

Non Valvular Atrial Fibrillation Related Ischaemic Stroke at the Teaching Hospital of Yalgado Ouédraogo, Burkina Faso

Mandi D Germain¹, Samadoulougou K André^{1,2}, Yaméogo R Aristide^{1*}, Millogo RC Georges^{1,2}, Naïbé D Temoua¹, Kaboré PK Hervé¹, Kologo K Jonas¹ and Zabsonré Patrice^{1,2}

¹Service de Cardiologie du Centre Hospitalier Universitaire Yalgado Ouédraogo (CHU-YO), Burkina Faso

²Unité de Formation et de Recherche en Sciences de la Santé/ Université de Ouagadougou, Burkina Faso

Abstract

Objectives: We aim to describe the epidemiological and prognostic characteristics of non valvular atrial fibrillation related stroke.

Patients and methods: We retrospectively analyzed data of hospitalized patients from January 1st 2010 to June 30th 2012 in the two contiguous departments of cardiology and neurology, at the teaching hospital of Yalgado Ouédraogo, Burkina Faso.

Results: We recorded 391 cases of ischaemic stroke. Cardioembolic stroke was observed in 159 patients out of who, non valvular atrial fibrillation accounted for 43.5%. Atrial fibrillation was persistent/permanent in 60 cases (87%). The mean age \pm SD was 63.3 ± 14.2 years (extremes: 26-91 years). Hypertension was observed in 85.5% of the cases. The mean CHA₂DS₂-VAsc score was 4.72 ± 1.16 . The mean HAS-BLED score was 2.35 ± 0.92 with a low to intermediate bleeding risk score (≤ 2) in 60.9 % of patients. The rate of vitamin K antagonists use was 52%. They were introduced at least a week after stroke onset in 34 cases. A mean follow up of two weeks in hospital noticed haemorrhagic transformation and ischaemic recurrence in respectively 8.7% and 2.9% of the cases. Mortality rate of 21.7% during hospitalization was predicted by large sized cerebral infarction and congestive heart failure ($p < 0.05$).

Conclusion: Non valvular atrial fibrillation stroke is associated with in-hospital high mortality and is subject to early recurrence.

Keywords: Ischaemic stroke; Non valvular atrial fibrillation; Anticoagulation; Hemorrhagic transformation; Mortality; Burkina Faso

Introduction

Ischaemic stroke is a leading cause of acquired disability and death in adults [1]. Cardioembolic stroke accounts for 14-30% of all ischaemic strokes and appears to be associated with higher mortality and early recurrence [2,3]. Atrial fibrillation (AF) is the most common cardiac source of cerebral embolism with many associated risk factors [4,5]. Managing AF alone or with stroke is challenging and costly [6-8]. Data regarding AF related stroke are scarce in Sub-Saharan African including Burkina Faso. We aim to describe the epidemiological and prognostic characteristics of Non Valvular Atrial Fibrillation (NVAf) related stroke during hospitalization period.

Patients and Methods

We retrospectively analyzed data of hospitalized patients from January 1st 2010 to June 30th 2012 in the two contiguous departments of cardiology and neurology, at the teaching hospital of Yalgado Ouédraogo, Burkina Faso, west Africa. Those were included in the study, patients with ischaemic stroke diagnosed by cranial Computed Tomographic (CT) scan and/or by clinical stroke (persistence of focal neurological symptoms for over 24 hours period) who presented AF confirmed by a standard 12-lead electrocardiogram (ECG) or 24-hours Holter ECG. Transthoracic echocardiography (TTE) was used to screen patients with non valvular AF in the absence of rheumatic or degenerative cardiac valvular disease and valvular prosthesis.

TTE and transoesophageal echocardiography (TOE) were performed to look for other concomitant cardiac sources of cerebral embolism [9]. Doppler ultrasonography was used to eliminate cervical

large-artery atherosclerotic sources of embolism (obstructive carotid and vertebro-basilar artery disease).

Lone AF was defined as a condition without associated concomitant cardiac source of embolism. The cerebral infarction was assumed large-sized in case of infarct diameter above 30 mm at baseline. Congestive heart failure included shortness of breath weakness, edema, rales, rhonchi, or wheezes, presence of a third or fourth heart sound. Left ventricular ejection fraction (LVEF) was assessed by TTE in all patients. Urban area was defined by both Ouagadougou and Bobo-Dioulasso, the two biggest cities of Burkina Faso where International Normalized Ratio (INR) could be performed. Thromboembolic risk was evaluated according to CHA₂DS₂Vasc score [10]. Bleeding risk stratification was based on HAS-BLED score [11]. Cardiovascular vascular risk factors were evaluated according to the 2013 European Society of Hypertension/European Society of Cardiology [12].

For statistical analysis, EPI info TM software (version 7.0.9.34) was used. The categorical variables were expressed as percentages.

***Corresponding author:** Yameogo R Aristide, Service de Cardiologie du Centre Hospitalier Universitaire Yalgado Ouédraogo (CHU-YO), P.O: 11 BP 804 CMS Ouagadougou 11, Burkina Faso, Tel: 00226-66 48 58 58; E-mail: yraristide@hotmail.fr

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Continuous variables were expressed in terms of means \pm SD. Chi square test or Fisher's exact test were used for proportions comparison as appropriate. A logistic regression model was used to identify risk factors independently associated with death. For each analysis, a significant difference was defined as $p < 0.05$.

Results

During the study period, 2010 patients were hospitalized at both departments. We recorded 391 cases of ischaemic stroke. Cardioembolic stroke was observed in 159 patients out of who, NVAF accounted for 43.5% (43 females and 26 males). Atrial fibrillation was persistent/ permanent in 60 cases (87%) and paroxysmic in nine cases (13%). The mean age was 63.3 ± 14.2 years (extremes: 26-91 years). Forty five patients (65.2%) were ≥ 60 years old. Cardiovascular risk factors included hypertension in 85.5% ($n=59$), dyslipidemia in 24.6% ($n=17$) and diabetes in 21.7% ($n=15$) of patients. Alcohol abuse was observed in 25 cases (36.2%). Neurological deficit occurred in 63 cases and congestive heart failure was noticed in nine patients. The sociodemographic and clinical characteristics of the study patients at admission are shown in Table 1.

Cranial CT scan was normal in four cases (5.8%) and found a hypodensity in 65 cases (94.2%). The localization of such lesion was unique in 61.5% and had multiple foci in 38.5% of patients. The cerebral infarct was large-sized in 18 patients (27.7%).

Concomitant potential cardiac sources of ischaemic stroke were noticed in 45 cases (65.2%). These underlying sources included hypertensive dilated cardiomyopathy in 15 cases and left sided thrombus in 10 cases (Table 2). Mean LVEF was $61.6\% \pm 14.6$ (28-80). Eight patients had a LVEF $< 40\%$ and eleven had a LVEF between 40 and 54%. Cervical arterial Doppler ultrasonography performed in 28 patients has shown plaque in 23 cases without significant atherothrombotic stenosis ($< 50\%$).

The mean CHA2DS2-VASc score was 4.72 ± 1.16 (extremes 2 and 7) and all patients had high thromboembolic risk. The mean HAS-BLED score was 2.35 ± 0.92 (extremes: 1 and 5) with a low to intermediate bleeding risk score (≤ 2) in 60.9 % of patients (Figure 1). Characteristics comprising both CHA2DS2-Vasc stroke risk score and HAS-BLED bleeding risk are shown in Table 3.

Low molecular weight heparin (LMWH), enoxaparin in our context was used for secondary prevention of stroke recurrence in 55 patients before switching to vitamin K antagonist (VKA) in 36 cases (52%). VKA were introduced at least a week after stroke onset in 34 cases and sooner in two cases. VKA were prescribed in 60.9% ($n=31$) of 51 patients without large sized cerebral infarction versus 27.8% ($n=5$) of those with larger cerebral infarction ($RR=2.19$; $CI95\%=[1.01-4.76]$; $p=0.02$). VKA treatment was observed in 66.7% of the 42 patients from urban area versus 29.6% of 27 patients from other areas ($RR=2.25$; $CI95\%=[1.21-4.18]$; $p=0.003$). Antiplatelet therapy was prescribed in 94.2% of the study patients. It was associated with VKA in 35 cases and used alone in 14 patients. Ventricular rate control was obtained using antiarrhythmic drug in 55% of the cases comprising amiodarone ($n=14$), β -blockers ($n=19$) and digoxine ($n=5$). Table 4 indicates therapy received by study population during hospitalization period.

A mean follow up of 12.8 days ± 7.8 (extremes: two and 45 days) in hospital noticed complete regression of neurological deficit in 18 patients (26.1%). Complications were observed in 17 patients including haemorrhagic transformation in 8.7% ($n=6$), seizures in 8.7% ($n=6$) and ischaemic stroke recurrence in 2.9% ($n=3$). Five out

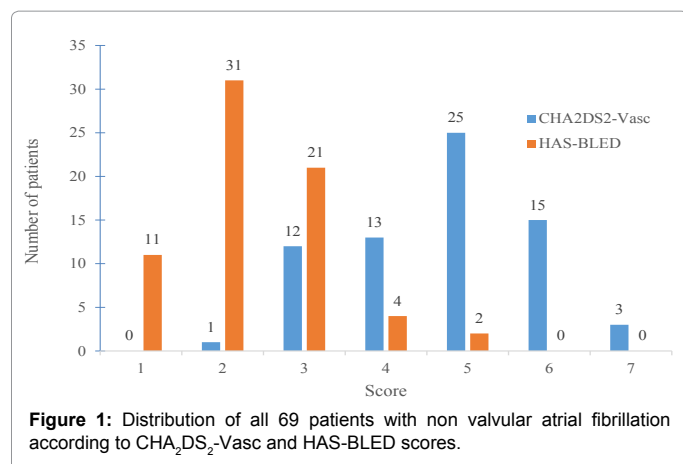
of 18 patients with larger cerebral infarct developed haemorrhagic transformation ($RR=14.17$; $CI95\%=[1.77-113.25]$; $p=0.003$). Only three patients among those under VKA ($n=36$) developed haemorrhagic transformation ($RR=0.41$; $CI95\%=[0.09 - 2.34]$; $p=0.46$). Mortality rate during hospitalization period was 21.7% ($n=15$). It was associated on univariate analysis with older age ≥ 75 years, large sized cerebral infarct, haemorrhagic transformation and congestive heart failure. On multivariate analysis, large sized cerebral infarct and congestive heart failure were independent and significant predictor death (Table 5). Immediate cause of death was of cardiac ($n=4$) and neurological ($n=7$) origin. Table 6 showed distribution of complications and causes of death in study population.

Characteristic	Number (n)	Percentage (%)
Mean age (years)	63.3 \pm 14.2	-
Age rage		
<60	11	16
60-74	45	65.2
≥ 75	13	18.8
Sex	Females/Males	43/26
		62.3/37.7
Type of atrial fibrillation		
Paroxysmic	9	13
Persistent	17	24.6
Long-standing persistent	19	27.5
Permanent	24	34.8
Cardiovascular risk factors		
Hypertension	59	85.5
Dyslipidemia	17	24.6
Smoking	17	24.6
Diabetes mellitus	15	21.7
Obesity	10	14.5
Prior ischaemic stroke	12	17.4
Clinical features		
Congestive heart failure	9	13
Pure motor weakness	63	91.3
Impaired verbal processing	42	60.9
Weakness of face	26	37.7
Association of the three types of deficit	43	62.3
Syncope	21	30.4
Altered consciousness	11	16
Palpitations	19	27.5
Ongoing antiplatelet therapy	19	27.5

Table 1: Socio-demographic and clinical characteristics of study patients at baseline.

Concomitant potential cardiac sources of embolism	Number (n)	Percentage (%)
High-risk sources of embolism		
Hypertensive dilated cardiomyopathy	15	21.7
Cardiothyreosis†	2	2.9
Left sided thrombus	10	14.5
Restrictive cardiomyopathy	4	5.8
Medium-risk sources of embolism		
Spontaneous echo contrast	16	23.2
Hypertrophic hypertensive cardiomyopathy	2	2.9
Ischaemic cardiomyopathy (>4 weeks)	5	7.3
Patent foramen ovale	2	2.9
Communicant interatrial septal aneurysm	1	1.4

Table 2: Concomitant potential cardiac sources of cerebral embolism in 69 patients (†with dilated left cavities).



Risk factor	Number	Percentage
Thromboembolic risk factors (CHA₂DS₂-Vasc)		
Congestive heart failure/ LVEF<0,40	14	20.3
Hypertension	59	85.5
Age ≥ 75 years	13	18.8
Diabetes mellitus	15	21.7
Ischaemic stroke	69	100.0
Vascular disease	5	7.2
Age 65-74 years	23	33.3
Female sex	43	62.3
Bleeding risk factors (HAS-BLED)		
Hypertension (SBP >160 mmHg)	5	7.2
Altered kidney function	12	17.4
Hepatic function impairment	0	0.0
Stroke	69	100.0
Bleeding	0	0.0
Labile INRs	0	0.0
Age>65 years	36	52.2
Antiplatelet therapy	19	27.5
Alcohol	25	36.2

Table 3: Distribution of CHA₂DS₂-Vasc and HAS-BLED scores risk factors in study patients (LVEF: left ventricular ejection fraction; SBP: systolic blood pressure; INR: International Normalized Ratio).

Treatment	Number	Percentage (%)
Anticoagulants	55	79,7
LMWH alone	19	27,5
LMWH VKA	36	52,0
None	14	20,3
Antiplatelet therapy	65	94,2
Alone	14	20,3
With VKA	35	50,7
With LMWH	16	23,2
None	4	5,8
Antiarrhythmic drugs		
Digoxin	5	7,3
Amiodarone	14	20,3
β-blockers	19	27,5
Other drugs		
ACE/ARBs	55	79,7
Statins	51	74,0
Early rehabilitation	55	79,7

Table 4: Distribution of study treatment in 69 patients during hospitalization period (LMWH: low molecular weight heparin (enoxaparin), VKA: vitamin K antagonist; ACE: angiotensin-converting enzyme inhibitors; ARBs: angiotensin receptor blockers).

Factor	Death n/N	Univariate analysis		Multivariate analysis*	
		RR (CI 95%)	p	OR (CI 95%)	p
Age (years)	<75	9/56	1.00	1.00	
	≥ 75	6/13	2.87 (1.24-6.64)	4.06 (0.83 – 19.68)	0.082
Congestive heart failure	Non	10/60	1.00	1.00	
	Oui	5/9	3.33 (1.48-7.52)	6.32 (1.04 – 38.37)	0.045
Haemorrhagic transformation	Non	11/63	1.00	1.00	
	Oui	4/6	3.82 (1.75-8.33)	3.77 (0.39 – 36.53)	0.252
Infarct size (cm)	<3	6/51	1.00	1.00	
	≥ 3	9/18	4.25 (1.76-10.27)	4.40 (1.01 – 19.26)	0.049

Table 5: Factors associated with death on univariate and multivariate analysis in the 69 study patients during hospitalization period (RR: Risk ratio; OR: Odds Ratio; CI 95%: confident Interval at 95% of association measure; *Adjustment for variables listed on the table).

Complications	Number (n)	Percentage (%)
Haemorrhagic transformation	6	8.7
Stroke recurrence	2	2.9
Seizures	6	8.7
Mesenteric infarction	1	1.5
Venous thromboembolic disease	1	1.5
Pressure ulcers	1	1.5
Causes of death		
Congestive heart failure	4	-
Cerebral herniation	3	-
Haemorrhagic transformation	2	-
Stroke recurrence	2	-
Sepsis	3	-
Mesenteric infarction	1	-

Table 6: Complications occurred during hospitalization period and immediate causes of death in all 69 patients with atrial fibrillation.

Discussion

The retrospective pattern of the study and lack of ambulatory follow up data may have underestimated the assessment of some parameters. Nevertheless current results gave an overview of the problem in our setting. All study patients did not benefit from large-artery atherosclerosis research based on the fact that it was a retrospective study and we just reported data of those who underwent this Doppler ultrasonography. Moreover Doppler ultrasonography was not performed in patients with an obvious cardiac cause of ischaemic stroke and/or in those who could not afford such exam (knowing Burkina Faso belongs to low income countries with no share care system). Arterial angiography was not available at that time.

NVAF, the most common source of cardioembolic stroke was observed in 43.5% of all cardiac causes of cerebral embolism in our study. Damorou et al. [13] in Togo and Paciaroni et al. [14] in Italia have reported lower rates in patients presenting their first episode of ischaemic stroke with respectively 19.8% and 20.3% of the cases. Conversely, Yip et al. [15] at Taiwan observed 69% of AF in a subgroup of cardioembolic stroke. Discrepancies in rates may be explained by patients' selection criteria and quality of AF screening methods used after stroke onset. A possible underuse of VKA for primary prevention of thromboembolism in AF may have played a role in low income regions such as Burkina Faso.

NVAF is frequently associated with other cardiac sources of stroke which were similarly found in Kim et al. series [16] and ours with respectively 65.2% and 68% of the cases.

In a Japanese study [17] including 234 patients suffering from NVAF related stroke, AF was classified as paroxysmic and permanent in respectively 42.3% and 57.7% of the cases. Our data have supported results from Marini et al. [18] study in Italia with a persistent to permanent AF rate being above 80%. These marked differences in types of AF between studies are probably related to weight carried by 24-hours Holter ECG in detecting paroxysmic AF after ischaemic stroke onset. Regardless of the type of AF (paroxysmic or permanent), the annual risk of cerebral embolism in the absence antithrombotic treatment is identical and assessed to range from 3 to 5% but widely depends on CHA2DS2-VASc score [6]. The mean CHA2DS2-VASc score in our study was 4.72 and all patients had a score ≥ 2 indicating a very high risk of embolism and a need of antithrombotic treatment except contraindications. Moreover, bleeding risk was low to intermediate (HAS-BLED score: 1-2) in 60.9% of our study patients suggesting safer initiation of anticoagulation therapy. This bleeding risk was high (HAS-BLED score ≥ 3) in 39.1% of patients indicating cautious introduction of anticoagulation therapy with a close follow-up [19]. Secondary prevention of cerebral embolism in NVAF is widely addressed in series worldwide. Accordingly, it is recommended to quickly start treatment with heparinoïds in patients at very high risk of thromboembolism after an individual assessment of risk/benefit ratios [14,20,21]. For long term secondary prevention of ischaemic stroke in AF, VKA remain the gold standard treatment in reducing the risk of recurrence by 70% [22]. In a survey of practice patterns of anticoagulation therapy in acute ischaemic stroke in Korea among physicians, the most common method of immediate treatment initiation was heparin followed by warfarin (68%) and then warfarin alone or warfarin with aspirin in the absence of large-sized infarct and haemorrhagic transformation [23]. In the PREFER in AF study, the rate of oral anticoagulation use in 2012 was $>80\%$ in Europe including patients at high risk of bleeding since publication of 2010 ESC Guidelines on atrial fibrillation [24]. Only 52% of our study patients benefit from VKA treatment. This relatively low rate of VKA use in our setting is partly due to physician's worry about bleeding risk and also geographic and financial constraints on accessing frequent International Normalized Ratio (INR) follow-up. However, new oral anticoagulants a great progress in therapeutics could be an alternative to VKA in a near future and modify our practice [3], due to their simpler way of use and comparative reduction of major bleeding risk [25,26].

Early haemorrhagic transformation risk in AF related stroke accounts for 2.7% at one week [3]. Our results supported data from a prospective multicentric study of 1125 patients nevertheless suffering from ischaemic stroke of all origin with a rate of 8.7% and this haemorrhagic transformation is significantly associated with large-sized infarct [27]. Ischaemic stroke recurrence in AF is assessed to be 2.5% and 5% at one week and one month respectively [2,3]. We reported recurrence rate of 2.9% at two weeks period.

Atrial fibrillation related ischaemic stroke is classically severe with high mortality rate during the acute phase in comparison to other sources of cerebral embolism. We found in hospital rate of death (21.7%) that supported data from literature [2,13,28]. Mortality was predicted by large sized cerebral infarct and congestive heart failure ($p<0.05$). Death in cardioembolic stroke is mainly due to neurological complications and cardiac comorbidities [2].

Conclusion

NVAF related stroke is associated with higher mortality during hospitalization and subject to early recurrence. A better use of international guidelines on primary and secondary prevention of cerebral embolism in AF may contribute to reduce the burden of the problem. Introduction of INR self-measurement equipment in remote areas or new oral anticoagulants could be an alternative way of treatment follow-up in rural and semi-urban areas with poorly equipped hospitals.

Author's Contribution

All authors did fully participate in the study. Paper writing process was a team work.

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