al. [10], the reduction in mortality at 30 days post-cerebral infarction, found in Sweden, between 1994 and 2011, was made independently of the comorbidities, which remains a strong prognostic factor of short-term and long term mortality. Indeed, a significant correlation was frequently reported between the high age or the comorbidities and the occurrence of post-stroke medical complications [25-27]. Among the comorbidities, atrial fibrillation, coronary artery disease and diabetes mellitus, are those whose significant negative impacts on the vital and functional prognosis, at short or medium term post cerebral infarction, were the more often reported [28,29]. A pre-existing functional handicap to stroke is also often reported as an independent indicator of unfavorable functional and vital outcome [22-24].

Cerebral infarctions of the elderly are characterized by heavier early and short-term mortality and a darker functional and cognitive outcome, due to prolonged hospitalization, particularly high frequency of medical complications, especially infectious, poly-pathological context and more frequent comorbidities whose decompensation increases the risk of early death. Moreover, prior physical and/or cognitive handicap preexisting to stroke, exposes these patients to a greater risk of the under optimal management "ageism" of the Anglo-Saxons [30,31].

The implementation of SUs in African hospitals, the training of specialists in stroke pathology, associated with early admission of stroke patients to SUs, use of specific therapies to reduce the size of infarctions such as fibrinolysis, in the acute phase, associated with early detection and efficient management of comorbidities in particular, cardiac, are an effective way to reduce early and short-term mortality post-cerebral infarction.

Limits of Our Study

- The small size of our study population, linked to our inclusion criteria that excluded patients whose ischemic stroke was more than 72 hours during hospitalization, probably helped to reduce the statistical power of certain results.
- This is a hospital series in a third-level reference hospitals, hence a possible bias of selection of the most serious patients was probably observed.
- Causal research has not been possible in all our patients, due to high costs, thereby introducing a causal classification bias of cerebral infarctions.

Conclusion

The one-month mortality of inpatient cerebral infarctions remains high in Ouagadougou, about 20%, consistent with data from SSA. The initial clinical severity of the infarction, the advanced age and the comorbidities are its independent predictive factors. The early admission of stroke patients to SUs, the use of specific therapies to reduce the size of infarctions such as fibrinolysis, in the acute phase, associated with early detection and the efficient management of comorbidities in particular, cardiac, is an effective way to reduce early and short-term mortality post cerebral infarction.

Recommendations

In order to contribute significantly to the reduction of early mortality after cerebral infarction, in hospitals in SSA, we recommend:

- Implement SUs integrated into high-performance stroke networks in hospitals in SSA,
- Make available recanalization therapies for cerebral infarctions, including fibrinolysis,
- Establish and disseminate care protocols and procedures for acute stroke care at the hospital level,
- Train neurovascular specialists in SSA.

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