

# Determinants and Risks Factors of Renal Failure in Patients with Heart Failure in Cardiology Department of CHU Sylvanus Olympio of Lomé (Togo)

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## Abstract

**Introduction:** The morbidity and mortality of patients with heart failure are known to increase rapidly in the presence of renal insufficiency, which is usually the cause but may be a consequence. To organize better prevention of renal failure, we undertook this study to identify the determinants of renal failure in the population of patients with heart failure. **Methodology:** This was a retrospective descriptive and analytical study of heart failure (HF) cases hospitalized from January 1st to December 31st, 2016, over a period for twelve (12) months at CHU Sylvanus Olympio. Patients who performed cardiac Doppler ultrasound were included in our study. Renal failure was defined as eGFR (estimated glomerular filtration rate) less than 60 ml/min/1.73m<sup>2</sup>. Multivariate logistic regression was performed to investigate associated factors. The dependent variable was DFG status: coded 1 if the GFR is less than 60 ml/min and 0 if not. **Results:** A total of 216 patients were included. The majority were female (54.17%). The median age of patients was 53 years [IQI = 32 - 61 years] with extremes of 15 and 96 years. 16.49% of patients had a GFR of less than 60 ml/min. In multivariate analysis the average standard of living (OR = 2.40, p = 0.0456), diabetes (OR = 2.67, p = 0.0300), hypertension (OR = 5.66, p = 0.0399), alcoholism (OR = 4.00, p = 0.0063) were the main factors in the development of an RF/HF. **Conclusion:** The average standard of living, diabetes, hypertension, and chronic alcoholism are the determinants of renal failure in HF.

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## Keywords

Heart Failure, Renal Failure, Determinants, Togo

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## 1. Introduction

Heart failure (HF) is a serious and frequent pathology whose evolution is enlarded of several complications with a risk of sudden death at all stages. It is an important public health problem because of its frequency, its impact on mortality and the significant medical and economic resources it absorbs [1] [2]. It is responsible for nearly 1 million hospitalizations in the United States and affects 1% to 2% of the population between 50 and 59 years [2]. In Togo, the work of Pio *et al.* [3] reveals that heart failure is the leading cause of hospitalization in cardiology at the Sylvanus Olympio University Hospital Center (CHU-SO). It is known that the morbidity and mortality of patients with heart failure increase rapidly in the presence of renal failure, which is usually the cause but may be a consequence [4]. In Togo, the prevalence of renal failure is estimated at 73.2% in nephrology consultation, with 11.6% of patients referred by cardiologists in heart failure [5]. In a context where health care is self-funded by the patient, kidney failure becomes inevitable and its treatment overwhelming for the patient. We therefore considered it necessary, to organize better prevention, to undertake this study to identify the determinants of renal failure in the population with heart failure.

## 2. Patients and Methods

The Cardiology Department of CHU-SO of Lomé which is the reference hospital of Togo served as a framework for our study. This was a descriptive and analytical retrospective study of hospitalized heart failure cases from January 1st to December 31st, 2016, over a twelve (12) month period. Patients with heart failure syndrome who performed a Doppler ultrasound scan were included in our study. Patients who did not have an HF or who had a clinical syndrome of HF and did not perform a cardiac Doppler ultrasound were not included in the study.

Questionnaire data were extracted from inpatient hospital registers during the study period. It was designed by the team of nephrologists of the department. It was first tested on a sample of 25 heart failure patients randomly selected to ensure that the questions and their answers were understood. The variables studied were of order:

- Sociodemographic: frequency, age, sex, place of residence, marital status, profession;
- Clinics: blood pressure (BP), body mass index (BMI), existence of diabetes, alcoholism, smoking, sedentary lifestyle, clinical signs of heart failure;
- Electrocardiographic: search for ischemia, ventricular hypertrophy, rhythm

disorders;

- Biological: glomerular filtration rate (GFR) calculated according to the formula of the Renal Diseases Modification (MDRD), hemoglobin level, lipid balance disorder, proteinuria, hydroelectrolytic disorder, phosphocalcic disorders, infection to the human immunodeficiency virus;
- Cardiac Doppler ultrasound: the appearance of the myocardium and valves, type of cardiomyopathy, left ventricular ejection fraction (LVEF).

#### **Operational Definitions**

- Renal failure was defined as eGFR (estimated glomerular filtration rate) less than 60 ml/min/1.73m<sup>2</sup> according to the simplified MDRD;
- Socio-economic groups were defined according to the SMIG (70\$) as follows: low level, for a monthly income below seventy dollars (70\$); average level, for a monthly income of between seventy and three hundred dollars (70 - 300\$); high level, for a monthly income exceeding three hundred dollars (300\$).

#### **Data processing**

The statistical analysis was performed with Studio software version 3.3.2. It consisted of a descriptive analysis, a comparative analysis and the logistic regression. It was a descriptive analysis of the population of heart failure patients with GFR < 60 ml/min. The results were expressed in terms of size and percentage for the qualitative or median and interquartile range variables for the quantitative variables. All variables were cross-referenced to the degree of GFR. A comparative analysis was carried out to find a difference between the variables collected at inclusion, depending on whether the GFR is less than 60 ml/min or not. The statistical tests used were the Pearson Chi-square test or Fisher's exact test for qualitative variables and the Student's test for quantitative variables. The threshold of significance was set at 0.05. Missing data were not considered in.

Multivariate logistic regression was performed to investigate associated factors. The dependent variable was GFR status: coded 1 if the GFR is less than 60 ml/min and 0 if not. The explanatory variables were some sociodemographic, clinical and biological variables. The step-down procedure was used to select the final model. It consisted of including all the variables chosen in the initial model and then gradually removing the least significant variables. At each step, it was checked that there was no major confusion between the removed variable and those remaining in the model by checking the modifications of their Odds ratio (tolerated variation: 20%) or even radical changes in their degrees of significance. The multivariate analysis made it possible to estimate the Adjusted Coast Ratio (RCa) and its 95% confidence interval (CI) for each selected variable. After obtaining the final model, interactions were sought between the different variables of the final model by including interaction terms (product of the 2 variables concerned) in the model and verifying their non-significance. The adequacy of the model has been verified based on the R<sup>2</sup> value.

#### **Ethical aspect**

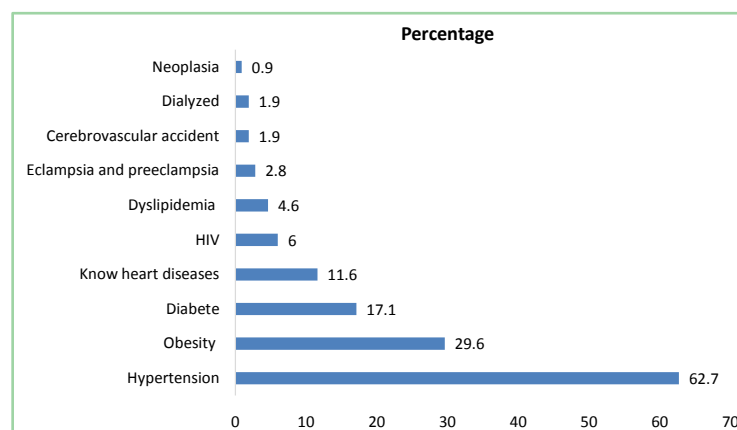
All the medical information collected was anonymised before being transmitted to the investigations. The study was made according to the recommenda-

tions of the ethics committee of the University of Lomé and in accordance with national and local regulations.

### 3. Results

A total of 216 patients with heart failure with a cardiac Doppler ultrasound were included. Of these patients, the majority were female (54.17%). The median age of patients was 53 years [IQI = 32 - 61 years] with extremes of 15 and 96 years. **Table 1** groups the other socio-demographic data of the population. **Figure 1** shows the co-morbidities of the study population. The main comorbidities were hypertension in 62.7% of cases and obesity in 29.6% of cases. The median systolic blood pressure was 130 mmHg [IIQ = 110 - 151 mmHg]. Of the 188 patients who achieved serum creatinine, 31 patients (16.49%) had a GFR of less than 60 ml/min/1.73m<sup>2</sup> and 2.13% of patients had a GFR of less than 15 ml/min. The median proteinuria was 940 mg/day [IIQ = 500 - 2350 mg/day]. The prevalence of renal failure in the study population was estimated at 16.49%. Male patients ( $p = 0.0087$ ), those older than 53 years ( $p = 0.0254$ ), patients with medium socioeconomic status ( $p = 0.0313$ ) were more likely to renal failure. The comorbidities according to the GFR are presented in **Table 1**. Hypertensive patients ( $p = 0.0005$ ); diabetics ( $p = 0.0016$ ); sedentary ( $p = 0.0011$ ); antecedents of self-medication ( $p = 0.0405$ ), alcoholism ( $p = 0.0004$ ); HIV infection ( $p = 0.0017$ ); with a hospital stay of more than 9 days ( $p = 0.0002$ ) had a high risk of having a GFR < 60 ml/min/1.73m<sup>2</sup>. Renal failure with GFR < 60 ml/min, was associated with impairment of left ventricular ejection fraction (LVEF) ( $p = 0.0289$ ), left ventricular hypertrophy (LVH) ( $p = 0.0424$ ), left atrial hypertrophy (LAH) ( $p = 0.0248$ ), ECG ischemia ( $p = 0.0102$ ) in our patients.

**Table 2** presents the result of the univariate analyzes. A total of thirteen variables were associated with renal failure: males, age greater than 53 years, average socio-economic status, hypertension, diabetes, smoking, self-medication, alcoholism, lengths of hospital stay, impaired LVEF, LVH, LAH, ischemia. The risk of developing kidney failure is higher for males ( $p = 0.0107$ ) in subjects older than 53 years ( $p = 0.0289$ ).



**Figure 1.** Distribution of patients by comorbidities related to heart failure.

**Table 1.** Distribution of patients by comorbidities, lifestyle and socio-demographic data.

	Univaried model				
	n/N	%	OR	CI à 95%	P
<b>Gender</b>					0.0107
Femal	10/101	9.9	1		
Male	21/87	24.1	2.9	[1.31 - 6.80]	
<b>Age (year)</b>					
<53	9/89	10.11	1		
≥53	22/99	22.2	2.54	[1.13 - 6.14]	0.029
<b>Socio-economic level</b>					
Hight	16/128	12.5	1		
Average	15/60	25	2.33	[1.06 - 5.14]	0.034
<b>Geographical area</b>					
Townsmen	23/158	14.6	1		
Rural	8/30	26.7	2.13	[0.81 - 5.24]	0.107
<b>Obesity</b>					
No	18/136	13.2	1		
Yes	13/52	25	2.18	[0.97 - 4.85]	0.055
<b>High blood pressure</b>					
No	2/62	3.23	1		
Yes	29/126	23	8.97	[2.57 - 56.75]	0.003
<b>Diabete</b>					
No	19/153	12.4	1		
Yes	12/35	34.3	3.68	[1.55 - 8.57]	0.003
<b>Smoking</b>					
No	30/174	17.2	1		
Yes	1/14	7.14	0.369	[0.02 - 1.96]	0.3459
<b>Self-medication</b>					
No	17/132	12.9	1		
Yes	14/56	25	2.25	[1.01 - 4.97]	0.044
<b>Alcoholism</b>					
No	16/143	11.2	1		
Yes	15/45	33.3	3.7	[1.76 - 8.97]	8E-04
<b>Sédentarity</b>					
No	20/158	12.6	1		
Yes	11/30	30.7	3.99	[1.63 - 9.58]	0.002
<b>Hospitalization duration</b>					
<9 days	13/131	9.92	1		
>9 days	18/57	31.6	4.19	[1.90 - 9.50]	4E-04

## Continued

<b>LEVF</b>						
Preserved	5/62	8.07	1			
Weathered	26/126	20.6	2.96	[1.16 - 9.14]	0.035	
<b>Hemoglobin level</b>						
<11 g/dl	12/75	16	1			
≥11 g/dl	19/113	16.8	1.06	[0.48 - 2.39]	0.883	
<b>LVH</b>						
No	11/98	11.2	1			
Yes	20/90	22.2	2.26	[1.03 - 5.18]	0.046	
<b>LAH</b>						
No	11/101	10.9	1			
Yes	20/87	23	2.44	[1.11 - 5.61]	0.029	
<b>Rythm disorder</b>						
No	10/55	18.2	1			
Yes	21/133	15.8	0.84	[0.37 - 2.00]	0.688	
<b>Ischemia</b>						
No	11/106	10.4	1			
Yes	20/82	24.4	2.78	[1.28 - 6.40]	0.012	

LVH: left ventricular hypertrophy; LAH: left atrial hypertrophy; LEVF: left ventricular ejection fraction; N = total number of patients; n = effective of patient with GFR < 60; CI = confidence interval (95%); OR = odds ratio.

**Table 2.** Effective and percentage of factors associated with renal failure in univaried model.

	Effective			GFR < 60			GFR ≥ 60			p
	N = 188	n	%	N <sub>1</sub> = 31	n <sub>1</sub>	%	N <sub>2</sub> = 157	n <sub>2</sub>	%	
<b>Gender</b>										0.0087
Female		101	53.7		10	32.3		91	58	
Male		87	46.3		21	67.7		66	42	
<b>Age (year)</b>										0.0254
<53		89	47.3		9	29		88	51	
≥53		99	52.7		22	71		77	49.1	
<b>Socio-economic level</b>										0.0313
Hight		128	68.1		16	51.6		112	71.3	
Average		60	31.9		15	48.4		45	28.7	
<b>Geographical area</b>										0.1012
Townsmen		158	84		23	74.2		135	86	
Rural		30	16		8	25.8		22	14	

## Continued

<b>Obesity</b>						0.0518
No	136	72.3	18	58.1	118	75.2
Yes	52	27.7	13	41.9	39	24.8
<b>Diabete</b>						0.0016
No	153	81.4	19	61.3	134	85.4
Yes	35	18.6	12	38.7	23	14.7
<b>High blood pressure</b>						0.0005
No	62	33	2	6.45	60	38.2
Yes	126	67	29	93.6	97	61.8
<b>Smoking</b>						0.3272
No	174	92.6	30	96.8	144	91.7
Yes	14	7.45	1	3.23	13	8.28
<b>Self-medication</b>						0.0405
No	132	70.2	17	54.8	115	73.3
Yes	56	27.8	14	45.2	42	26.8
<b>Sedentary</b>						0.0011
No	158	84	20	64.5	138	87.9
Yes	30	16	11	35.5	19	12.1
<b>Alcoholism</b>						0.0004
No	143	76.1	16	51.6	127	80.9
Yes	45	23.9	15	48.4	30	19.1
<b>HIV</b>						0.0017
No	147	90.7	23	85.2	124	91.9
Yes	9	5.56	0	0	9	6.67
N/A	6	3.7	4	14.8	2	1.48

N = total number of patients; N1 effective of patient with GFR < 60; N2 = effective of patient with GFR ≥ 60.

**Table 3** represents the multivariate analysis after adjustment for socioeconomic level, diabetes, hypertension, alcohol, length of stay, ischemia, LVH, alcoholism, analysis shows that : mean standard of living (OR = 2.40, 95% CI [1.02 - 5.10],  $p = 0.0456$ ), diabetes (OR = 2.67, 95% CI [1.31 - 4.68],  $p = 0.0300$ ), HTA (OR = 5.66, 95% CI [1.30 - 10.20],  $p = 0.0399$ ), alcoholism (OR = 4.00, 95% CI [1.49 - 11.13],  $p = 0.0063$ ) are the main factors in the development of renal failure associated with heart failure.

#### 4. Discussions

This work really suffers from its retrospective character with the absence of data like proteinuria. Nonetheless, this kind of study is the first one in Togo and

concerns a population with the main goal of isolating the factors that can be used for prevention. There are several risk factors for kidney disease: diabetes, hypertension, a family history of kidney disease, and congenital uropathies that are modifiable while aging and race are unmodifiable [6] [7]. Several studies have shown that Asians, South Asian, Pacific, African and Caribbean have a higher risk of chronic kidney disease [8]. The population of heart failure is a population at risk with a prevalence of renal failure at 16.49%. This high prevalence found is like the result of Bouilly *et al.*, who found 20% renal failure in a French heart failure population [9].

**Table 3.** Effective and percentage of factors associated with renal failure in analysis.

	Initial model				Final model		
	n/N	OR	CI à 95%	p value	ORa	CI à 95%	P
<b>Gender</b>							
Femal	10/101	1					
Male	21/87	0.85	[0.19 - 3.68]	0.8233			
<b>Socio-economic level</b>							
Hight	16/128	1			1		
Average	15/60	2.59	[0.73 - 9.54]	0.1418	2.40	[1.02 - 5.10]	0.0456
<b>Age (year)</b>							
<53	9/89	1					
≥53	22/99	1.98	[0.59 - 7.03]	0.2733			
<b>Obesity</b>							
No	18/136	1					
Yes	13/52	0.91	[0.28 - 2.85]	0.8780			
<b>Diabete</b>							
No	19/153	1			1		
Yes	12/35	2.39	[0.74 - 7.76]	0.1431	2.67	[1.31 - 4.68]	0.0300
<b>High blood pressure</b>							
No	2/62	1			1		
Yes	29/126	3.14	[0.56 - 26.68]	0.2292	5.66	[1.30 - 10.20]	0.0399
<b>Self-medication</b>							
No	17/132	1					
Yes	14/56	1.23	[0.37 - 3.99]	0.7291			
<b>Alcohol</b>							
No	16/143	1			1		
Yes	15/45	3.71	[1.14 - 13.25]	0.0337	4.00	[1.49 - 11.13]	0.0063
<b>Geographical area</b>							
Townsmen	23/158	1					
Rural	8/30	1.99	[0.49 - 7.87]	0.3252			



## Continued

<b>Hospitalization duration</b>							
<9	13/131	1					
≥9	18/57	5.72	[1.85 - 19.69]	0.0034	5.92	[2.10 - 18.54]	0.0012
<b>Sedentarity</b>							
No	20/158	1					
Yes	11/30	2.48	[0.71 - 8.79]	0.1532			
<b>Ischemia</b>							
No	11/106	1			1		
Yes	20/82	2.67	[0.92 - 8.35]	0.0762	2.27	[1.10 - 4.54]	0.0020
<b>LVH</b>							
No	11/98	1			1		
Yes	20/90	4.23	[1.12 - 17.58]	0.0378	4.50	[1.57 - 10.53]	0.0075
<b>LAH</b>							
No	11/101	1					
Yes	20/87	1.97	[0.66 - 6.22]	0.2339			

N = total number of patients; n = effective of patient with GFR < 60; CI = confidence interval (95%); ORa = adjusted odds ratio; LVH: left ventricular hypertrophy; LAH: left atrial hypertrophy.

We have identified in multivariate analysis, the average standard of living, diabetes, hypertension, chronic alcoholism as the determinants of kidney failure in heart failure.

Crew *et al.* in 2013 showed that low socioeconomic status can contribute to the development of the chronic kidney diseases (CKD) [10]. With a 2.4 RCa the standard of living in our work appears as a very important determinant. This is explained by the fact that the health is still self-financed by the patient in Togo. There is no social security system and most patients have no health coverage. Heart failure is a heavy economic burden and patients become financially exhausted during treatment; this leads to complications of various kinds, which may be renal failure through cardiorenal syndrome type 1 which is a functional renal insufficiency. Susanne B, in a conceptual model, illustrated the relationship between the onset of renal disease chronic and poverty through, low birth weights, obesity, diabetes, hypertension and cardiovascular pathologies [8] [11] [12] [13].

High blood pressure is one of the major risk factors for the development and progression of renal failure [8]. With diabetes, it is a fatal duo and is the etiology of more than half of patients who have dialysis [14] [15]. In the literature, 50% to 80% of patients have hypertension at the time of diagnosis of type 2 diabetes [14]. There is a strong link between diabetes and hypertension, which seems to be a two-way street. In a large cohort work done on cardiovascular risk factors in Hong Kong, only 42% of diabetic patients had normal BP [16]. The high preva-

lence of hypertension in type 2 diabetics is explained by entangled pathophysiology of the two diseases [14]. Obesity has been identified as a risk factor for hypertension and diabetes. It is associated with an increase in blood mass and a decrease in peripheral resistance. However, the influence of obesity on BP goes through changes in blood flow and heart rate. In our study, 17.13% of patients were diabetic, 29.6% obese and 62.96% hypertensive. The economic burden of these two diseases is difficult to determine but it appears that controlling them would be a good way to slow the onset of kidney failure in the population with heart failure [12]. Indeed, among our patients, the risk of developing renal failure was high with diabetes (RCa = 2.67) and much greater with hypertension (RCa = 5.66).

Prenatal exposure to alcohol adversely affects kidney development, leading to a reduction in the number of nephrons [17] [18]. However, the mechanism by which alcohol acts to disrupt kidney development is little known. Several studies on the effects of alcohol on the heart muscle clearly demonstrate its deleterious effect [19] [20]. This involves the development of high blood pressure, the activation of complex inflammatory mechanisms, these mechanisms would probably explain the renal failure [19] [20]. The etiologies of heart failure in Togo are mainly hypertension, HIV, chronic alcoholism, pregnancy, degenerative and rheumatic valvulopathies, ischemic heart disease, tuberculous pericarditis and sickle cell disease [3] [21]. These main etiologies also appear to be the main determinants of renal failure.

Like any retrospective study, our study is skewed by its retrospective nature which justifies the lack of certain important data such as the elements that can enable us to classify renal insufficiency as acute (AKI) or chronic (CKD).

In addition, we relied on the estimation of glomerular filtration rate using the simplified MDRD equation. Although it is much better than the Cockcroft and Gault equation, because it is indexed on the surface of the body and not on the muscle mass, this MDRD equation is well known for its inaccuracy in extreme values of DFG, ie in the alterations severe or early renal function. The last consensus of KDIGO recommended the use of the CKD-EPI equation which in our context remains illusory because of the absence of international indexing of creatinine. Despite this, the MDRD equation holds its place because it has been validated in several reference works.

## 5. Conclusion

It appears that the average standard of living, diabetes, high blood pressure, chronic alcoholism were the determinants of renal failure in heart failure. The youth of the study population testify to the high frequency of heart failure in young people in developing countries and therefore the possibility of kidney failure. The renal failure is not only being the renal failure, a major comorbidity of heart failure, but also a two-way interaction between the heart and the kidney that is life-threatening. The control of these determinants will reduce the occur-

rence of kidney disease in the population particularly of heart failure. This will require new studies that will identify the survival and mortality of patients with these comorbidities.

## Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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