



## Original Article

## Cardiac Arrhythmia during Chronic Hemodialysis: A Cross-Sectional Holter ECG Study in Patients from North Cameroon

### *Arythmies cardiaques chez les patients hémodialysés chroniques: Une étude transversale au Nord Cameroun utilisant le Holter ECG*

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### ABSTRACT

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**Key words:** Arrhythmias, chronic hemodialysis patients, North Cameroon.

**Mots-clés :** Troubles du rythme cardiaque, hémodialysés chroniques, Nord Cameroun.

**Background.** Cardiac arrhythmia is frequently observed in patients with end-stage renal disease (ESRD), and it is associated with a high morbidity and mortality, but ECG studies in this group are rare. The aim of our study was to describe the occurrence, severity, and risk factors of cardiac arrhythmia in patients with ESRD in the North Cameroon region. **Methods.** We carried out a cross-sectional study in the hemodialysis units of two regional hospitals in the cities of Maroua and Garoua, Cameroon. Over a four month period in 2015, we consecutively recruited consenting adult patients on maintenance hemodialysis for at least three months. A 24-hour Holter ECG monitor was placed just before dialysis. Ventricular arrhythmia was classified according to Lown classification. **Results.** 30 participants (63.3% males) were included in the study. Their mean age was  $42 \pm 15.7$  years (range 30 – 67 years). Hypertension was the most frequent co-morbid condition, present in 21 cases (70%). On standard ECG, 25 patients (83.3%) had normal sinus rhythm while 5 (16.7%) had sinus tachycardia. The mean ejection fraction (EF) was  $64.4 \pm 15\%$ , and ranged from 32 to 83%. The most frequent pericardial finding was effusion (46.6%). The overall average heart rate was  $85.7 \pm 14.8$  bpm, and ranged from 62 to 120 bpm. The most frequent arrhythmia on Holter ECG was PVC of varying degrees seen in 26 (86.7%) of patients. This was followed by supraventricular premature contractions (21, [70%]), which were all junctional in origin. Of those with PVC, 12 (46.2%) had complex arrhythmia. Six (20%) patients had salves of Premature Ventricular Contractions (PVC). **Conclusion.** Complex Premature ventricular contractions frequently occurred in patients on maintenance hemodialysis. This was associated with left ventricular systolic dysfunction. This stresses the need for a comprehensive cardiac evaluation including Holter-ECG recordings this group of patients.

### RÉSUMÉ

**Introduction.** Les troubles du rythme cardiaques sont fréquemment observés chez les patients en insuffisance rénale chronique terminale (IRCT) et sont associés à une grande morbidité et mortalité. Le but de notre étude était d'identifier les principaux troubles du rythme cardiaque au HOLTER ECG de 24H chez les patients hémodialysés chroniques suivis dans deux centres d'hémodialyse au Nord Cameroun. **Méthodes.** Notre étude transversale descriptive a été menée dans 2 centres d'hémodialyse au Nord Cameroun (Garoua et Maroua) de Février à Mai 2015. Tous les patients hémodialysés depuis plus de 03 mois ayant accepté de participer à l'étude ont été inclus. Un enregistrement électrocardiographique de longue durée (HOLTER ECG) a été réalisé pendant 24H et débutait peu avant chaque séance de dialyse. Les extrasystoles ventriculaires (ESV) ont été classées selon la classification de LOWN. **Résultats.** 30 patients ont été retenus. La moyenne d'âge était de  $42 \pm 15.65$  ans, et les hommes représentaient 63.3% de l'effectif. La principale comorbidité retrouvée était l'hypertension artérielle (21 patients, 70%). A l'ECG standard 25 patients étaient en rythme sinusal normal tandis que 5 patients étaient en tachycardie sinusale. A l'échodoppler cardiaque la fraction d'éjection ventriculaire gauche moyenne était de  $64.4 \pm 15\%$ . On a retrouvé dans 46% des cas un épanchement péricardique. Au Holter ECG la fréquence cardiaque moyenne de 24h était de  $85.7 \pm 14.8$  bpm. Parmi les troubles du rythme détectés, les ESV étaient présentes dans 86,7% des cas dont 46,2% étaient classées comme complexes. Les extrasystoles supraventriculaires (ESSV) étaient retrouvées chez 70% des patients. Parmi les 12 (46,2%) patients qui avaient des ESV complexes, 6 patients avaient des salves d'ESV. **Conclusion.** Les ESV sont fréquentes chez les patients hémodialysés chroniques. Ces ESV sont associées à une altération de la fonction systolique ventriculaire gauche. Cela souligne la nécessité d'une évaluation cardiaque complète incluant un enregistrement Holter-ECG de 24h chez ce groupe de patients.

## INTRODUCTION

Chronic Kidney Disease (CKD) has an insidious onset, and can progress to end-stage renal disease (ESRD) that will require renal replacement therapy [1,2]. The incidence is on the rise, with the greatest impact in East Asia [3–6]. Despite the therapeutic advances, the five year survival rarely goes beyond 36 to 53%. This is associated with the high rates of complications, especially cardiovascular [7,8]. Cardiovascular disorders represent the first cause of mortality in patients with end-stage CKD, with a rate ten to thirty times more frequent than the general population. Dialysis and renal transplantation are the mainstay of treatment in ESRD [4]. Sudden death is seen in up to 22% of patients treated with hemodialysis, and mainly due to arrhythmia from dyskalemia [9,10]. Arrhythmias are frequently seen during hemodialysis sessions, and can persist several hours after dialysis [11–14]. In low-income settings south of the Sahara, there is a constant rise in the number of people with CKD, and hemodialysis remains the only treatment modality [5,6]. To the best of our knowledge, no local data exist on the frequency, risk factors and the types of arrhythmia in patients on maintenance hemodialysis. Our study aimed to fill this gap. The result of this cross-sectional Holter ECG will guide informed decisions for patient care and policy making in this low-income setting.

## METHODS

### Study design and setting:

Between February and May 2015 (four months), we carried out a cross-sectional Holter ECG study in the hemodialysis units of two regional hospitals in the cities of Maroua and Garoua in Cameroon, sub-Saharan Africa. Maroua is the regional headquarter of the Extreme North region. The reference regional hospital has a hemodialysis unit with eight functional Fresenius 4008S dialysis generators, and has a catchment population of about 3.5 million inhabitants. Garoua is the regional headquarter of the North region. The reference regional hospital has a hemodialysis unit with six functioning Fresenius 4008S dialysis generators, and has a catchment population of about 2.5 million inhabitants. Both are neighboring regions located in the Savanah zone of Cameroon, where outdoor temperatures can reach 40 to 50°C during the day. Both hemodialysis centers are managed by two nephrologists. The lone Cardiologist (BH) works at the Garoua regional hospital, and serves both regions and the environs.

### Participants

Participants were consenting adult patients of both sexes, aged  $\geq 18$  years, who had end-stage renal disease, and had been on maintenance hemodialysis for at least three months. Those with known cases of arrhythmia were not included.

## Variables

Patients were interviewed and examined (MM). We obtained the following clinical informations. Socio-demography (age and sex), symptoms suggestive of heart disease (dyspnea, orthopnea, paroxysmal nocturnal dyspnea, cough, chest pain, palpitation), cardiovascular risk factors (hypertension, diabetes, tobacco use, alcohol misuse, dyslipidemia, sedentarity), history of chronic kidney disease (cause, duration of pre-dialysis, duration in dialysis, mode of entry into dialysis, number and duration of dialysis sessions), anthropometric parameters (weight, height, waist circumference), hemodynamic parameters (blood pressure, pulses, respiratory rate), and clinical signs of left and right heart failure. Then, we performed standard ECG, cardiac ultrasound, and placed the 24-hour Holter ECG monitor.

### Measurements

**Electrocardiography:** This was performed at rest using a commercially available ECG machine (Mac 500 GE), using standard speed (25 mm/s) and voltage (1 mV/10mm) in a calm environment with normal room temperature. The recording was read by BH and aimed to obtain baseline data for the presence of arrhythmia.

**Trans-thoracic Echocardiography:** This was performed by an experienced cardiologist (BH) with the patient in the left lateral decubitus position using a commercially available echocardiograph (Mindray).

Left ventricular end-diastolic diameter (LVEDd) expressed in millimeters was measured in the long parasternal window view. Patients with LVEDd  $\geq 60$  mm were retained for the study. Left atrial surface area was measured in end-systole in the apical four chamber view. Left atrial enlargement was considered if this was  $\geq 20$  cm $^2$ . Right ventricular diameter (mm) was measured in the long parasternal window view. This was considered dilated when it was  $> 45$  mm.

Left ventricular ejection fraction (EF) was measured using the Teicholz method when there was no segmental wall motion anomaly, or using the Simpson method when there was a regional wall motion anomaly. This was considered normal if EF  $\geq 55\%$ , mildly reduced if EF 45 – 55%, moderately reduced if EF 30 – 45%, and severely reduced if EF  $< 30\%$ . Diastolic function was assessed from the trans-mitral pulse wave and lateral mitral annulus tissue Doppler measurements. This was classified using the Appleton classification [17].

**Holter ECG:** This was measured for 24 hours using a commercially available long duration ECG recorder and analyzed using the software EasyScope of ELA Medical (Sorin Group) MultiDay Version 3.10. The recorder was placed just before the dialysis session, and the recordings were read by BH. The findings were classified using the Lown classification [18].

### Sample size

Patients were consecutively recruited for the study during the period of research. A consecutive sample of all possible eligible patients was considered.

### Statistical analysis

Data was analyzed with the Statistical Package for the Social Sciences software (SPSS) version 20.0 (IBM Corp. Released 2012). We expressed Categorical variables as frequencies and proportions, and continuous variables as means (SD). We grouped patients in to two, those with severely reduced EF and those with mild to moderately reduced or normal EF and compared the occurrence of the various arrhythmias using Student t-test. A p value < 0.05 was considered statistically significant for observed difference or trends.

## RESULTS

### Participants and descriptive data

30 patients were included in this study, of whom there were 19 (63.3%) males and 11 (36.7%) females. Their mean age was  $42 \pm 15.7$  years and ranged from 30 to 67 years. 14 patients [46.7%] were aged between 40 to 60 years, 12 (40%) were aged less than 40 years, and 4 (13.3%) were aged more than 60 years. The socio-economic and cardiovascular risk factors are shown in Table 1. Most of the patients had low or average socio-economic status, and hypertension was the most frequent risk factor. Palpitations and chest pains were the most frequent complaints. The mean duration in maintenance hemodialysis was  $22 \pm 27$  months, and ranged from 3 to 108 months.

**Table I: Socio-economic status, cardiovascular risk factors, and presenting symptoms of patients**

Characteristics	N	%
<b>Revenue status</b>		
Fixed	8	26.7
Retired	4	13.3
No fixed	12	40
None	6	20
<b>Socio-economic status</b>		
Low	11	36.7
Average	15	50
High	4	13.3
<b>CV Risk factors</b>		
Hypertension	25	83.3
Diabetes	3	10
Tobacco	0	0
Alcohol	0	0
Obesity	1	3.3
Gout	3	10
Chronic glomerulonephritis	3	10
<b>Symptoms</b>		
Precordial pain	13	43.3
Palpitations	13	43.3
Dyspnea	4	13.3

Most of the patients (27, [90%]) had 8 hours of dialysis per week, and 3 (10%) had 12 hours of dialysis per week. Most patients (26, [86.7%]) did not receive specialist Nephrologist care prior to entering the chronic hemodialysis program, and 23 (76.7%) of them presented as emergencies.

### Outcome data and main results

On standard ECG, 25 (83.3%) were in normal sinus rhythm while 5 (16.7%) had sinus tachycardia. Six (20%) patients had premature ventricular contractions (PVC) at baseline.

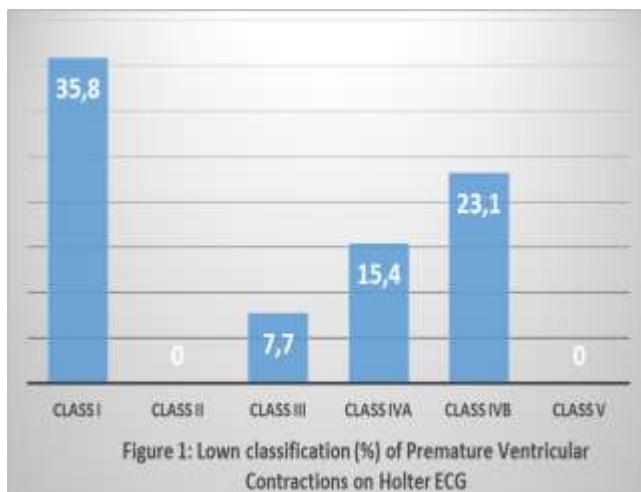
The findings on cardiac ultrasound are shown in Table 2: The mean ejection fraction (EF) was  $64.4 \pm 15\%$ , and ranged from 32 to 83%. The most frequent finding was pericardial effusion (46.6%), followed by left ventricular hypertrophy (LVH) and low EF (33.3%).

The findings on Holter ECG are shown in Table 2. The average of the minimum heart rate was  $55.4 \pm 15.2$  beats per minute (bpm), and ranged from 20 to 87 bpm. The average of the maximum heart rate was  $138 \pm 30.1$  bpm, and ranged from 96 to 212. The overall average heart rate was  $85.7 \pm 14.8$  bpm, and ranged from 62 to 120 bpm.

**Table II: Echocardiographic and Holter ECG findings of the patients**

Findings	N	%
<b>Echocardiography</b>		
Left Ventricle dilation	7	23.3
Left ventricle Hypertrophy	10	46.6
Pericardial effusion	14	33.4
Mitral valve regurgitation	7	23.3
Aortic valve regurgitation	2	6.7
Low Ejection Fraction	10	33.4
<b>Holter ECG</b>		
Premature supraventricular contraction	21	70
Supra-Ventricular Tachycardia	7	23.3
Atrial fibrillation	1	3.3
Premature Ventricular contractions (PVC)	26	86.7

The most frequent arrhythmia on Holter ECG was premature ventricular contractions of varying degree seen in 26 (86.7%) of patients. This was followed by supraventricular premature contractions (21, [70%]), which were all junctional in origin. The distribution of PVC is shown in Figure 1. Of those with PVC, 12 (46.2%) had complex arrhythmia. Salves of PVC were significantly associated low ejection fraction (40% versus 5%,  $p=0.037$ ).



## DISCUSSION

We carried out a cross-sectional Holter ECG study in a group of patients on maintenance hemodialysis for at least three months in a low-income setting in Cameroon, sub-Saharan Africa. Complex premature ventricular contractions frequently occurred in this group of patients on maintenance hemodialysis. This was associated with left ventricular systolic dysfunction.

Despite the relatively lower rate of patients with chronic kidney disease (CKD), the burden of disease appears higher in low income settings. Patients with end-stage chronic kidney disease on maintenance hemodialysis in low income settings are relatively younger, compared with those in high income settings [19]. They are at least twenty years younger, with a male predominance, and in the prime of their working age [20]. This has serious economic implications as they are less productive, and the cost of care is high for the patients and their families, and the society as a whole. Most of the patients had low socio-economic status, thus limiting access to timely quality nephrology care.

This manifests as late referrals [21] or no pre-dialysis preparation as shown by our data. The end result is a very mortality rate with loss of man power needed for economic growth [7,20]. As expected, hypertension was the most frequent co-morbid condition, which could be a cause or consequence of CKD in this population [8]. Hypertension has been shown to be the second cause of CKD after chronic glomerulonephritis in this low income setting [22]. Also, heart failure and valvular lesions are frequently seen in this group of patients [8].

Coupled with the high economic burden of end-stage CKD, our patients were under-dialyzed. Most of them had just eight hours of hemodialysis per week, compared to the recommended 12 to 16 hours per week. This was due to a high patient demand for the scarce human and material resources in our low-income setting. The end result is a drastic reduction in survival, which we expect to be less

than 36 to 53% at 5-years as reported in medium-to-high income settings [7,20]. With this situation in our setting, we expected high rates of death due cardiac causes, especially the arrhythmias [4]. Most of our patients had PVCs, and almost half of whom had complex forms, and it mostly occurred in those with low ejection fraction. This stresses the need for a comprehensive cardiac evaluation including cardiac ultrasound in all patients admitted for chronic hemodialysis. Those with low ejection fraction should receive further care aimed at reducing the risk of fatal arrhythmias and improve on survival in low income settings.

Our findings should be interpreted in the light of some limitations. Our sample size was small due to logistic difficulties for research. This did not permit us capture other risk factors for arrhythmia. Serum electrolytes and other metabolic panel were not performed during the time of the study due financial constraints. The effects of metabolic distortion could not be controlled for, especially as patients were under-dialyzed. Despite these limitations, this study has some merits. We have provided the first evidence on the occurrence and severity of cardiac arrhythmia in a group of patients on maintenance hemodialysis in a low-income setting, where outdoor temperatures can reach 40 to 50°C most time of the year.

## CONCLUSION

Complex Premature ventricular contractions frequently occurred in patients on maintenance hemodialysis in Cameroon. This was associated with left ventricular systolic dysfunction. This stresses the need for a comprehensive cardiac evaluation including Holter-ECG recordings this group of patients.

## AUTHORS' CONTRIBUTION

Study Conception: BH, MPH, SK.

Study Design: BH, MPH, AM, SK.

Data collection: BH, SNA, BJ, CNN, FK, MAM.

Data analysis and interpretation: BH, MAM, MPH, JB, LKM, AM, SK.

Draft of Manuscript: BH, MPH, MAM, JB, LKM, CNN, AM, SK.

All the authors read and approved the final manuscript and the decision to publish the work.

**Ethical statement.** We carried out this work in accordance with the declarations of Helsinki [15]. Ethical clearance was obtained from the ethical committee of the Faculty of Medicine and Pharmaceutical Sciences, University of Douala. We report this work in accordance with the Standard for Reporting Observational Studies (STROBE) checklist [16].

**Acknowledgements.** We thank the patients and support staff of the hemodialysis units.

**Conflict of Interest.** We declare no conflict of interest.

**Funding.** No funding was received for this work.

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