

## Sinus Variability in Patients Followed for Stroke at the Yaounde Central and General Hospitals

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### Abstract

**Objective:** Since 2015, our center has been actively promoting methods of surgical correction of atrial fibrillation, in particular, in patients with coronary heart disease. The study presents a comparative analysis of the late postoperative period in patients with coronary artery bypass grafting and atrial fibrillation.

**Methods:** The study included 189 patients with ischemic heart disease and atrial fibrillation for the period from 2015 to 2021. Patients were divided into 2 groups. The first group is represented by patients with ischemic heart disease and atrial fibrillation who underwent coronary bypass surgery and surgical treatment of atrial fibrillation (N = 68). The second group is represented by patients with ischemic heart disease and atrial fibrillation who underwent only myocardial revascularization (N = 121). Patients were comparable in age, gender, initial severity of the condition.

**Results:** Average follow-up for group 1 and group 2 was 28 and 52 months respectively. There was only 1 patient in group 1, who had died from cardiovascular diseases in follow up. Freedom of atrial fibrillation was in 80,6% in group 1. In group 2 there were 7 patients who had died from cardiovascular diseases and total freedom of atrial fibrillation was in 50,5% of patients. Combined endpoints (death, stroke/TIA, progression heart failure, myocardial infarction, bleeding, repeat ablations) were achieved in 22,2% in group 1 and 39,8% in group 2, respectively.

**Conclusion:** Surgical treatment of atrial fibrillation helps to reduce adverse events in the late postoperative period and contributes to the regression of heart failure.

**Keywords:** Atrial Fibrillation; Ischemic Heart Disease; Coronary Artery Bypass Grafting; Pulmonary Vein Ablation

## Introduction

Stroke is characterized by the American Stroke Society as a neurological deficit attributed to acute focal damage to the central nervous system (CNS) by a vascular cause, including cerebral ischemia, intracerebral hemorrhage and subarachnoid hemorrhage [1]. Despite advances in modern medicine, stroke remains a pandemic that affects one person every 5 seconds [2]. It is the second leading cause of death worldwide from non-communicable diseases behind coronary heart disease and is the leading cause of disability in adults [2-4]. In addition, the WHO projects an increase in incidence from 16 million in 2005 to 23 million in 2030 [2]. In sub-Saharan Africa, its incidence is 316/100000 inhabitants, with a prevalence of up to 981/100000 inhabitants [5]. In this region of the world, non-communicable diseases are the leading cause of death, stroke is the leading cause with 16% mortality among individuals aged 55-74 and 18% among individuals over > 74 years old, without gender difference [5]. In Cameroon, stroke accounts for half of neurology consultations with a mortality rate of up to 76% in patients hospitalized in intensive care [6,7]. The main risk factors for stroke in sub-Saharan Africa and Cameroon remain broadly similar to the rest of the world: hypertension blood pressure, type 2 diabetes, dyslipidemia, smoking and atrial fibrillation [5,7,8]. In Cameroon, the main prognostic factors found are the Glasgow score below 8, hyperglycaemia, a modified Rankin score above 5, leukocytes above 10,000/mm<sup>3</sup> and pneumonia [6,9]. However, it is suggested that cardiovascular mortality linked to stroke is induced by neurological stress and disturbances of the heart-brain axis via dysfunctions of the autonomic nervous system [10]. Heart Rate Variability (HRV) is a non-invasive method used to assess the coordination of the autonomic nervous system over the sinus node [11,12]. Low HRV index levels often indicate dysfunction of the autonomic nervous system [13]. Correlations are increasingly found between dysfunctions of the autonomic nervous system and cardiovascular mortality, as well as cardiovascular mortality and sinus variability [12,14]. Research is therefore also focused on the relationship between neurological disorders and sinus variability. Indeed, a systematic review strongly suggests a decrease in sinus variability as a factor in the severity of stroke in the acute phase [15]. We conducted this study to determine the values of sinus variability and the factors associated with its alteration in subjects with stroke.

## Methods

### Study design and setting

We carried out a cross-sectional study over a period of 3 months (June and August 2021) in the neurology and cardiology departments of the Yaoundé central hospital, and in the cardiology department of the Yaoundé general hospital.

### Participants

All adult patients who had stroke and who gave their informed consent were included in the study. We excluded patients who were not in sinus rhythm or those whose Holter ECG recording was uninterpretable.

### Sample size

We carried out a consecutive and exhaustive sampling.

### Data collection

Sociodemographic data, cardiovascular risk factors, comorbidities, clinical and paraclinical signs were collected from the patients' medical records using a pre-established questionnaire. All those with baseline sinus rhythm underwent 24-hour rhythmic Holter to assess sinus variability. We used Schiller Medilog Ar Holter ECG devices, HOLTER SYSTEM TF. DARWIN MEDIALOG and 3 HOLTER ECG software were used for the analysis of the recordings with the time-based and frequency-based methods.

### Measurement of heart rate variability

We will use time based analysis and frequency based analysis on 24H holter ECG.

### Notion of NN interval

RR intervals represent the time between each sensed heartbeat, measured from peak (R) to peak (R) on the QRS complex. The NN interval represents RR interval data but with additional filtering to remove artifacts in the data that make some RR intervals unreliable.

### Time-based analysis

Two types of indices are distinguished:

Short term variability (STV) representing rapid changes in heart rate and long term variability (LTV) representing slow changes in heart rate (less than 6 minutes).

Both being calculated by the variations of RR in a window of time (generally between 0.5 and 5 minutes).

Have been calculated:

- The standard deviation of NN intervals: SDNN
- The standard deviation of the means of the NN intervals in all 5-minute segments of the entire SDAN record
- The mean root square of the successive interval difference: RMSSD
- The number of successive interval differences that differ by at least 50 ms expressed as a percentage of the total number of ECG cycles analyzed: pNN50%.

**Frequency-based analysis**

Frequency-based analysis measures the cyclical fluctuation of R-R intervals by performing Fourier transform spectral analysis. This analysis method quantifies the spectral energy by determining the area under the curve, measured in ms<sup>2</sup>, for a given frequency. It makes it possible to distinguish the low frequency band (LF = 0.04 to 0.15Hz) which is mainly a reflection of sympathetic activity and the high frequency band (HF = 0.15 to 0.50Hz) which is a reflection of parasympathetic activity. The normalized ratio of these spectral indices (LF/HF) is used to assess the sympatho-vagal balance.

**Statistical analyzes**

They were made using Epi Info version 7 and Microsoft Excel 2016 software. Quantitative variables obeying the normal law were presented as means ± standard deviations. Quantitative variables not obeying the normal distribution were expressed by their median and interquartile range. We have presented the qualitative variables by their numbers and percentages. Chi-square or Fisher tests, as appropriate, were used for the comparison of proportions. The Student test was used for the comparison of means. The threshold of statistical significance was set for a value p < 0.05.

**Ethical considerations**

All participants gave their informed consent before inclusion in the study. An ethical clearance was obtained from the institutional ethics and research committee of the Faculty of Medicine and Biomedical Sciences of the University of Yaoundé I. The fundamental principles of medical research were strictly respected.

**Results**

In total, we included 40 patients in the study, including 25 men (65%). The average age was 64 ± 15 years. The most common comorbidities were high blood pressure (67.5%), diabetes (17.4%) and excessive alcohol consumption (15.0%). Two thirds of the participants had an ischemic stroke and the majority of them had a mild stroke according to the NIHSS score (Table 1). The results of the sinus variability analysis are presented in table 2. On time-based analysis, median SDNN was 71.0 ms, SDAN 73.3 ms, median RMSSD 49.6, and median PNN50 4.91%. After spectral analysis, the median LF was 97.8 ms<sup>2</sup>, the median HF 106.6 ms<sup>2</sup> and the median LH/FH ratio 0.86.

Overall clinical characteristics		Numbers (N = 40)	Percentages (%)
Age (years)	Less than 40	3	7.50
	[40-50[	5	12.50
	[50-60[	3	7.50
	[60-70[	13	32,50
	[70-80[	11	27.50
	Less than 80	5	12.50
Past history of stroke		9	22.20
Comorbidities	High blood pressure	27	67.50
	Diabetes	7	17.40
	Obesity	4	10.00
	Active smoking	5	12.50
	Alcoholism	6	15.00
	HIV infection	2	5.00
	LMWH	1	2.50
Type of stroke	Takayasu Disease	1	2.50
	Hemoragic stroke	14	35.00
	Ischemic stroke	26	65.00
Stroke severity (NIHSS)	Minor	3	8.89
	Light	20	58.80
	Serious	10	29.41
	Severe	1	2.90

**Table 1:** Overall clinical characteristics of the study population.

VFC parameters		Minimum	Maximum	Mean $\pm$ dst	Median [IQ]
Heart rate (bpm)					
	Maximum HR	47	133	116( $\pm$ 28.9)	115[94-133]
	Minimal HR	40	96	64( $\pm$ 15.2)	63[49-76]
	Mean HR	46	105	79( $\pm$ 14.5)	79[71-105]
Markers of sympathetic activity					
	SDNN(ms)	18.09	165.5		71[35.15-96.57]
	SDAN(ms)	29.5	848		73.30[52.3-108.15]
	LF(ms <sup>2</sup> )	20.3	414.1		97.85[65.11-137.5]
Markers of parasympathetic activity					
	RMSSD (ms)	6.24	187.7		49.6[23.4-72.81]
	PN50(%)	0.08	39.09		4.91[8.5-11.9]
	HF(ms <sup>2</sup> )	22.2	986.5		106.6[75.15-206.5]
Sympathovagal balance					
	LF/HF	0.48	1.29		0.86[0.64-0.93]

**Table 2:** Measures of Heart Rate Variability in Stroke Patients.

None of the measures of sinus variability were associated with age  $\geq$  64 years, gender, hypertension, diabetes, type of stroke, Rankin score and NIHSS score.

## Discussion

We aimed to describe the parameters of sinus variability and to determine the associated factors in patients followed for stroke in our context. The average age of the participants was relatively higher than that of epidemiological studies in Cameroon which generally find an average or median age close to 58 years for stroke [8,16]. We also found a male predominance like Mapoure., *et al.* in Douala [8]. Knowing that World Bank data show a proportion of 50% of men in the Cameroonian population [17], this could imply a higher prevalence and incidence of stroke in Cameroonian men. We found 2/3 of cases of ischemic stroke just like Chiasseu and Mbahe [16] in the city of Douala, but higher than the proportion of 52% found by Mapoure., *et al.* All this contrasts with the 80% of ischemic strokes expected according to the literature and suggests a higher incidence of hemorrhagic strokes in Cameroon [18].

There are no recommended values for heart rate variability. However, studies in healthy subjects generally find mean SDNN of 160 ms, LF and HF of 1337 ms<sup>2</sup> and 289 ms<sup>2</sup> respectively, RMSSD of 49 ms and an LF/HF ratio greater than 1 as noted by Shaffer., *et al.*

[19]. We found lower median values in our patients. They were also lower than those found by Nganou., *et al.* in diabetic patients [20]. We looked for other factors besides stroke associated with lower sinus variability, but no association was statistically significant. This suggests that stroke alone is responsible for this autonomic dysfunction.

## Conclusion

This study suggests a significant decrease in heart rate variability in subjects with stroke in Cameroon. There is also an imbalance between the sympathovagal balance in these subjects. Thus we can conclude an increased dysfunction of the autonomic nervous system in these subjects.

## Bibliography

1. Sacco RL., *et al.* "An updated definition of stroke for the 21<sup>st</sup> century: a statement for healthcare professionals from the American Heart Association/American Stroke Association". *Stroke* 44.7 (2013): 2064-2089.
2. Mendis S., *et al.* "Global atlas on cardiovascular disease prevention and control / edited by: Shanthi Mendis ... [et al.]". Geneva: World Health Organization (2011).
3. Mathers CD and Loncar D. "Projections of global mortality and burden of disease from 2002 to 2030". *PLoS Medicine* 3.11 (2006): 442.

4. Wang Y and Wang J. "Modelling and prediction of global non-communicable diseases". *BMC Public Health* 20.1 (2020): 822.
5. Owolabi MO., et al. "The burden of stroke in Africa: a glance at the present and a glimpse into the future". *Cardiovascular Journal of Africa* 26 (2015): S27-38.
6. Mapoure NY., et al. "Predictors of in-hospital mortality for stroke in douala, cameroon". *Stroke Research and Treatment* 68 (2014): 120-129.
7. Beyiha Q., et al. "Aspects épidémiologiques et facteurs de gravité des accidents vasculaires cérébraux au Cameroun". *Journal of Maghréb Anesth-Réanimation Médecine Urgence* 66.15 (2008): 293-297.
8. Mapoure YN., et al. "Stroke Epidemiology in Douala: Three Years Prospective Study in a Teaching Hospital in Cameroon". *World Journal of Neuroscience* 04.5 (2014): 406-414.
9. Kuate-Tegueu C., et al. "Mortalité par Accident Vasculaire Cérébral et ses Déterminants dans un Hôpital de Référence de Douala (Cameroun)". *Health Science and Disease* 17.1 (2016).
10. Manea MM., et al. "Brain-heart axis--Review Article". *Journal of Medicine and Life* 8.3 (2015): 266-271.
11. Catai AM., et al. "Heart rate variability: are you using it properly? Standardisation checklist of procedures". *Revista Brasileira de Fisioterapia* 24.2 (2020): 91-102.
12. Rajendra Acharya U., et al. "Heart rate variability: a review". *Medical and Biological Engineering and Computing* 44.12 (2006): 1031-1051.
13. Vanderlei LCM., et al. "Basic notions of heart rate variability and its clinical applicability". *Revista Brasileira de Cirurgia Cardiovascular* 24.2 (2009): 205-217.
14. I C W Z. "Heart rate variability". *Handbook of Clinical Neurology* (2013): 117.
15. Yperzeele L., et al. "Heart rate variability and baroreceptor sensitivity in acute stroke: a systematic review". *International Journal of Stroke* 10.6 (2015): 796-800.
16. Chiasseu Mbeumi M and Mbahe S. "Etude descriptive des accidents vasculaires cérébraux à Douala, Cameroun". *Medecine Tropicale* 71 (2011): 492-494.
17. Population, hommes (% du total) - Cameroon | Data.
18. Truelsen T., et al. "Stroke incidence and prevalence in Europe: a review of available data". *European Journal of Neurology* 13.6 (2006): 581-598.
19. Shaffer F and Ginsberg JP. "An Overview of Heart Rate Variability Metrics and Norms". *Frontiers in Public Health* 5 (2017): 258.
20. Nganou-Gnindjio CN., et al. "Poor glycemic control impacts heart rate variability in patients with type 2 diabetes mellitus: a cross sectional study". *BMC Research Notes* 11.1 (2018): 599.