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RESEARCH ARTICLE

Challenges of Sodium-glucose Transporter-2 Inhibitors Use in a low Socioeconomic Setting

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ABSTRACT

Background: Sodium-glucose transporter-2 (SGLT2) inhibitors have shown efficacy in reducing major adverse cardiovascular events and hospitalizations for heart failure in patients with type 2 diabetes mellitus and concomitant heart failure.

Aim: To compare the short-term effectiveness between empagliflozin and dapagliflozin.

Methods: A single-center observational cohort study was implemented in a Dominican tertiary-care center, where patients with heart failure and reduced ejection fraction were divided into two groups and treated with different SGLT2 inhibitor molecules, empagliflozin and dapagliflozin. Two-step cluster analysis was conducted for the interim analysis of the study.

Results: We enrolled a total of 60 patients, with a median age of 69. The majority of these were men (70%) and comprised 75.0% of the Dapagliflozin 10 mg group and 62.5% of the Empagliflozin 10 mg group. Most participants (61.7%) were categorized as NYHA-II in functional class. The main cause of heart failure was ischemic (55%), while the predominant state of the disease was chronic with 65% patients in this group.

Conclusion: This preliminary manuscript evaluated the effectiveness of SGLT2 inhibitors in a Dominican heart failure patient cohort, finding notable gender, age, and risk factor variations, and emphasizing the need for standardized research methods in future investigations.

Keywords: heart failure, sodium-glucose transporter-2 inhibitors, heart diseases, cluster analysis.

Introduction

Heart failure (HF) is characterized as a clinical condition presenting symptoms and indications arising from an abnormality in the structure and function of the heart, confirmed by increased levels of natriuretic peptides and objective proof of pulmonary or systemic congestion.[1] It affects around 26 million people worldwide, being associated with soaring resource utilization and cost of healthcare.[2] Current treatment guidelines are based on pharmacotherapy, including angiotensin-converting enzyme inhibitors (ACEi), angiotensin II receptor blockers (ARBs), beta-blockers, angiotensin receptor-neprilysin inhibitors, aldosterone antagonist and statins as needed. In advanced stages, treatment options include heart transplant, inotropes, mechanical circulatory support, experimental therapies, palliative care, hospice, and deactivating implantable cardioverter defibrillators. Most recently, Sodium-glucose transporter-2 (SGLT2) inhibitors have upsurged as one of the pilar drugs for managing heart failure with reduced ejection fraction.[3]

The use of SGLT2 ihibitors in HF stems from the EMPA-REG OUTCOME trial (Empagliflozin Cardiovascular Outcome Event Trial in Type 2 Diabetes Mellitus Patients), which resulted in a significant 35% relative risk reduction in hospitalization for heart failure in patients with type 2 diabetes and established atherosclerotic cardiovascular disease (ASCVD) who were treated with empagliflozin.[4] Diabetes independently increases the risk of developing heart failure, with a more than twofold surge in risk in men and an over fivefold increase in women. In diabetic patients, the prevalence of heart failure is four times higher than in the general population, with 25% having chronic heart failure and up to 40% experiencing acute heart failure.[5] It has been described that the primary mechanism of these drugs in protecting against heart failure consists of improving ventricular loading through preload reduction due to their diuretic and natriuretic effect.[6]

Sodium-glucose transporter-2 inhibitors have demonstrated efficacy in reducing major adverse cardiovascular events, hospitalizations for heart failure, and all-cause mortality in patients with type 2 diabetes mellitus and concomitant heart failure. Furthermore, studies have shown that in patients with heart failure with reduced and preserved ejection fraction, regardless of type 2 diabetes, SGLT2 inhibitors can minimize disease progression, hospitalizations, and deaths from all causes.[7,8] Nonetheless, the mechanism of SGLT2 inhibitors in cardiovascular protection is complex and warrants further study. Outside of phase III studies, there is limited information concerning the characterization of each agent and the situations where each one would stand out as the better option, especially in Latin America. There is no record of such information in the Dominican Republic (DR). Therefore, our study objective is to compare the short-term effectiveness between empagliflozin and dapagliflozin.

Methods

STUDY DESCRIPTION

A single-center, non-randomized, open-label observational cohort was implemented at the Estrella Ureña Regional University Hospital in Santiago de los Caballeros, Dominican Republic. The study included patients with heart failure and reduced ejection fraction, divided into two parallel groups treated with different SGLT2 inhibitor molecules, empagliflozin, and dapagliflozin.

PARTICIPANTS

Inclusion criteria stipulated that participants should be over 18 years old, with a diagnosis of heart failure classified as NYHA II-IV, and either normal or reduced ejection fraction. Patients with hypotension, recent cardiac surgery, continuous use of parenteral inotropic agents, estimated glomerular filtration rate less than 30 mL/min/1.73m^2, current pregnancy, or those requiring hemodialysis or peritoneal dialysis were excluded.

INTERVENTION

Eligible patients received either empagliflozin (10-25 mg/day for six months) or dapagliflozin (5-10 mg/day for six months) without randomization or masking.

SAMPLE CALCULATION

As this was an observational study, non-probabilistic sampling was employed, and all eligible patients who presented at the hospital during the recruitment period were included.

STATISTICAL METHODS

R Studio 4.2 and various statistical tests were utilized for data analysis. For continuous variables with a normal distribution, the Student's t-test was applied, while non-normally distributed continuous variables were analyzed using the Mann-Whitney U test. Categorical variables were examined using the chi-square test.

A two-step cluster analysis was conducted for the interim analysis of the study, using both categorical and continuous variables. To determine the optimal number of clusters, a pre-clustering validation stage established that the most suitable number was three. ANOVA was employed to compare clusters for

continuous variables, while the chi-square test was used for categorical variables.

RESULTS

Table 1. Baseline characteristics of participants

Variables	Value
Gender	
Male, N (%)	42 (70)
Female, N (%)	18 (30)
Age, Median (IQR)	69.00 (20.25)
BMI, Median (IQR)	26.67 (5.62)
Diabetes N (%)	24 (40)
Diabetes evolution time in years,median (IQR)	24.00 (150.00)
Atrial fibrillation, N (%)	8 (13.3)
Smoking status	
Current smoker, N (%)	1 (1.7)
Never smoked, N (%)	23 (38.3)
Former smoker, N (%)	36 (60)

The study enrolled a predominantly male group, with 75.0% in the Dapagliflozin 10 mg group and 62.5% in the Empagliflozin 10 mg group. In contrast, women comprised 25.0% and 37.5% of these groups. Both the Dapagliflozin 5 mg and Empagliflozin 25 mg groups only had one participant each, which were female. In terms of age, the median age for participants in the Dapagliflozin 10 mg group was 66.9 years (IQR=14.9), while the Empagliflozin 10 mg group had a median age of 66.2 years (IQR=12.6). Meanwhile, participants in the groups of Dapagliflozin 5 mg and Empagliflozin 25 mg had mean ages of 50 and 45 years, respectively.

Additionally, a significant majority of over 60% in both 10 mg groups did not have diabetes. Among those with diabetes, the median duration since diagnosis was longer for Dapagliflozin 10 mg users, at 104 months (IQR=136). Another notable aspect was the prevalence of atrial fibrillation, affecting 20% of Dapagliflozin 10 mg users compared to a mere 6.25% among those in Empagliflozin 10 mg. Regarding body mass index (BMI), many patients in the 10 mg groups had values within 18.5-24.9 kg/m2, precisely, 37.5% in the Dapagliflozin group and 18.8% in the Empagliflozin group (Table 2).

Table 2. Comparison between different doses and types of SGLT2 inhibitors according to baseline characteristics

Variables	**Dapagliflozin 10 mg**	**Dapagliflozin 5 mg**	**Empagliflozin 10 mg**	**Empagliflozin 25 mg**	**p.overall**
	N=40	N=1	N=16	N=1	
Sex:					0.106
Female, %	10 (25.0%)	1 (100%)	6 (37.5%)	1 (100%)	
Male, %	30 (75.0%)	0 (0.00%)	10 (62.5%)	0 (0.00%)	
Age, Median (IQR)	66.9 (14.9)	50.0 (.)	66.2 (12.6)	45.0 (.)	0.320
Diabetes mellitus:					0.424
No, %	24 (61.5%)	0 (0.00%)	10 (62.5%)	0 (0.00%)	
Yes, %	15 (38.5%)	1 (100%)	6 (37.5%)	1 (100%)	
DM evolution time, Median (IQR)	104 (136)	48.0 (.)	58.0 (111)	156 (.)	0.728

Variables	Dapagliflozin 10 mg	Dapagliflozin 5 mg	Empagliflozin 10 mg	Empagliflozin 25 mg	p.overall
History of Atrial Fibrillation:					0.575
Yes, %	7 (20.0%)	0 (0.00%)	1 (6.25%)	0 (0.00%)	
No, %	28 (80.0%)	1 (100%)	15 (93.8%)	1 (100%)	
BMI, Median (IQR)					0.393
< 18,5 kg/m2, %	3 (7.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	
18,5-24,9 kg/m2, %	15 (37.5%)	0 (0.00%)	3 (18.8%)	0 (0.00%)	
25-29,9 kg/m2, %	14 (35.0%)	1 (100%)	8 (50.0%)	0 (0.00%)	
> 30 kg/m2, %	8 (20.0%)	0 (0.00%)	5 (31.2%)	1 (100%)	
LDL, Median (IQR)	80.3 (41.8)	-	95.2 (41.5)	78.0 (.)	0.641
HDL, Media (SD)	43.8 (13.2)	-	42.3 (5.87)	51.0 (.)	0.776
Hemoglobin A1c, Mean (SD)	8.18 (2.13)	11.7 (.)	6.12 (0.76)	8.10 (.)	0.098
Fasting blood glucose, Median (IQR)	114 (51.6)	368 (.)	124 (39.9)	96.0 (.)	<0.001
Blood sodium, Median (IQR)	140 (3.33)	-	131 (36.0)	142 (.)	0.349
Creatinine, Median (IQR)	1.68 (2.57)	0.79 (.)	1.53 (1.48)	1.03 (.)	0.970
Microalbuminuria/proteinuria:					0.044
No, %	8 (20.0%)	1 (100%)	3 (18.8%)	0 (0.00%)	
Yes, %	10 (25.0%)	0 (0.00%)	9 (56.2%)	1 (100%)	

Discrepancies were evident in fasting glucose levels between groups ($p<0.001$): Dapagliflozin 10 mg users had a median of 114 mg/dL (IQR=51.6), while the Empagliflozin 10 mg group was established at 124 mg/dL (IQR=39.9). On the other hand, Hemoglobin A1c levels reached 11.7% in the Dapagliflozin 5 mg group, while the Empagliflozin 10 mg group averaged 6.12% (SD=0.76). Regarding LDL cholesterol, the Empagliflozin 10 mg group recorded the highest median levels, reaching 95.2 mg/dL (IQR=41.5). When assessing renal function, a significant difference emerged. Microalbuminuria or proteinuria was considerably more prevalent among Empagliflozin 10 mg users, affecting 56.2%, compared to only 25.0% in the Dapagliflozin 10 mg group, marking this difference as statistically notable ($p=0.044$) (Table 2).

Chronic heart failure was another prominent condition, affecting 60% of Dapagliflozin 10 mg users and 81.2% of those treated with Empagliflozin 10 mg. Ischemic etiology emerged as a leading cause of this heart failure, with 58.8% and 68.8% occurrences, respectively. Most participants in both groups were categorized as NYHA-II in functional class. Additionally, Empagliflozin 10 mg users experienced a higher rate of heart failure-related hospitalizations, at 31.2%, in contrast to the 17.5% observed in the Dapagliflozin 10 mg group. Regarding duration since the diagnosis of heart failure, the median range was reasonably consistent, between 22.2 and 24.9 months in both groups. Concerning NT-pro-BNP results, patients in the Dapagliflozin 10 mg group had the higher values, with a mean of 10,129, while patients in the Empagliflozin 25 mg had the lower values (Table 3).

Based on the Kansas City Cardiomyopathy Questionnaire, quality of life evaluation revealed that most patients in the Dapagliflozin 10 mg group reported having a moderate impairment of quality of life (42.5%), followed by good quality of life (35.0%) and severe impairment of quality of life (22.5%). Regarding the Empagliflozin 10 mg cohort, 37.5% of participants reported having moderate impairment of quality of life, 37.5% stated they had severe impairment of quality of life and only 25.0% described having a good quality of life (Table 3).

Table 3. Comparison between different doses and types of SGLT2 inhibitors according to heart failure characteristics

Variables	Dapagliflozin 10 mg	Dapagliflozin 5 mg	Empagliflozin 10 mg	Empagliflozin 25 mg	p.overall
	N=40	N=1	N=16	N=1	
Heart failure status:					0.662
De novo, %	2 (5.00%)	0 (0.00%)	1 (6.25%)	0 (0.00%)	
Acute, %	7 (17.5%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	
Chronic, %	24 (60.0%)	1 (100%)	13 (81.2%)	1 (100%)	
Chronic decompensated, %	7 (17.5%)	0 (0.00%)	2 (12.5%)	0 (0.00%)	
Cause of heart failure:					0.934
Ischemic, %	20 (58.8%)	1 (100%)	11 (68.8%)	1 (100%)	
Non-ischemic, %	8 (23.5%)	0 (0.00%)	3 (18.8%)	0 (0.00%)	
NYHA functional status					0.935
NYHA-I, %	13 (32.5%)	0 (0.00%)	5 (31.2%)	0 (0.00%)	
NYHA-II, %	24 (60.0%)	1 (100%)	9 (56.2%)	1 (100%)	
NYHA-III, %	3 (7.50%)	0 (0.00%)	2 (12.5%)	0 (0.00%)	
Hospitalization due to heart failure:					0.172
Yes, %	7 (17.5%)	0 (0.00%)	5 (31.2%)	1 (100%)	
No, %	33 (82.5%)	1 (100%)	11 (68.8%)	0 (0.00%)	
Time of evolution of heart failure, Median (IQR)	24.9 (34.3)	24.0 (.)	22.2 (35.6)	36.0 (.)	0.980
Ejection fraction, Mean (SD)	33.5 (12.0)	32.0 (.)	28.7 (8.55)	34.0 (.)	0.540
NT-pro-BNP, Median (IQR)	10129 (24605)	3072 (.)	2413 (1898)	651 (.)	0.726
Quality of life by KCCQ12					0.795
KCCQ12 <50, Good quality of life, %	14 (35.0%)	0 (0.00%)	4 (25.0%)	0 (0.00%)	
KCCQ12 50-75, moderate impairment, %	17 (42.5%)	1 (100%)	6 (37.5%)	1 (100%)	
KCCQ12 >75, severe impairment, %	9 (22.5%)	0 (0.00%)	6 (37.5%)	0 (0.00%)	
MAP, Media (SD)	95.4 (14.7)	127 (.)	94.4 (11.5)	113 (.)	0.093

Cluster analysis generated three distinct groups (Table 4). In Group 1, most subjects were prescribed Empagliflozin 25mg as their primary SGLT2 inhibitor and typically consumed more than four medications. Their average BMI fell within the 25-29.9 kg/m2 range. Laboratory tests revealed a LDL level of 108.57 mg/dL, HDL of 38.59 mg/dL, and a total cholesterol of 181.31 mg/dL. Clinically, these subjects predominantly fell into NYHA Class III functional status, with an ejection fraction below 40%. Their NT-pro-BNP scores and KCCQ12 scores were 2952.93 pg/mL and between 45-59, respectively.

On the other hand, Group 2 patients predominantly took Dapagliflozin 10mg and maintained a medication count between 1-3. They had a BMI over 30 kg/m^2 and exhibited LDL levels of 99.96 mg/dL, HDL of 40.60 mg/dL, and a total cholesterol level of 165.27 mg/dL. This group primarily consisted of subjects in NYHA Class II functional status, with their ejection fraction ranging between 40-49%. They recorded an NT-pro-BNP level of 1481.65 pg/mL and had KCCQ12 scores exceeding 75.

Finally, Group 3 had Empagliflozin 10mg as the primary medication, with the majority of members taking more than four medications. They had BMIs below 24.9 kg/m2, LDL and HDL levels of 109.77 mg/dL and 39.28 mg/dL, respectively, and a total cholesterol reading of 177.94 mg/dL. NYHA Class II was the predominant functional status, their ejection fraction ranged between 50 and 59%, and they presented with NT-pro-BNP levels of 1055.50 pg/mL, and KCCQ12 scores between 60 and 74.

Table 4. Cluster analysis according to cardiovascular characteristics

Characteristics	Cluster 1	Cluster 2	Cluster 3	p-value
SGLT2 inhibitor	**Empagliflozin 25mg**	**Dapagliflozin 10mg**	**Empagliflozin 10mg**	**0.181**
No. drugs	> 4	1-3	> 4	0.236
BMI	25-29.9 kg/m2	> 30 kg/m2	< 24.9 kg/m2	0.827
LDL	108.57 mg/dL	99.96 mg/dL	109.77 mg/dL	0.090
HDL	38.59 mg/dL	40.60 mg/dL	39.28 mg/dL	0.871
Total cholesterol	181.31 mg/dL	165.27 mg/dL	177.94 mg/dL	0.207
Functional status	NYHA III	NYHA II	NYHA II	0.491
Ejection fraction	< 40%	40-49%	50-59%	0.193
NT-pro-BNP	2952.93 pg/mL	1481.65 pg/mL	1055.50 pg/mL	0.201
KCCQ12	45-59	> 75	60-74	0.864

Similarly, a cluster analysis was conducted to observe patterns among the metabolic characteristics of the participants (Table 4). Regarding the SGLT2 inhibitor, all groups were prescribed Empagliflozin (10-25mg for Group 1) or Dapagliflozin (5-10mg for Groups 2 and 3), with a p-value of 0.953, indicating no significant differences. Creatinine levels were consistent among the groups: 1.05 mg/dL, 0.95 mg/dL, and 1.06 mg/dL for Groups 1, 2, and 3, respectively (p=0.936). The prevalence of diabetes varied significantly: Group 1 had 37.50%, Group 2 had no cases, while Group 3 reported an incidence of 100%, but the p-value of 0.327 suggests that the differences could be due to chance. Hemoglobin A1c percentages were 5.95% for Group 1, 5.50% for Group 2, and 7.20% for Group 3, with a p-value of 0.996. Microalbuminuria/proteinuria was present in 15% of Group 1, absent in Group 2, and observed in 18% of Group 3 (p=0.087). (Table 5)

The functional class was assessed using NYHA classifications. Group 1 was predominantly NYHA-III, while Groups 2 and 3 were NYHA-I (p=0.394). Ejection fraction ranged from 40-49% for Group 1 and 50-59% for Groups 2 and 3 (p=0.958). Notably, NT-pro-BNP levels showed significant differences: Group 1 had 392.7 pg/mL, Group 2 had a much higher value of 6674.2 pg/mL, and Group 3 reported 227.2 pg/mL, with a significant p-value of <0.001. Finally, KCCQ12 scores were 71.6, 54.6, and 83.9 for Groups 1, 2, and 3, respectively, with a p-value of 0.412. (Table 5)

Table 5. Cluster analysis according to metabolic characteristics

Characteristics	Cluster 1	Cluster 2	Cluster 3	p-value
SGLT2 inhibitor	**Empagliflozin 10-25mg**	**Dapagliflozin 5-10mg**	**Dapagliflozin 5-10mg**	**0.953**
Creatinine	1.05 mg/dL	0.95 mg/dL	1.06 mg/dL	0.936
Diabetes	37.50%	0%	100%	0.327
Hemoglobin A1c	5.95%	5.50%	7.20%	0.996
Microalbuminuria/proteinuria	15%	0%	18%	0.087
Functional status	NYHA-III	NYHA-I	NYHA-I	0.394
Ejection fraction	40-49%	50-59%	50-59%	0.958
NT-pro-BNP	392.7 pg/mL	6674.2 pg/mL	227.2 pg/mL	< 0.001
KCCQ12	71.6	54.6	83.9	0.412

Discussion

Our aim was to provide information regarding the preliminary effectiveness of SGLT2 inhibitors in a Dominican cohort.

We found that 70% of the sample consisted of males, a deviation from the findings of a previous study on sex differences in HF. In that study, which explored heart failure with both preserved and reduced ejection fraction, the disease's prevalence was higher among women, reaching a ratio of approximately 2:1.[9] Several factors could potentially explain this discrepancy. Firstly, men typically have a greater cardiac mass and may also experience a higher incidence of subclinical coronary artery disease. Additionally, it's worth

noting that estrogens are known to have cardioprotective effects, which could influence these contrasting results.[10] On the other hand, the median age of the participants in our study was 69 years, with an interquartile range of 20.25. Interestingly, this age distribution closely resembles that of a cohort from Costa Rica, where the average age was reported as 69 ± 13.6 years.[11] Such similarities in age distribution are to be expected in heart failure studies. With increasing age, cardiac reserve and physiological function tend to decline, contributing to the progression of the disease.[12]

Regarding risk factors for heart failure, only 40% of the sample in our study received a diagnosis of type II diabetes mellitus (T2DM). This proportion appears lower compared to a similar cohort, where the prevalence of T2DM in the sample was 46%.[11] This observation implies that the development of heart failure in our studied population likely arises from other contributing risk factors, including coronary artery disease, high blood pressure, smoking, and unhealthy habits.[13] Concerning smoking habits, it's notable that 61.7% of the participants in our study were either former smokers or current smokers, underscoring its significance as a potential cause for the development of heart failure within our sample. Smoking has been widely categorized as the "most significant" modifiable risk factor for cardiovascular disease, doubling the risk of suffering from heart failure in individuals who smoke.[14,15]

With respect to the specific causes of heart failure within our study, ischemic heart disease was identified as the cause for 55% of the patients. This finding aligns with global trends, as evidenced by a study conducted in 195 countries in 2017, where ischemic heart disease was recognized as the leading cause of heart failure, accounting for 26.5% of cases. However, it's worth noting that when examining regional variations, such as in Latin America and the Caribbean, high blood pressure emerged as the predominant cause, relegating ischemic heart disease to the second position.[16] These findings highlight the complex interplay of risk factors and regional variations in the etiology of heart failure, emphasizing the need for comprehensive risk assessment and tailored prevention strategies.

After conducting a cluster analysis to discern patterns among subjects due to noticeable data heterogeneity, three distinct groups emerged, each with unique characteristics related to cardiovascular status. One of the clusters comprised patients under Empagliflozin 25mg, taking more than four medications, having increased LDL and decreased HDL, with a BMI corresponding to overweight. The predominant functional class was NYHA Class III, showing reduced ejection fraction and elevated NT-pro-BNP levels despite the excellent quality of life measured by the KCCQ12 questionnaire. The number of drugs for cardiovascular or non-cardiovascular disorders is notorious in this type of patient. It is acknowledged that heart failure patients tend to use a high number of prescribed or non-prescribed drugs, increasing the risk of adverse events during treatment.[17]

Furthermore, the use and dosage of multidrug regimes show considerable differences among patients, possibly due to cultural and economic circumstances instead of the medical doctor's guidance.[18] On the other hand, attention is given to the quality of life of this cluster despite their cardiovascular deterioration. Other authors also observed this tendency.[19] In this regard, the improvement in hemodynamics and reduction of cardiac fibrosis might be related to the subjective benefit of SGLT2 inhibitors.[20]

In a distinct cluster of patients under Dapagliflozin 10mg treatment, we observed a modest medication regimen, typically comprising 1-3 medications. Intriguingly, despite having a BMI indicative of obesity type I, their cholesterol levels consistently remained within the normal range. Furthermore, their ejection fraction (EF) demonstrated robust preservation, placing them in NYHA functional Class II. However, a striking contrast emerged with their NT-pro-BNP levels, which exceeded the anticipated range, paralleled by KCCQ12 scores indicating significant impairment in daily functioning.

Regarding NT-pro-BNP levels, prior studies have established an inverse correlation between this neurohormone and physical capabilities.[21] Moreover, these studies have also noted a proportional relationship between NT-pro-BNP and disease severity.[22] Thus underscoring the rationale behind the diminished health-related quality of life observed in clusters with elevated relative BNP concentrations. However, it's noteworthy that lipid profiles have been recognized as predictive indicators of potential cardiovascular outcomes in heart failure patients.[23] Nevertheless, the presence of patients within this particular cluster displaying a less favorable heart failure profile despite maintaining normal lipid levels prompts a compelling call for more rigorous research on this intriguing topic.

In Cluster 3, Empagliflozin 10mg emerged as the predominant treatment, often administered alongside more than four medications. Interestingly,

the patients in this group presented with a BMI, suggesting an average weight, although their LDL and HDL levels exhibited slight deviations from the expected range. They were classified under NYHA Class II, reflecting a moderate functional status, and their ejection fraction (FE) fell within the anticipated range. While their NT-pro-BNP levels were elevated, this elevation was less pronounced than observed in the initial two clusters. What makes this finding particularly paradoxical is the KCCQ12 assessments, which indicated severe impairment in daily activities attributed to the underlying disease. Despite their seemingly favorable clinical metrics, these patients reported significant limitations in their ability to carry out everyday tasks, raising intriguing questions about the nuanced factors contributing to their overall well-being.

It is noteworthy to ponder the idea that increased weight and high lipid profile are related to the development of heart failure, along with weight loss and weight maintenance leading to a better cardiovascular profile and heart failure improvement, considering the features of this cluster. Genetic predisposition, dietary patterns, and physical activity levels might play an essential role in the worsening condition of these patients.[24-28]

In this study, several limitations were encountered. Firstly, the researchers could not strictly assess the duration between the patient's HF diagnosis and their participation in the study. But rather, asked participants for a reference of the amount of time since their diagnosis, which limits the interpretation to memory bias. This factor could have provided valuable insights into the progression of the condition. Additionally, the precise duration of their SGLT2 inhibitor usage remained unspecified, hindering a comprehensive evaluation of treatment duration and its potential impact on outcomes. Furthermore, the study lacked information regarding whether patients had a previous diagnosis of hypertension, a variable that could potentially influence the effectiveness of these medications.

Another notable challenge was the difficulty in conducting specific imaging and laboratory tests, leading to limitations in collecting precise clinical data. Additionally, the study participants' diverse educational backgrounds posed data collection and interpretation challenges. Finally, significant heterogeneity among the patients introduced complexity to the analysis, rendering it challenging to arrive at definitive conclusions regarding the comparative efficacy of the two SGLT2 inhibitors. These limitations underscore the necessity for more comprehensive and standardized data collection methodologies in future research to yield more robust and informative results.

Conclusion

This manuscript aimed to assess the preliminary effectiveness of SGLT2 inhibitors in a Dominican cohort of heart failure patients. Key findings revealed a higher proportion of males in the sample, a median age consistent with global trends, and a lower prevalence of type II diabetes mellitus compared to similar cohorts. Smoking emerged as a significant risk factor, and ischemic heart disease was the leading cause of heart failure, highlighting variations in etiology. Cluster analysis identified distinct patient groups with varying characteristics related to cardiovascular status and medication regimens, prompting further investigation through more standardized research approaches in the future.

Conflicts Of Interest Statement

No conflict of interest to disclose.

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Appendix

Table 1. Characteristics of disease and treatment

Variables	Value
State of heart failure	
De novo, N (%)	3 (5)
Acute, N (%)	9 (15)
Chronic, N (%)	39 (65)
Chronic decompensated, N (%)	9 (15)
Cause of heart failure	
Ischemic, N (%)	33 (55)
Non-ischemic, N (%)	13 (21.7)
Unknown, N (%)	8 (13.3)
NYHA functional status	
NYHA-I, N (%)	18 (30)
NYHA-II, N (%)	37 (61.7)
NYHA-III, N (%)	5 (8.3)
Hospitalization due to heart failure	13 (21.7)
Time of evolution of heart failure, Median (IQR) [months]	11.00 (20.00)
SGLT2 Inhibitor	
Dapagliflozin 10 mg, N (%)	40 (66.7)
Empagliflozin 10 mg, N (%)	16 (26.7)
Dapagliflozin 5 mg, N (%)	1 (1.7)
Empagliflozin 25 mg, N (%)	1 (1.7)
Ejection fraction, Mean (SD)	32.51 (11.79)
NT-pro-BNP, Median (IQR)	2635.00 (4271.50)
No. of drugs, Median (IQR)	7.00 (2.00)
Quality of life by KCCQ12, Median (IQR)	66.67 (28.79)
Systolic blood pressure, Median (IQR)	130.00 (20.00)
Diastolic blood pressure, Median (IQR)	80.00 (12.50)
Median arterial pressure, (SD)	95.89 (14.12)
Heart frequency, Mean (SD)	74.42 (12.57)
FR, Median (IQR)	20.00 (2.00)
Hemoglobin A1c, Mean (SD)	7.77 (2.10)
Fasting blood glucose, Median (IQR)	104.00 (32.00)
Total Cholesterol, Mean (SD)	153.96 (46.43)
LDL, Median (IQR)	76.00 (49.00)
HDL, Mean (SD)	43.43 (11.24)
Blood sodium, Median (IQR)	140.00 (3.00)
Creatinine, Median (IQR)	1.20 (0.39)
Microalbuminuria/proteinuria	
Yes, N (%)	20 (33.3)
No, N (%)	12 (20)