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Sodium-Glucose Co-Transporter 2 (SGLT2) Inhibitors: Indications, Safety, and Efficacy Experienced at Yaoundé General Hospital

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Abstract

Introduction: Sodium-glucose co-transporter type 2 (SGLT2) inhibitors have demonstrated proven cardiovascular and renal benefits in the Caucasian population, independent of diabetes. Their use extends to cardio-nephrology. This study aims to evaluate their use in cardiology and nephrology at the Yaoundé General Hospital (YGH). **Methods:** This was an observational study with retrospective and prospective data collection that included adult patients on SGLT2 inhibitors for at least three months. Sociodemographic, clinical, paraclinical, therapeutic, and evolutionary variables were collected after a review of adult case files of patients who had been on SGLT2 inhibitor treatment for at least 3 months for chronic kidney or heart disease. Outcomes were left ventricular ejection fraction (LVEF), blood pressure, estimated glomerular filtration rate (eGFR), and proteinuria. Associations between variables were analyzed with a 95% confidence interval (CI) at a significance level of 5%. **Results:** A total of 101 patients were included (61.4% men, median age 70 years [62.5 – 78]). Side effects were: 3 cases of urinary tract infections and 1 case of amputation. Improvements in systolic ($p < 0.001$), diastolic ($p < 0.001$), and LVEF ($p < 0.001$) blood pressure were observed. eGFR improved with a median increase from 42 [26 – 69] mL/min/1.73m^2 to 45 [24.5 – 64] mL/min/1.73m^2 ($p < 0.001$), serum creatinine from 16.6 [11.3 – 23.8] mg/L to 15.2 [11.8 – 25.9] mg/L, and proteinuria from 0.7 [0.3 – 0.9] g/g to 0.5 [0.3 – 0.7] g/g. Men (OR = 7.5; $p = 0.039$) and patients receiving concomitant renin-angiotensin-aldosterone system blocker (OR = 10.2; $p = 0.018$) had more observed benefits. Good adherence (Morisky score = 0) was strongly associated with perceived benefits (OR = 9.26; $p = 0.001$). **Conclusion**: SGLT2 inhibitors are effective

and well tolerated in the cardio-nephrological context in Yaoundé, with significant clinical benefits and few adverse effects.

Keywords

SGLT2 Inhibitors, Chronic Kidney Disease, Proteinuria, Heart Failure, Cameroon

1. Introduction

Sodium-glucose co-transporters (SGLT2) are transmembrane proteins that are found in the proximal tubule of the nephron. They ensure the reabsorption of around 90% of filtered glucose, as well as some sodium. Their inhibition makes it possible to limit this reabsorption, thus promoting urinary elimination of glucose and sodium. SGLT2 inhibitors, also known as gliflozins, are a pharmacological class originally developed to treat type 2 diabetes. However, large-scale clinical studies have revealed that, in addition to controlling blood sugar levels, these drugs provide significant cardiovascular and renal benefits [1].

These properties have been confirmed by several studies around the world, such as Empagliflozin Outcome Chronic Heart Failure Reduced Ejection Fraction (EMPEROR-Reduced), Dapagliflozin-Heart Failure (DAPA-HF), Dapagliflozin Chronic Kidney Disease (DAPA-CKD), and Empagliflozin Chronic Kidney Disease (EMPA-KIDNEY), demonstrating a reduced risk of cardiovascular mortality, hospitalizations for heart failure, and slowing of the progression of chronic kidney disease, including in non-diabetic patients [2]-[5]. Thus, this class is now part of the therapeutic arsenal recommended for cardio-renal protection regardless of glycemic status. However, the use of SGLT2 inhibitors is not free of side effects. Among the most common are an increase in urogenital tract infections, as well as the risk of hypotension, volume depletion, and, more rarely, amputation [6]. In this context, it is essential to better understand the use of these treatments in different regions, particularly in Africa where the prevalence of chronic kidney disease and heart failure remains a major public health issue.

In Africa, the overall prevalence of chronic kidney disease (CKD) is estimated at 6.28%, with an annual heart failure mortality rate of 34% [7] [8]. In this context, the progression of the disease is favored by non-communicable factors, including type 2 diabetes, hypertension, obesity, lifestyle, and infectious diseases [9]. In Cameroon, heart failure and CKD are growing public health problems due to the increasing prevalence of risk factors such as high blood pressure and diabetes. Congestive heart failure is estimated to affect a significant proportion of adults, with a prevalence of 29.6% [10]. CKD is also common, with a prevalence of 11% among adults in urban areas [11]. These two pathologies lead to high healthcare costs, which are often difficult for patients and their families to bear, especially when complications arise.

In this context, SGLT2 inhibitors could be a promising option in terms of public health and long-term cost reduction. We therefore propose to evaluate their place in local cardiology and nephrology practices.

2. Material and Method

2.1. Setting and Patient Selection

This was an observational study, including retrospective and prospective collection, conducted in the Cardiology and Nephrology Departments of the Yaoundé General Hospital (Cameroon). The retrospective phase involved collecting information from eligible files. The prospective stage consisted of evaluating the functional symptoms (dyspnea, orthopnea, cough, nocturia, edema) and biological parameters (creatinine, left ventricular ejection fraction) of interest after convening and obtaining consent from eligible participants. Included patients were 18 years of age or older, followed for heart failure, chronic kidney disease, or both, and treated with SGLT2 inhibitors for at least three months between the 1st of January and the 30th of June 2025. Those with no work-up (blood creatinine, proteinuria, and cardiac ultrasound) at initiation and during follow-up were excluded, as were those with acute kidney injury and acute heart failure. Data were collected using validated standardized sheets and included sociodemographic, clinical, biological, and therapeutic parameters. Therapeutic adherence was assessed by the Morisky score [12].

The effects of SGLT2 inhibitors were analyzed on left ventricular ejection fraction (LVEF), blood pressure, estimated glomerular filtration rate (eGFR), serum creatinine, and proteinuria.

The information was collected using a pretested questionnaire.

2.2. Statistical Analyses

The word processing was done with the epidemiology software EPI INFO 3.5.1. The data were analyzed using the Statistical Package for the Social Sciences (SPSS) software. Microsoft Excel and Word application software were used for data processing. Categorical variables were described in the form of percentages, proportions, and/or frequencies. Median values were expressed with a 95% confidence interval with a significance threshold set at $p < 0.05$.

2.3. Ethical Considerations

We have obtained research authorization n˚107524 from the YGH, and ethical clearance has been issued to us by the institutional committee on research ethics of the Faculty of Medicine and Biomedical Sciences of Yaoundé I University.

2.4. Terms Definition

We considered the following terms in our study:

- Chronic Kidney Disease (CKD): presence for more than 3 months of an estimated glomerular filtration rate (eGFR) less than 60 mL/min/1.73m^2 and/or

proteinuria > 30 mg/g or 30 mg/24h.

- Cardiac failure was defined as the presence of New York Heart Association Class II-IV symptoms and objective evidence of cardiac dysfunction via echocardiography. Cardiac function was considered reduced for a Left Ventricular Ejection Fraction (LVEF) of less than 40% and preserved for an LVEF of more than 50%.
- Benefits: were assessed based on the comparison of parameters at baseline and after more than three months of regular treatment. Parameters will be LVEF, proteinuria, and serum creatinine-based eGFR.
- Side effects: were defined by all the following conditions after SGLT2 initiation regardless of other treatment: urogenital infections, hypotension, ionic disorders, ketoacidosis, amputation.
- Adherence: was defined by the four-item Morisky score and classified into good adherence (score = 0), mean adherence (score = 1 to 2), and poor adherence (score = 3 to 4) [12].
- The benefits of the treatment were an improvement in the functional symptoms of heart failure and/or a lack of decline in renal function, as assessed by an improved glomerular filtration rate and decreased proteinuria.

3. Results

1) General characteristics of the study population

The median age of patients was 70 [62.5 - 78] years, with a predominance of male subjects (61.4%). Hypertension was prevalent (84.2%), followed by type 2 diabetes (38.6%) as illustrated in Table 1.

Table 1. Comorbidities and clinical profile of the population.

Variables	Frequency (N = 101)	Percentage (%)
Median age [IQR], in years	70 [62.5 - 78]	
Gender		
Male	62	61.4
Women	39	38.6
Comorbidities		
High blood pressure	85	84.2
Diabetes	39	38.6
Viral hepatitis C	7	6.9
HIV	7	6.9

IQR: interquartile range.

2) Types, indications, associations, and side effects of SGLTi2

Dapagliflozin was widely prescribed (96%) in our context, with heart failure as the main indication (53.5%). The other indications are given in Table 2.

Table 3 illustrates the low frequency of side effects encountered in the study population, with 3 cases of urinary tract infection and 1 case of amputation.

Table 2. Distribution, indications, combinations, and adherence to SGLT inhibitor treatment.

Variables	Frequency (N = 101)	Percentage (%)
Type of SGLT2 inhibitor		
Dapagliflozin	97	96
Empagliflozin	4	4
Indication of SGLT2 inhibitor		
Heart failure	54	53.5
Chronic kidney disease	45	44.6
Isolated proteinuria	2	2
Associated treatments		
RAAS inhibitor	80	79.2
Beta Blocker	45	44.6
Loop diuretic	43	42.6
Calcium channel blocker	38	37.6
Anti-aldosterone	34	33.7
Statins	34	33.7
Adherence to therapy		
Good compliance	14	13.9
Moderate compliance	71	70.3
Poor compliance	16	15.8

RAAS: Renin-Angiotensin-Aldosterone System.

Table 3. Adverse reactions related to SGLT2 inhibitor treatment.

Variables	Frequency (n = 4)
Urinary tract infection	3
Amputation	1

3) Benefits of SGLT2 inhibitor

Effect on functional signs

Figure 1 shows the frequency of the main functional signs observed at baseline and at follow-up. There is a decrease in the frequencies of dyspnea, lower limb edema, orthopnea, cough, and nocturia.

Effects on blood pressure

There was a statistically significant improvement ($p < 0.001$) in systolic and di-

astolic blood pressure from baseline to the course followed, as illustrated in Figure 2(a) and Figure 2(b).

The data show a significant improvement ($p < 0.001$) in diastolic blood pressure at follow-up (Figure 4).

4) Effects on cardiac function

A statistically significant improvement ($p < 0.001$) in LVEF between baseline and follow-up was observed, with LVEF increasing from 53% [32.5 - 63.5] to 58% [42.5 - 65], respectively.

Also, patients with reduced left ventricular ejection fraction (LVEF) improved their cardiac function (from 31.5% to 41.5% LVEF) as illustrated in Figure 3.

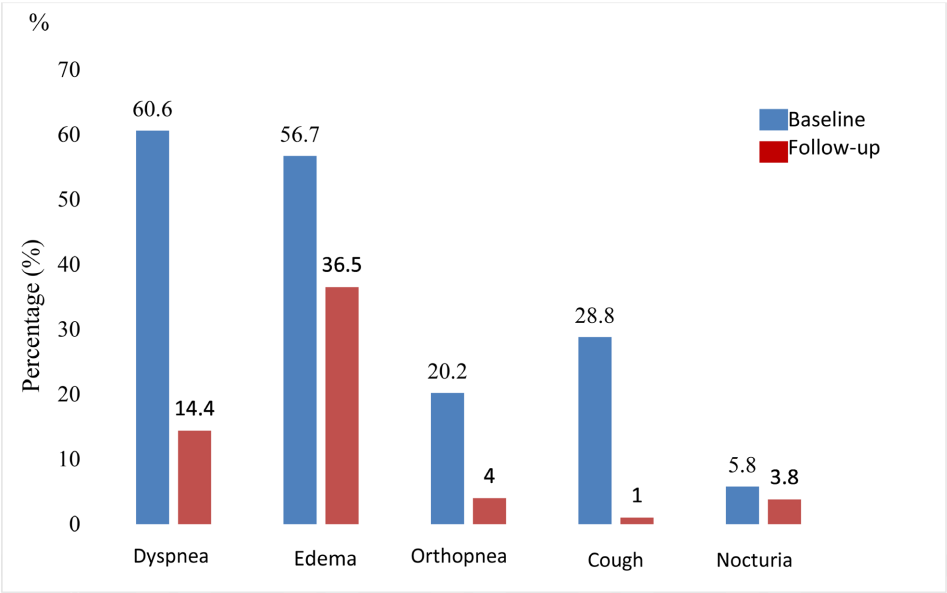
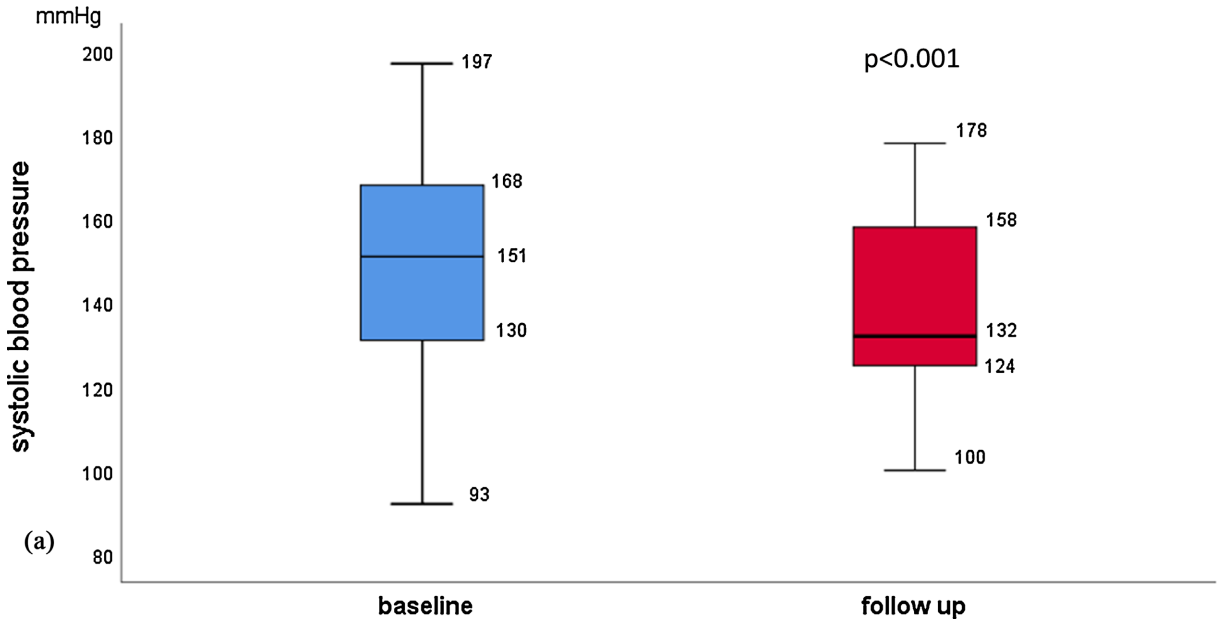


Figure 1. Evolution of functional signs at baseline and follow-up.



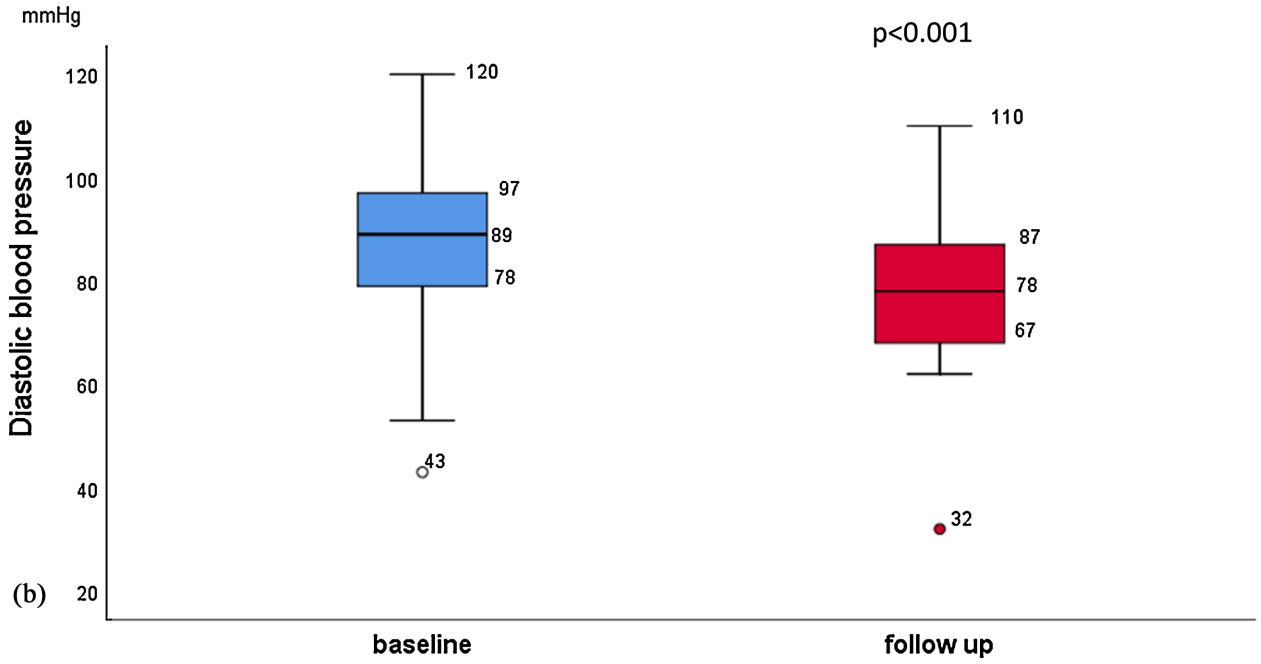


Figure 2. (a) Baseline and follow-up systolic blood pressure distributions; (b) baseline and follow-up distribution of diastolic blood pressure.

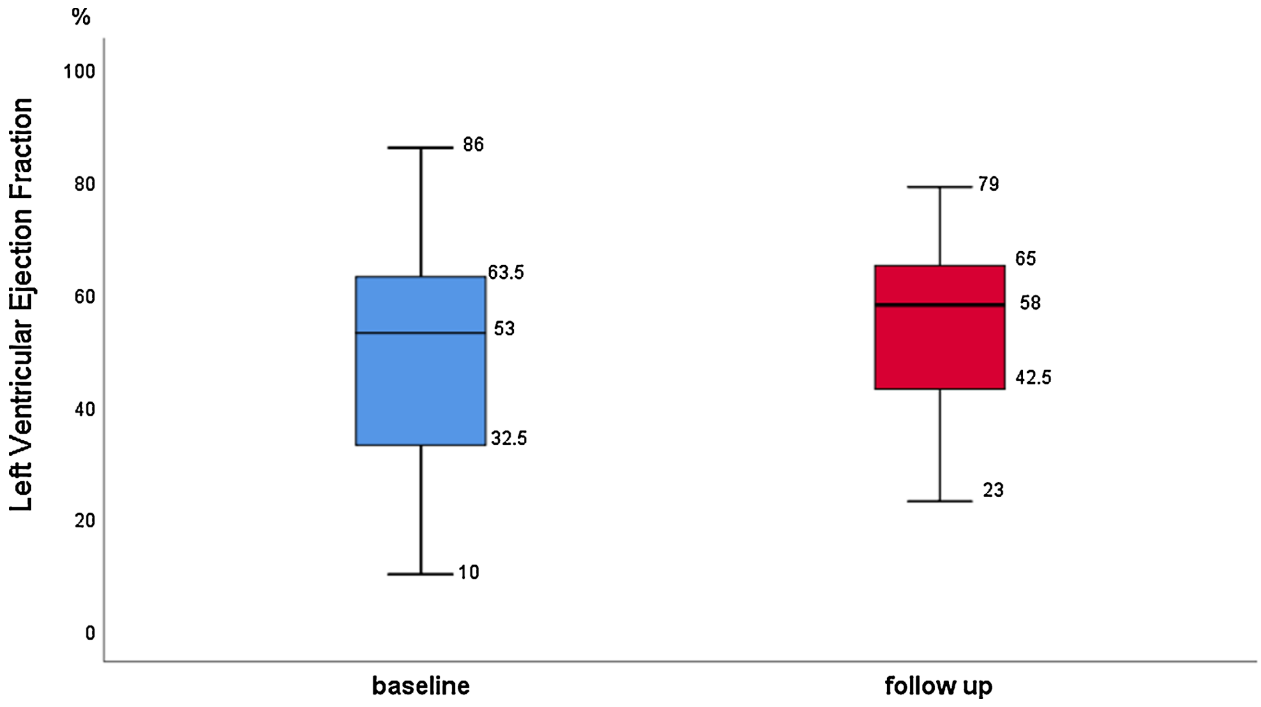


Figure 3. Baseline and follow-up left ventricular ejection fraction distribution.

5) Effects of SGLT2 Inhibitors on Renal Function

A modest but significant improvement ($p < 0.001$) in the glomerular filtration rate from 42 [26 - 69] mL/min/1.73m^2 to 45 [24.5 - 64] mL/min/1.73m^2 was observed during follow-up (Figure 4). Proteinuria also decreased under SGLT2 inhibitors, from 0.7 to 0.5, a decrease of 28.6% (Figure 5).

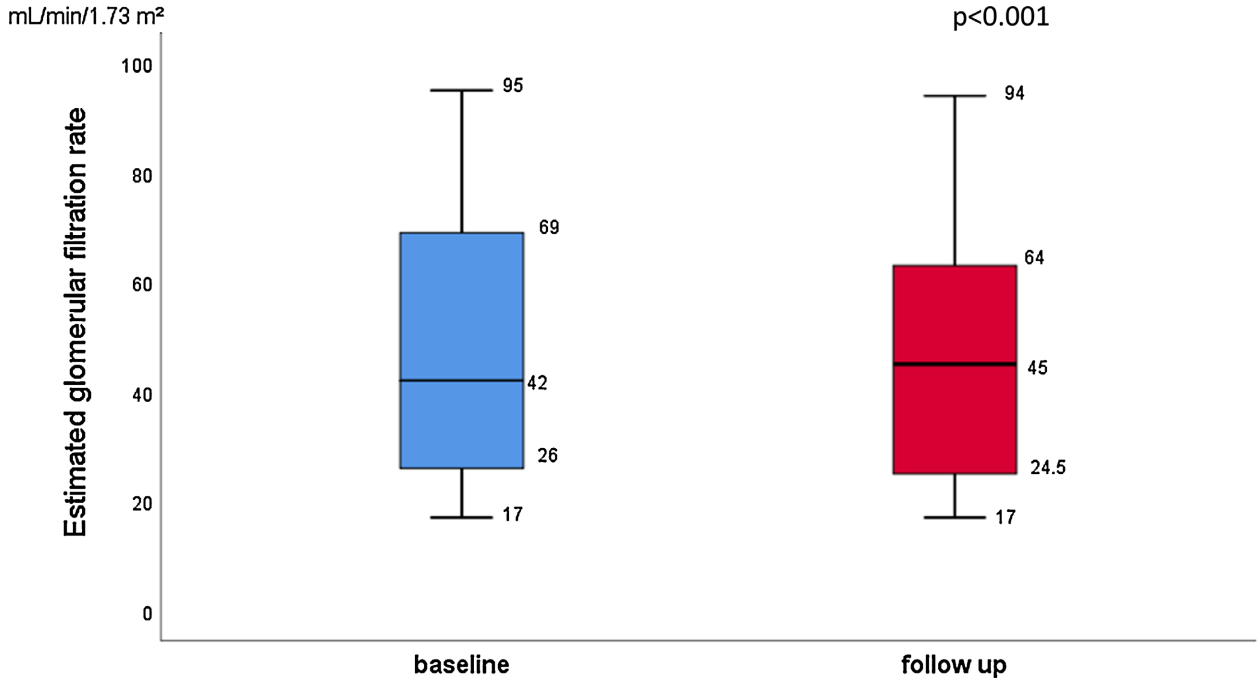


Figure 4. Estimated glomerular filtration rate at baseline and during follow-up.

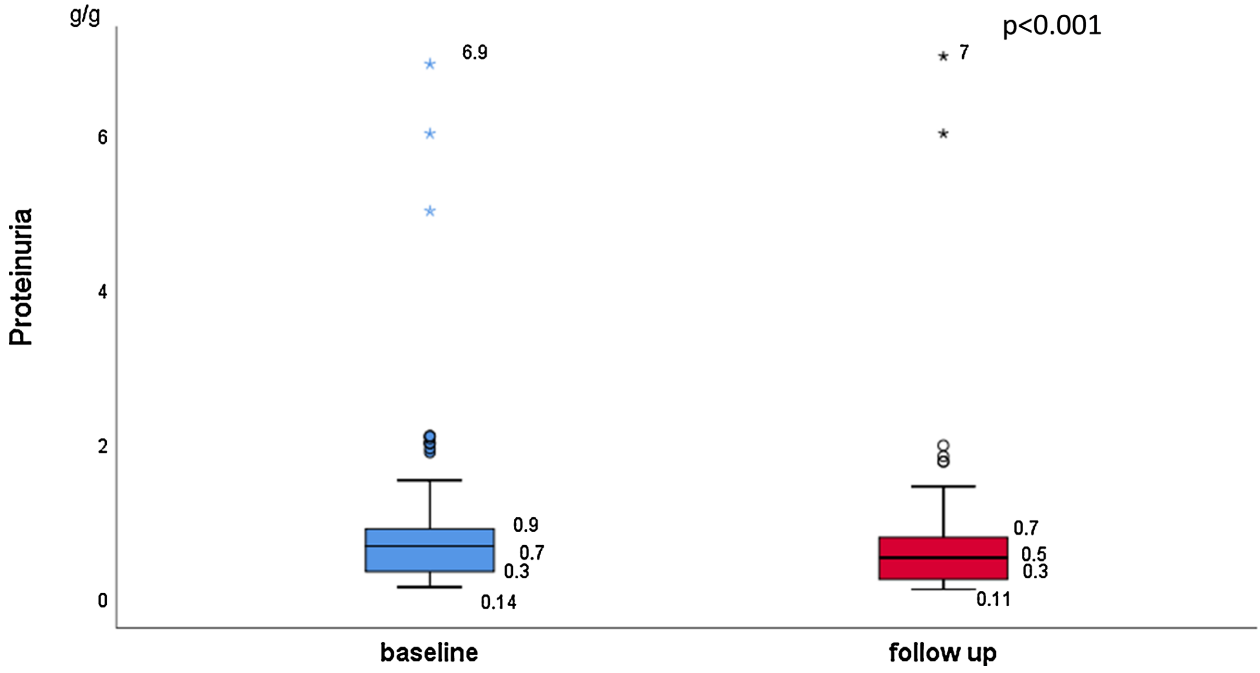


Figure 5. Proteinuria at baseline and during follow-up.

6) Factors associated with the effects of SGLT2 inhibitors

Male sex, concomitant use of renin-angiotensin-aldosterone system (RAAS) blockers, and especially good adherence to treatment were correlated with the observed benefits in bivariate analysis ($p < 0.001$), as shown in Table 4. In multivariate analysis, only good therapeutic compliance was associated with benefit (Table 5).

Table 4. Analysis of factors influencing response to treatment (bivariate analysis).

Variables	Benefits		OR [95% CI]	p value
	Yes n = 66	No n = 35		
Median age	70 [64 - 77]	70 [62 -78]	0.95 [0.90 - 1]	0.086
Male, n (%)	66 (65.4)	35 (34.6)	7.5 [1.10 - 50.8]	**0.039**
HBP, n (%)	54 (63.5)	31 (36.5)	1.3 [0.2 - 8.5]	0.823
Diabetes, n (%)	23 (59)	16 (41)	0.6 [0.3 - 1.5]	0.293
Indication, n (%)	66 (65.4)	35 (34.7)	0.36 [0.03-4.35]	0.424
RAAS Blocker, n (%)	53 (66.3)	27 (33.7)	10.2 [1.5 - 69.5]	**0.018**
Anti-aldosterone, n (%)	23 (67.6)	11 (32.4)	3.5 [0.6 - 18.9]	0.150
Beta blocker, n (%)	31 (68.8)	14 (31.1)	2 [0.5 - 7.4]	0.331
Calcium channel blocker, n (%)	23 (60.5)	15 (39.5)	0.4 [0.08 - 2.5]	0.367
Loop diuretic, n (%)	31 (72)	12 (28)	3.6 [0.6 - 20]	0.137
Statins, n (%)	22 (64.7)	12 (35.3)	0.6 [0.2 - 3.4]	0.592
Antithrombotic, n (%)	15 (83.3)	3 (16.6)	3.6 [0.6 - 22.8]	0.165
Morisky score, n (%)				
Good compliance	13 (92.8)	1 (7.2)	9.26 [1.9 - 4.5]	**0.001**
Average adherence	50 (70.4)	21 (29.6)	10.7 [1.1 - 109.3]	0.046
Poor compliance	3 (18.75)	16 (81.3)	0.8 [0.1 - 0.3]	**0.001**

HBP: high blood pressure; RAAS: Renin-Angiotensin-Aldosterone System; LVEF: Left Ventricular Ejection Fraction.

Table 5. Analysis of factors influencing response to treatment (multivariate analysis).

Variables	OR [95% CI]	p value
Male, n (%)	1.574 [0.683 - 3.632]	0.286
RAAS Blocker, n (%)	1.208 [0.447 - 3.268]	
Score de Morisky, n (%)		
Good compliance	8.68 [1.043 - 66.690]	**0.020**
Poor compliance	0.82 [0.021 - 0.310]	**0.000**

RAAS: Renin-Angiotensin-Aldosterone System.

4. Discussion

At the end of this observational study conducted in two reference hospitals in the city of Yaoundé on the indications and benefits of sodium-glucose cotransporter type 2 inhibitors in patients followed in cardiology and nephrology, it emerges that:

- The indication profiles for SGLT2 inhibitors were dominated by heart failure

with reduced LVEF and chronic kidney disease.

- The side effects found were mainly three cases of urinary tract infections and one case of amputation not directly linked to SGLT2 inhibitor.
- Treatment improved cardiac symptoms, blood pressure, and heart function. There is also stabilization of kidney function.

In our series, SGLT2 inhibitors were prescribed mainly in the context of heart failure or chronic kidney disease, regardless of whether there was diabetes mellitus. This use profile reflects the evolution of therapeutic indications, following the results of major trials such as Dapagliflozin-Heart Failure (DAPA HF), Empagliflozin Outcome Chronic Heart Failure Reduced Ejection Fraction (EMPEROR-Reduced), and Dapagliflozin Chronic Kidney Disease (DAPA-CKD), which demonstrated the efficacy of SGLT2 inhibitors in patients with cardiac dysfunction and/or impaired renal function, regardless of glycemic status, with 50.2% of patients included who were not diabetic for EMPEROR-Reduced, 45% in DAPA-HF, and 32% for DAPA-CKD. Most patients in our cohort (96%) received dapagliflozin, which is a testament to its availability and wider dissemination in our context. This hegemony of dapagliflozin could also reflect a better perceived cost-effectiveness or greater familiarity of prescribers with this molecule. Although a similar trend has been observed in most African countries, apart from South Africa and Togo, where the use of empagliflozin predominates, accessibility remains limited due to various economic and structural barriers [2] [3] [5].

In our study, SGLT2 inhibitors showed an overall satisfactory safety profile. Of the 101 patients included, four cases of adverse reactions were reported, representing a frequency of 4%. These were three cases of simple urinary tract infections and one case of non-traumatic amputation of the lower limb. UTIs are well-known adverse effects of SGLT2 inhibitors, supporting the results of the observational study by Uitrakul *et al.*, which confirms an association with a small but significant risk of UTIs and genital infections, related to treatment-induced glycosuria [13]. The case of amputation observed in our series, although rare, raises questions. Indeed, this complication was initially reported in the Canagliflozin and Cardiovascular Assessment Study (CANVAS) with canagliflozin but was not found with dapagliflozin or empagliflozin in the DAPA-HF or EMPEROR-Reduced studies. The interpretation of this event must therefore be done with caution, as several contributing factors, such as severe peripheral arterial disease, diabetic neuropathy, and infected diabetic foot wounds, can contribute to this type of complication independently of SGLT2 inhibitor treatment. No hypotension, ketoacidosis, or ionic disorders were reported during follow-up [13]-[15].

The effect of SGLT2 inhibitors on cardiac function was generally favorable, with a statistically significant improvement ($p < 0.001$) in LVEF, reduced LVEF, a downward trend in the percentage of patients with increased left ventricular filling pressures in patients with preserved LVEF ($p < 0.05$), suggesting an improvement in diastolic function, as well as a decrease in symptoms such as dyspnea, orthopnea, or peripheral edema. These improvements, although modest, are on the

basis of the [2] [16]. The mechanism behind these effects is the improvement in endothelial function and reduction in arterial stiffness [17].

The reduction of blood pressure also explains the cardiovascular importance of SGLT2 inhibitors. A meta-analysis on changes in systolic and diastolic BP showed significantly reduced BP in patients with type 2 diabetes [18]. In non-diabetics, the effect on blood pressure is slightly less than in diabetics (because there is less glucose-related osmotic diuresis), but it remains significant (approximately -2 to -3 mmHg on average) [2] [19].

On the kidney level, the effects observed are also encouraging. The increase in the estimated glomerular filtration rate, associated with a reduction in serum creatinine and proteinuria, indicates stabilization or even improvement in renal function. These effects are attributed to several mechanisms: reduction of glomerular hyperfiltration, decrease in intraglomerular pressure, natriuretic effect, and improvement of systemic hemodynamics. The results are consistent with robust data from the DAPA-CKD study, where dapagliflozin significantly slowed the progression of chronic kidney disease and reduced the risk of cardiovascular death [3].

The analysis of the factors associated with perceived benefits shows that male sex, the concomitant use of renin-angiotensin-aldosterone system (RAAS) blockers, and especially good treatment adherence are significantly correlated with the observed benefits. The statistically significant association between male sex and SGLT2 inhibitor benefit (OR = 7.5; $p = 0.039$) warrants cautious interpretation. Indeed, our sample is predominantly male (61.4%), which may have influenced this association. This gender imbalance can introduce a confounding bias, especially since sex is not recognized as a determinant of the therapeutic response to SGLT2 in large multicenter studies [20]. Co-prescribing of RAAS blockers is also significantly associated with a better clinical response (OR = 10.2; $p = 0.018$). This result is consistent with the pathophysiological and clinical data, which suggest a synergy between SGLT2 inhibitors and RAAS blockers in cardio-renal protection. This is also found in the study of Vart *et al* in non-diabetic patients with chronic kidney disease associated with albuminuria, demonstrating the benefit of this combination [21]. These data support the role of SGLT2 inhibitors as an adjunct therapy in an optimized treatment regimen. The high Morisky score (good adherence) is associated with a particularly high odds ratio (OR = 9.26; $p = 0.001$), highlighting the critical importance of treatment adherence in achieving clinical goals. These results underline the need to strengthen the patient's therapeutic education, as well as the rigorous monitoring of the prescription. Conversely, variables such as age, diabetes, hypertension, or baseline LVEF do not show a statistically significant association with benefit, suggesting that SGLT2 inhibitors may be effective independently of these traditional risk factors, which is in line with the findings of major trials such as DAPA-HF and EMPEROR-Reduced, which have shown beneficial effects in highly heterogeneous patients [2] [5]. Indeed, a greater clinical benefit is observed in patients treated with SGLT2 inhibitors, despite initial vari-

ations in renal biological parameters. These results suggest that the improvement of clinical status, particularly in terms of cardiovascular morbidity and mortality and progression of renal failure, does not depend exclusively on classical markers of renal function. Thus, the isolated interpretation of a decrease in GFR or an increase in serum creatinine at the beginning of treatment must be qualified, as these fluctuations reflect more a transient hemodynamic adjustment than a real functional decline that could result in a lack of statistically significant association between biological parameters (eGFR, serum creatinine, proteinuria) and the achievement of a benefit. This phase, often misinterpreted as kidney deterioration, usually precedes a stabilization or lasting improvement in kidney function in the medium to long term. Thus, in an early follow-up evaluation such as ours, these fluctuations can mask the real renal benefit, especially in the absence of prolonged follow-up beyond one year.

5. Conclusion

Sodium-glucose co-transporter type 2 inhibitors appear to be effective and well-tolerated therapeutic agents in patients with cardio-renal pathologies at the Yaoundé General Hospital. Their use is associated with a significant improvement in clinical and biological parameters, with a low frequency of adverse effects. These results support their systematic integration into local protocols for the management of heart failure and chronic kidney disease, even in the African context.

Declarations

Availability of Data and Materials

The materials described in the manuscript, including all relevant raw data, will be freely available to any scientist wishing to use them for non-commercial purposes. The data that support the findings of this study are also available from the corresponding author.

Funding

This work was carried out with own funds.

Ethical Considerations

All stages of this work have been carried out in accordance with the Declaration of Helsinki.

Author Contributions

All authors contributed to the study conception. The study was designed by Menanga Alain and Maimouna Mahamat. Material preparation, data collection, and analysis were performed by Bouba Bame, Nono Aristide, Ndobo Valerie, and Nzana Bandolo. The first draft of the manuscript was written by Maimouna Mahamat and Menanga Alain. All authors read and approved the final manuscript.

Conflicts of Interest

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

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