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Research Article

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Determinant and Impact of Left Ventricular Hypertrophy (LVH) in Chronic Renal Failure (CRF) Patients

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ABSTRACT

Left ventricular hypertrophy is the most common cardiovascular complication in chronic renal failure. It appears to be associated with excess mortality. Objective: To determine the factors associated with left ventricular hypertrophy (LVH) in patients with chronic kidney disease (CKD), and to describe their influence on renal function. Patients and methods: This was a descriptive and analytical study conducted over 6 years (January 1, 2012 to December 31, 2017) on CKD patients who had an electrocardiogram or cardiac ultrasound. Results: A total of 329 patients were included. LVH was found in 223 patients, a prevalence of 68%. The sex ratio M/F was 2.1. Mean age was 51.05±14.17 years (range 11-95 years). Arterial hypertension predominated (97% of cases), followed by diabetes (26%).Univariate and multivariate analysis showed that LVH was associated with: age ≤51 years (p=0.0037) and with arterial hypertension (p=0.0018) and anemia (p=0.0018). Over a 5-year period, CKD patients with LVH experienced a more rapid decline in renal function than those without LVH (p<0.0001). There was also a higher rate of death in patients with LVH (83%) than in those without (46%) during a 5-year follow-up. Conclusion: LVH is an important factor in the poor prognosis of CKD. This calls for systematic screening and early management by a multidisciplinary team.

Keywords: CKD, Left Ventricular Hypertrophy, Cardiovascular Complication, Hypertension, Togo

Introduction

According to ISN, chronic kidney disease (CKD) affects around 850 million people worldwide today, and will be the 5th leading cause of death by 2060[1]. It leads to a number of formidable systemic complications, including cardiovascular complications. Indeed, cardiovascular complications are the main cause of death in populations with chronic kidney disease (CKD) in developed countries [2]. Among cardiovascular complications, left ventricular hypertrophy (LVH) appears to be the most frequent, with a proportion ranging from 40% to 70%, depending on the severity of renal disease [3]. In addition to known traditional risk factors, non-traditional risk factors such as chronic volume overload, anemia, oxidative stress and bone mineral disorders have been identified in Western populations [4]. However, in sub-Saharan Africa, there is little data on this subject from a local population. In Togo, as in many African countries south of the Sahara, CKD is discovered in the terminal stage, with numerous complications [5]. Access to replacement therapy is low, and mortality high. This implies a more upstream approach to reducing mortality. We hypothesized that in CKD patients, as in Western data, LVH would lead to a more rapid deterioration in renal function. The aim of this study was therefore to identify the factors associated with LVH in patients with chronic kidney disease, and to determine its influence on changes in renal function.

Patients and Methods

Setting and Type of Study

The Nephrology and Hemodialysis Department of the Sylvanus Olympio University Hospital in Lomé was the setting for this study. Lomé is a city of 3 million inhabitants, and the CHU SO is the country's largest hospital. The nephrology department consisted of a conventional nephrology unit and a hemodialysis unit.

The study was a descriptive, cross-sectional and analytical case series with retrospective data collection. Data collection covered a period from January 1, 2012 to December 31, 2017, i.e. 6 years. This period corresponded to the start of the department's management by a nephrologist.

Inclusion and Non-Inclusion Criteria

All complete records of patients with chronic renal failure of either sex and of any age, from the nephrology and hemodialysis department of CHU Sylvanus Olympio at stage III, IV and V non-dialyzed from the MRC KDIGO 2012 classification with

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mandatory electrocardiogram (ECG) or cardiac ultrasound were included.

This study did not include:
- patients with no criteria for CKD,
- patients with stage I or II chronic kidney disease,
- patients without an ECG or cardiac ultrasound,
- patients on dialysis at the start of the study
- renal transplant patients.

Studied Variables

The variables studied were :
- Socio-demographic data: age, gender, origin, etc.
- Personal history: cardiovascular risk factors (hypertension, diabetes, dyslipidemia, smoking, obesity, sedentary lifestyle and use of estrogen-progestogen pills), HIV, chronic alcoholism, SS or SC hemoglobinopathy.
- Clinical data: personal history, reason for admission Weight (W) and height (H), Body Mass Index, causative nephropathy, blood pressure.
- Paraclinical data: electrocardiogram (ECG), cardiac echocardiogram cardiac ultrasound and biological tests, including blood urea and creatinine, hemoglobin, calcium, phosphorus, natremia, magnesium, chloramia, kalemia, 24-hour proteinuria, blood glucose, glycosylated hemoglobin, C-reactive protein, lipid profile, liver enzymes, urine cytobacteriological examination.
- Prognostic and evolutionary data. GFR was calculated for all patients at entry using the MDRD equation, without the corrective factor of race.
- GFR was calculated every 3 months for one year, then every year for 5 years after the start of treatment, in patients with and without LVH. We then carried out a comparative analysis of GFR in these 2 populations.

We looked for the occurrence of cardiovascular events/ complications over 5 years. Events included acute coronary syndrome (ACS), stroke, acute pulmonary oedema (APO), hospitalization and death.

Data Analysis

Data were processed and analyzed using R Studio version 3.4.2. and Microsoft Office Excel 2019. Once the data had been processed, an analysis was carried out. Quantitative variables were presented as mean and standard deviation, while qualitative variables were expressed as headcount and percentage. Pearson's Chi-square or Fisher's exact test was used for qualitative variables, and Student's t-test for quantitative variables. The significance level was set at 0.05.

Logistic Regression

Univariate and multivariate logistic regression was performed to identify factors associated with LVH. The dependent variable was LVH, coded 1 if the patient had LVH at follow-up and 0 if not. The explanatory variables were clinical or prognostic socio-demographic variables. The association between each explanatory variable and the dependent variable was estimated using the Odds Ratio (OR) and its 95% confidence interval.

Variables statistically associated with LVH in the univariate analysis with a significance level of $p<0.20$ were introduced into the initial model. The top-down stepwise procedure was used to select the final model. This involved including all selected variables in the initial model and then progressively removing the least significant variables. At each step, we checked that there was no major confounding between the removed variable and those remaining in the model, by verifying changes in their Odds ratios.

Multivariate analysis was used to estimate the Adjusted Odds Ratio (aOR) and its 95% confidence interval for each variable retained. Once the final model had been obtained, we looked for interactions between the different variables in the final model by including interaction terms (product of the 2 variables concerned) in the model and checking that they were not significant. The adequacy of the model was checked on the basis of the R^2 value.

Operational Definitions

Chronic renal failure was defined by an estimated GFR of less than 60 ml/min/1.73m², characterized by normocytic normochromic anemia, hypocalcemia and renal atrophy. Estimated GFR was obtained by calculating creatinine clearance using the simplified MDRD (Modification of Diet in Renal Diseases) formula.

We selected the indices most commonly used in current practice to define left ventricular hypertrophy (LVH):
- On ECG, the Sokolow-Lyon index: SV1 + RV5 or V6 in favor of LVH when it exceeded 35 mm in a subject over 35 years of age. In subjects under 35, an amplitude greater than 45mm was required.
- Blondeau et Heller index: SV2 + RV7 in favor of LVH when it exceeded 35 mm.
- Casale or Cornell index: RaVL + SV3: LVH if >28 mm in men, > 20 mm in women.
- On cardiac ultrasound, left ventricular hypertrophy (LVH) was assessed using the left ventricular mass index (LVMI). LVMI was calculated as the ratio of left ventricular mass to body surface area. LVH was defined as LVMI greater than 115g/m² in men and greater than 95g/m² in women.

Ethical Considerations

To ensure the confidentiality of the information gathered, individualized forms were used and anonymized.

Results

Descriptive data

During the study period, 687 new patients were identified as having chronic renal failure. Of these, 329 were identified and 223 had left ventricular hypertrophy (LVH), representing a frequency of 67.8% of left ventricular hypertrophy among chronic renal failure patients. End-stage patients accounted for the majority (49%) (Table 1). They were predominantly male, with a sex ratio of 2.1. The median age was 51 years. The most represented age group was 51 to 60. Subjects with LVH were younger than those without LVH (p=0.0015), as shown in Table 1, which summarizes population data according to the presence or absence of LVH.

Table 1: Characteristic of the population distributed according to the presence or absence of LVH, CHUSO

		No LVH		Presence of LVH		
	Nombre	**n=223**	**(%)**	**n=106**	**(%)**	**p-value**
Gender						**0,0838**
Male	223	65	61,32	158	70,85	
Female	106	41	38,68	65	29,15	
Median age (Years)						**0,0015**
≤51	169	41	38,68	128	57,40	
>51	160	65	61,32	95	42,60	
Profession						**0,1496**
Student/Retired	104	41	38,68	63	28,25	
Liberal profession	165	49	46,23	116	52,02	
Residence						**0,6809**
Urban	265	84	79,25	181	81,17	
Rural	64	22	20,75	42	18,83	
HTA						**0,0249**
No	9	6	5,66	3	1,35	
Yes	320	100	94,34	220	98,65	
Diabetes						**0,0506**
No	243	70	66,04	173	77,58	
Yes	86	36	33,96	50	22,42	
Dyslipidemai						**0,5075**
No	204	63	59,43	141	63,23	
Ye	125	43	40,57	82	36,77	
Smoking						**0,9999**
No	320	103	97,17	217	97,31	
Yes	9	3	2,83	6	2,69	
Obesity						**0,4445**
No	321	105	99,06	216	96,86	
Yes	8	1	0,94	7	3,14	
VIH						**0,9999**
No	319	103	97,17	216	96,86	
Yes	10	3	2,83	7	3,14	
Anemia: Hb (g/dl)						**0,0226**
Sévère [1-8]	62	20	23,26	42	22,22	
Moderate [8-10]	147	48	55,81	99	52,38	
Mild[10-12]	66	18	20,93	48	25,40	
GFR (ml/min/173m²)						**0,6496**
< 15	161	53	53,00	108	49,09	
[15 - 29]	81	22	22,00	59	26,82	
[30 - 59]	78	25	25,00	53	24,09	
Cholesterol						**0,2600**
Normale	124	34	45,95	90	55,56	
Increased	112	40	54,05	72	44,44	
Calcémia (mg/l)						**0,8698**
Low (<90)	132	38	60,32	94	59,12	
Normal	90	25	39,68	65	40,88	
Phosphorémia (mg/l)						**0,6640**
Decreased	5	2	6,25	3	3,37	
Normal	73	20	62,50	53	59,55	
Increased	43	10	31,25	33	37,08	

Protéinurie						**0,7472**
No	13	3	13,04	10	17,54	
Yes	67	20	86,96	47	82,46	

Hypertension was the most common comorbidity (97%), followed by dyslipidemia (38.0%) and diabetes (26.1%). There was a statistically significant association between hypertension and the presence of LVH (p=0.0249). The initial nephropathy was vascular nephropathy in 72.3% of cases. Diabetic nephropathy was confirmed in 5.1% of cases, and HIV-associated nephropathy in 2.7%. There was no statistical association between initial nephropathy and the presence of LVH. No biological data were associated with LVH.

Evolutionary Data

Figure 1 shows the evolution of GFR after conservative treatment, according to the presence or absence of LVH. The mean GFR at entry, 19ml/min/1.73m² for patients with LVH (+), had risen to 27ml/min/1.73m² after 5 years.

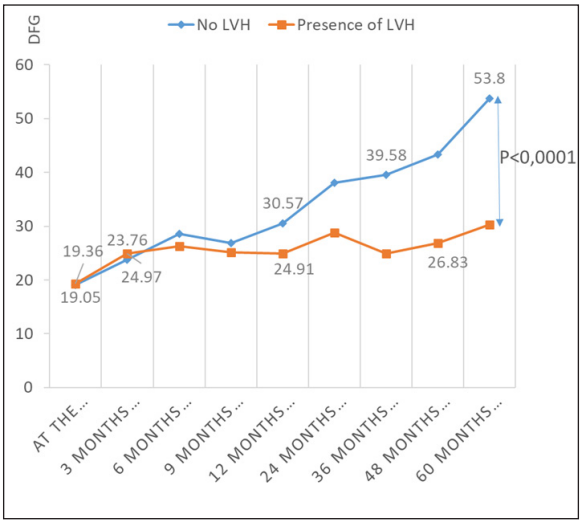

Figure 1: Comparative mean GFR curve for CKD patients with and without LVH

In patients without LVH (LVH (-)), mean GFR increased from 19ml/min/1.73m² to 53.8ml/min/1.73m².

Mortality was 37.6% in the LVH (+) group and 17.9% in the LVH (-) group. All complications (coronary syndrome, cerebrovascular accidents, acute lung edema, hospitalizations) were greater in the LVH (+) group, as shown in Table 2.

Table 2: Events/complications during the course of CKD in patients with and without LVH

	LVH (+) n(%)	LVH (-) n (%)
Acute coronary syndrom	57 (26%)	9 (8%)
Cerebrovascular accident	46 (21%)	12 (11%)
Acute lung oedema	88 (39%)	23 (22%)
Hospitalizations	218 (97%)	81 (76%)
Deahs	84 (38%)	9 (8%)
LVH (+) : present of LVH, LVH (-) : Absence of LVH		

Analytical Data

Factors associated with ventricular hypertrophy were age and arterial hypertension. In both the initial and final models, the risk of having left ventricular hypertrophy was significantly higher for subjects under 51 than for those over 51 (RCa=2.04; 95% CI [1.27-3.33] p value=0.0037), as well as for patients with arterial hypertension (Rca=2.32; 95% CI [1.38-4.00] p value=0.0018) (table 3).

Table 3: Multivariate analysis

	Initial Model			Final Model		
	OR	**IC à 95%**	**P values**	**ORa**	**IC à 95%**	**P values**
Median Age (years)			0,0276			0,0037
>51	1,00			1,00		
≤51	1,84	[1,07-3,17]		2,04	[1,27-3,33]	
Anemia			0,0190			0,0015
No	1,00			1,00		
Yes	1,27	[1,59-2,73]		2,78		
HTA			0,0055			0,0018
No	1,00			1,00		
Yes	2,15	[1,26-3,73]		2,32	[1,38-4,00]	
OR : Odds Ratio, ORa :Odds ratio ajusted, IC : Confidence interval						

Discussions

The prevalence of LVH in African patients with chronic renal failure is variable. In our series it was 68%, whereas it was less frequent (43%) in the Amoako series in Ghana and more frequent (83%) in the Nwankwo series in Nigeria [6,7]. These differences can be explained by the heterogeneity of the populations studied, both in terms of sociodemographics and renal disease itself. Indeed, our population of kidney patients was young, with a median age of 51. In the African literature, it is common to find a young population of CKD patients, generally economically active [5,8].

Age was the primary factor associated with the occurrence of LVH in multivariate analysis. Subjects aged 51 and under were 2.04 times more likely to develop LVH than those over 51 (p=0.0037). Although this association is widely described in the nephrology literature, it is a two-way street. Indeed, Peterson and Tomilina found in their studies that young age was a socio-demographic factor significantly associated with LVH, whereas Nardi and Amoako found advanced age to be a risk factor [6,9-11].

The hypothesis of living conditions (smoking, precariousness, alcohol, drugs) in young populations was put forward by Peterson in the Afro-American population [9]. However, myocardial aging and the accumulation of cardiovascular risk factors could also explain LVH in elderly subjects.

Hypertension was the 2nd risk factor for LVH in our population. Hypertensive patients were 2.32 times more likely to have LVH than those without hypertension, i.e. 33.33% (p=0.0018). As found in several previous studies [6,12], this notion seemed important to us, given the importance of the proportion of people with hypertension in sub-Saharan African communities. In Togo, according to the EDS 3, hypertension affects 19% of the active population. Like many African countries, Togo has undergone an epidemiological transition since the 90s, with a surge in non-communicable diseases. This pain is twofold, as infectious diseases coexist and are by no means under control [13,14]. With regard to other comorbidities such as diabetes, obesity and smoking, in our series there was no correlation with the occurrence of LVH, as in the work of Stack and Vigan [15,16].

In addition to these known traditional risk factors (DRFs), there are non-traditional risk factors such as anemia, hydrosodium overload, inflammation and hyperhomocysteinemia [17]. In CKD patients, LVH is described as the first feature of uremic heart disease [12]. The second feature of uremic cardiomyopathy, apart from LVH, is the development of myocardial fibrosis followed by dilatation of the heart. These descriptions could explain the other cardiovascular complications found in our patients. In the LVH (+) group, there was a 3-fold increase in coronary syndrome, and a 2-fold increase in acute pulmonary edema and stroke. Hospital admissions were high in both groups, no doubt due to the multiple non-cardiovascular complications. In fact, our results corroborate data thought to be Western. According to Cozzolino, at least 35% of patients with CKD show signs of an ischemic event (myocardial infarction or angina pectoris) at the time of presentation to a nephrologist [3].

Indeed, LVH is known to be an unfavorable prognostic factor in CKD [17]. In figure 1, the data showed that left ventricular hypertrophy significantly impaired recovery of improved renal function. Although it is difficult to draw conclusions from our experiments, the finding is clear in this series: patients with LVH, after 5 years of conservative treatment, did not significantly improve their GFR.

After 5 years of treatment, the mean GFR rose from 30 to 53 ml/min in patients with chronic renal failure without LVH, while in those with LVH it rose from 24.35 to 30.35, remaining virtually unchanged. In the space of 5 years with conservative treatment, it would be possible to regain up to 30 GFR points in the absence of left ventricular hypertrophy in patients with chronic renal failure. Several studies had already identified left ventricular hypertrophy as an independent factor in the deterioration of CKD [18]. However, these local data from an African population confirm the value of conservative treatment, and reiterate the vicious circle between CKD and cardiovascular complications. Thus, LVH will aggravate CKD, which in turn will lead to LVH [3].

The retrospective nature of our study was its main limitation. The way patients were recruited could be the source of bias (selection, information or confounding bias), making it difficult to generalize the results. Despite the limitations observed, this study remains of interest, as not only was it the first with similar objectives carried out in Togo, but its results could also contribute directly to better patient management.

Conclusion

Left ventricular hypertrophy is an important unfavorable prognostic factor in the chronic renal failure patients studied. In the absence of LV hypertrophy, patients gain GFR points with conservative treatment. When present, it not only leads to GFR stagnation, but also to other cardiovascular complications and a higher proportion of deaths. The risk factors for LVH in our CKD patients were: age, hypertension and anemia. Precautions must be taken rigorously in patients with chronic kidney disease, acting on these risk factors to slow disease progression as much as possible. The importance of multidisciplinary collaboration and cardiological follow-up in the management of chronic renal failure must be stressed once again.

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