



Research Article

Exploring the Impact of Dapagliflozin on Shock Therapy in Heart Failure Patients with Implantable Cardioverter Defibrillators: A Retrospective Cohort Study

Sabri Seyis*

Abstract

Background: Heart failure (HF) remains a leading cause of morbidity and mortality worldwide, with implantable cardioverter-defibrillators (ICDs) being crucial for managing life-threatening arrhythmias in these patients. Dapagliflozin, a sodium-glucose cotransporter 2 (SGLT2) inhibitor, has shown promise in improving cardiovascular outcomes in HF patients, yet its effects on those with ICDs have not been thoroughly explored.

Methods: This retrospective cohort study analyzed health records from 74 heart failure patients with ICDs who were treated with Dapagliflozin alongside standard HF therapy. We compared these patients' records before and after treatment with Dapagliflozin. Primary outcomes included the incidence of ICD shock therapy and arrhythmia episodes.

Results: No significant difference was found between the number of shocks observed in the 6-month follow-up before dapagliflozin treatment and the number of shocks observed in the 6-month follow-up after dapagliflozin treatment ($p=0.754$). Also, VT episodes were similar ($p=0.453$).

Conclusion: Dapagliflozin treatment in heart failure patients with ICDs has no adverse effects on arrhythmia episodes and ICD shock therapy. This aligns with the broader literature indicating dapagliflozin's role in reducing heart failure events and cardiovascular deaths without specifically addressing its impact on ICD shock occurrences.

Keywords: Dapagliflozin; Heart Failure; Implantable Cardioverter-Defibrillator; Arrhythmia; Cardiovascular Mortality

Introduction

Heart failure (HF) is a life-threatening disease with a growing incidence in developed countries due to better treatment options for heart failure, improvement of survival after myocardial infarction and increased life expectancy. The introduction of implantable devices such as implantable cardioverter defibrillators (ICD) has improved the overall survival of patients with heart failure [1]. Heart failure patients with an ICD are at elevated risk for ventricular arrhythmias and sudden cardiac death [2]. Also, an ICD shock is strongly associated with a poor prognosis [3,4]. Therefore, treatment capable of reducing ventricular arrhythmia burdens should be continued following ICD implantation. The utilization of sodium-glucose cotransporter 2 (SGLT2) inhibitors, such as dapagliflozin, has been linked to a reduction in cardiovascular mortality, yet the underlying mechanisms remain partially elucidated [5]. Dapagliflozin showed positive findings in the DAPA-HF trial [6]. However, the effect of dapagliflozin on sudden cardiac death had not

Affiliation:

Department of Cardiology, Yenisehir Hospital Mersin, Turkey.

*Corresponding authors:

Sabri Seyis, Department of Cardiology, Yenisehir Hospital Mersin, Turkey

Citation: Sabri Seyis. Exploring the Impact of Dapagliflozin on Shock Therapy in Heart Failure Patients with Implantable Cardioverter Defibrillators: A Retrospective Cohort Study. *Cardiology and Cardiovascular Medicine*. 8 (2024): 159-166.

Received: April 02, 2024

Accepted: April 12, 2024

Published: April 29, 2024

yet been reported. HF medications sometimes can cause ICD shocks as a side effect by deteriorating metabolic parameters [7]. This study aims to delineate the effect of dapagliflozin on the frequency of ventricular arrhythmias and ICD shocks in HF patients, thereby contributing to the understanding of SGLT2 inhibitors' cardiovascular benefits.

Methods

This retrospective cohort study meticulously investigated the impact of dapagliflozin on the frequency of ventricular arrhythmias and the subsequent requirement for ICD shocks in patients diagnosed with heart failure (HF), incorporating those with and without diabetes mellitus (DM). The study cohort consisted of 74 patients who had an implantable cardioverter-defibrillator (ICD) installed for HF management and were subsequently commenced on dapagliflozin treatment. Parameters such as baseline physical examination, risk factors, electrocardiography (ECG), and echocardiography and laboratory results were noted from the patient's files. The inclusion criteria were patients over 20 years of age, with ICD implantation for at least 6 months prior, and an ejection fraction of $\leq 35\%$. Patients were excluded if they had used any SGLT2 inhibitor in the 6 months before starting dapagliflozin, had interrupted dapagliflozin treatment, had a history of dapagliflozin allergy, type 1 DM, diabetic ketoacidosis, $\text{GFR} < 30 \text{ ml/min/1.73 m}^2$ or were on dialysis, suffered excessive fluid loss, were pregnant or suspected to be pregnant, underwent arrhythmia treatment modifications or ablation, had cardiac bypass or revascularization in the last 12 months, or if their ICD lacked arrhythmia recording capabilities. Standard programs were used in the defibrillators. When the heart rate is within the range of 130-161 bpm (Zone 1), the device recorded the event without giving any treatment. Ventricular arrhythmias faster than 162 bpm (Zone 2) were considered as VT, and the ICD was programmed to apply antitachycardia pacing (ATP) with 2 bursts and 2 ramps initially. If the arrhythmia persisted, the device delivered a defibrillator shock. When the rate of ventricular arrhythmia was faster than 210 bpm (Zone 3), the device was programmed to deliver a shock as the first treatment. In all devices, algorithms for discrimination of supraventricular tachycardia (SVT) and VT were activated to avoid inappropriate shocks. Data on ICD-detected arrhythmias and shock therapies were meticulously collected for two distinct intervals: the 6 months preceding and the 6 months following the initiation of dapagliflozin therapy. The primary study endpoints focused on the incidence of clinically significant ventricular arrhythmias and ICD shocks across these periods. The study protocol was approved by the local ethics committee.

Statistical Analysis

In this study, the effects of Dapagliflozin therapy on shock and ventricular tachycardia incidence among heart failure patients with implanted defibrillators were investigated. Data

were summarized using descriptive statistics; continuous (numerical) variables were presented as median, minimum, and maximum values in tables, while categorical variables were summarized by count and percentage. The normality of numerical variables was checked using Shapiro-Wilk, Kolmogorov-Smirnov, and Anderson-Darling tests. Statistical analyses were conducted using Pearson Chi-Square for categorical variables with expected counts of 5 or more in 2x2 tables, Fisher's Exact Test for tables with expected counts below 5, and Mann-Whitney U test for continuous variables. Odds Ratios (OR) were used to estimate the association strength between various risk factors and the incidence of ventricular tachycardia and shock. Univariable and multivariable ORs, with corresponding confidence intervals and p-values, were presented for each factor. Two models (Model 1 and Model 2) were used to explore the effects of different variables, with specific exclusions (hypertension in Model 1 and stroke history in Model 2) for certain variables. eGFR and primary prevention were statistically significant in both models. Statistical analyses were performed with Jamovi (Version 2.3.28) and JASP (Version 0.17.3), considering a significance level of 0.05 (p-value) for all statistical tests.

Results

The study included 74 patients, with a median age of 60 years. Of the participants, 24 (32.4%) were female and 50 (67.6%) were male. The median body mass index was 27. The majority of participants had ischemic etiology (77.0%, n=57), while 24.3% (n=17) had non-ischemic etiology. Diabetes mellitus was observed in 55.4% (n=41) and hypertension in 64.9% (n=48) of the patients. In the study, smoking was found in 51.4% (n=38) of participants, hyperlipidemia in 44.6% (n=33), and stroke in 16.2% (n=12). The proportion of participants with peripheral arterial disease was 33.8% (n=25). Pairwise comparisons between the groups with and without dapagliflozin use, in terms of shock development at 6-month follow-up, showed that the presence of hypertension and stroke history was significantly higher among those with shock development ($p=0.047$ and $p<0.001$, respectively). There were no significant differences between the groups in terms of age, gender, body mass index, etiology (ischemic and non-ischemic), diabetes mellitus, smoking, hyperlipidemia, and peripheral arterial disease ($p>0.05$ for each) (Table 1).

Pairwise comparisons revealed that patients with shock after dapagliflozin treatment had significantly lower ejection fraction compared to those without shock ($p<0.001$). Additionally, patients with shock had significantly higher rates of atrial fibrillation compared to those without shock ($p=0.002$). Primary prevention was significantly more common in patients without shock ($p<0.001$), while secondary prevention was significantly more common in patients with shock ($p<0.001$). There were no significant differences between the groups in terms of the use of RAS blockers, beta blockers, calcium channel blockers, and amiodarone ($p>0.05$ for each) (Table 2).

Table 1: Impact of Dapagliflozin on Shock Incidence in Heart Failure Patients with Implantable Defibrillators Over a 6-Month Period

Variables	Overall (n=74)	Shock at 6-Month Follow-up After Dapagliflozin		p-values
		No (n=62)	Yes (n=12)	
Age§	60.0 [38.0 – 79.0]	59.0 [38.0 – 79.0]	64.5 [51.0 – 72.0]	0.182**
Gender ‡				
Woman	24 (32.4)	21 (33.9)	3 (25.0)	0.740**
Male	50 (67.6)	41 (66.1)	9 (75.0)	
Body Mass Index§	27.0 [22.0 – 34.0]	27.0 [23.0 – 34.0]	27.5 [22.0 – 30.0]	0.751*
Ischemic etiology, yes ‡	57 (77.0)	48 (77.4)	9 (75.0)	0.999**
Non-Ischemic etiology, yes ‡	18 (24.3)	15 (24.2)	3 (25.0)	0.999**
Diabetes Mellitus, yes ‡	41 (55.4)	33 (53.2)	8 (66.7)	0.589**
Hypertension, yes ‡	48 (64.9)	37 (59.7)	11 (91.7)	0.047**
Smoking, yes ‡	38 (51.4)	31 (50.0)	7 (58.3)	0.831**
Hyperlipidemia, yes ‡	33 (44.6)	29 (46.8)	4 (33.3)	0.589**
History of Stroke, yes ‡	12 (16.2)	4 (6.5)	8 (66.7)	<0.001**
Peripheral Arterial Disease, yes ‡	25 (33.8)	18 (29.0)	7 (58.3)	0.092**

Footnote: Table 1 assesses the impact of Dapagliflozin on shock incidence in heart failure patients equipped with implantable defibrillators over a six-month timeframe, utilizing various statistical analyses and data representation methods. The § symbol denotes the median and range of values [Minimum-Maximum]. The ‡ symbol indicates data are presented in number and percentage format (n (%)), reflecting categorical variable distribution. Statistical significance is evaluated through the following symbols and tests: *. Mann-Whitney U test, utilized for comparing median values between two independent samples when the data distribution does not assume normality. **. Pearson Chi-Square or Fisher's Exact test, applied to examine the significance of association between two categorical variables.

Table 2: Comparison of Blood Pressure, Heart Rate, and Ejection Fraction Before and After 6 Months of Dapagliflozin Therapy in Heart Failure Patients with Implantable Defibrillators

Variables	Overall (n=74)	Shock at 6-Month Follow-up After Dapagliflozin		p-values
		No (n=62)	Yes (n=12)	
Systolic Blood Pressure §	130.0 [115.0 – 140.0]	130.0 [115.0 – 140.0]	130.0 [120.0 – 135.0]	0.288*
Diastolic Blood Pressure §	75.0 [60.0 – 85.0]	75.0 [60.0 – 85.0]	75.0 [70.0 – 80.0]	0.921*
Heart Rate §	66.0 [54.0 – 82.0]	66.0 [56.0 – 82.0]	66.0 [54.0 – 78.0]	0.488*
Ejection Fraction §	30.0 [18.0 – 35.0]	32.0 [20.0 – 35.0]	25.0 [18.0 – 32.0]	<0.001*
Atrial fibrillation, yes ‡	15 (20.3)	8 (12.9)	7 (58.3)	0.002**
Primary Protection, yes ‡	47 (63.5)	45 (72.6)	2 (16.7)	<0.001**
Secondary Protection, yes ‡	27 (36.5)	17 (27.4)	10 (83.3)	<0.001**
RAS Blocker Use, yes‡	62 (83.8)	51 (82.3)	11 (91.7)	0.677**
Beta Blocker Use, yes ‡	66 (89.2)	54 (87.1)	12 (100.0)	0.339**
Calcium Channel Blocker Use, yes ‡	19 (25.7)	16 (25.8)	3 (25.0)	0.999**
Amiodarone Usage, yes ‡	11 (14.9)	10 (16.1)	1 (8.3)	0.680**

Footnote: Table 2 explores the changes in blood pressure, heart rate, and ejection fraction among heart failure patients with implantable defibrillators before and after 6 months of Dapagliflozin therapy, using various statistical methods and data presentation formats. The ‡ symbol indicates data presented as the number and percentage (n (%)) for categorical variables. The § symbol represents values given as median and range [Minimum-Maximum], reflecting the distribution of continuous variables. The symbols for statistical significance are as follows: *. Mann-Whitney U test, utilized for comparing median values between two independent groups, especially when the data distribution is not assumed to be normal. **. Pearson Chi-Square or Fisher's Exact test, applied to assess the association and differences in frequencies or proportions between categorical variables across groups.

The analysis of pairwise comparisons revealed that patients with shock after dapagliflozin treatment had significantly higher CRP levels than patients without shock ($p < 0.001$). Patients with shock had significantly higher sodium levels compared to those without shock ($p = 0.025$). Additionally, patients with shock had significantly lower eGFR levels ($p < 0.001$). No significant differences were found in glucose and potassium levels in the presence of shock ($p = 0.256$ and $p = 0.769$, respectively) (Table 3).

When the number of shocks observed in the 6-month follow-up before dapagliflozin treatment was compared with the number of shocks observed in the 6-month follow-up after dapagliflozin treatment, no significant difference was found ($p = 0.754$) (Table 4).

When the number of VT episodes observed in the 6-month follow-up before dapagliflozin treatment was compared with the number of VT episodes observed in the 6-month follow-up after dapagliflozin treatment, no significant difference was found ($p = 0.453$) (Table 5).

At the 6-month follow-up after dapagliflozin treatment, a comparison was made between patients with and without VT attacks in terms of demographic and clinical variables. The results showed that patients with VT attacks had a

significantly higher presence of hypertension, history of stroke, and frequency of peripheral arterial disease compared to those without VT attacks ($p < 0.05$ for each). However, variables such as age, gender, body mass index, ischemic and non-ischemic etiology, diabetes mellitus, smoking, and hyperlipidemia were comparable in both groups, with and without VT ($p < 0.05$ for each) (Table 6).

When comparing patients with and without VT attacks at the 6-month follow-up after dapagliflozin treatment, it was found that ejection fraction was significantly lower in patients with VT attacks ($p < 0.001$). Additionally, the presence of atrial fibrillation was higher in patients with VT episodes ($p = 0.004$). Furthermore, the primary prevention rate was higher in patients without a VT episode ($p < 0.001$), while secondary prevention was more common in patients with a VT episode ($p < 0.001$). There were no significant differences in the development of VT attacks among variables such as systolic blood pressure, diastolic blood pressure, heart rate, RAS blocker use, beta-blocker use, calcium channel blocker use, and amiodarone use ($p > 0.05$ for each) (Table 7).

When comparing biochemical parameters in patients with heart failure and implantable defibrillator implantation after dapagliflozin treatment, those who experienced VT attacks

Table 3: Analysis of Glucose Levels, Inflammatory and Renal Markers Before and After 6 Months of Dapagliflozin Therapy in Heart Failure Patients with Implantable Defibrillators

Variables [§]	Overall (n=74)	Shock at 6-Month Follow-up After Dapagliflozin		p-values*
		No (n=62)	Yes (n=12)	
Glucose Level	113.5 [80.0 – 185.0]	113.0 [80.0 – 185.0]	138.5 [92.0 – 167.0]	0.256
CRP Level	0.2 [0.1 – 0.6]	0.2 [0.1 – 0.6]	0.4 [0.3 – 0.6]	<0.001
Sodium Level	136.5 [128.0 – 147.0]	136.0 [128.0 – 147.0]	138.0 [130.0 – 145.0]	0.025
Potassium Level	4.6 ± 0.6	4.6 [3.2 – 6.0]	4.8 [3.8 – 5.9]	0.769
eGFR	74.8 ± 17.0	81.0 [42.0 – 104.0]	51.5 [37.0 – 73.0]	<0.001

Footnote: Table 3 evaluates the effects of 6 months of Dapagliflozin therapy on glucose levels, inflammatory markers, and renal function in heart failure patients with implantable defibrillators, employing specific statistical methods and representations. The § symbol indicates that values are presented as median and range [Minimum-Maximum] for continuous variables. For the interpretation of statistical significance, the following symbol is used: *. Mann-Whitney U test is utilized for comparing median values between two groups, suitable for data not normally distributed. This footnote corrects the presentation of statistical symbols and their definitions to align with the data and analyses provided in

Table 4: Shock Incidence Before and After 6 Months of Dapagliflozin Therapy in Heart Failure Patients with Implantable Defibrillators

	Shock at 6-Month Follow-up After Dapagliflozin		p-value
	No (n=62)	Yes (n=12)	
Shock at 6-Month Follow-up Before Dapagliflozin			
No	56 (90.3)	4 (33.3)	0.754
Yes	6 (9.7)	8 (66.7)	

Footnote: Table 4 details the incidence of shock in heart failure patients with implantable defibrillators before and after 6 months of Dapagliflozin therapy. The data are presented using the McNamer test to evaluate the significance of differences between groups. The ‡ symbol indicates that data are shown in number and percentage format (n (%)), facilitating the comparison of shock occurrence rates pre- and post-treatment.

Table 5: Ventricular Tachycardia Episodes Before and After 6 Months of Dapagliflozin Treatment in Heart Failure Patients with Implantable Defibrillators

	VT Attack at 6-Month Follow-up After Dapagliflozin		p-value
	No (n=57)	Yes (n=17)	
VT Attack at 6-Month Follow-up After Dapagliflozin ‡			
No	52 (91.2)	2 (11.8)	0.453
Yes	5 (8.8)	15 (88.2)	

Footnote: Table 5 explores the episodes of ventricular tachycardia (VT) before and after 6 months of Dapagliflozin treatment in heart failure patients equipped with implantable defibrillators. The McNamer test is employed to determine the statistical significance of changes in VT episodes, with the ‡ symbol denoting data presented as counts and percentages (n (%)). This format highlights the comparative effectiveness of Dapagliflozin on VT incidence.

Table 6: Patient Characteristics and Ventricular Tachycardia Episodes After 6 Months of Dapagliflozin in Heart Failure Patients with Implantable Defibrillators

Variables	VT Attack at 6-Month Follow-up After Dapagliflozin		p-value
	No (n=57)	Yes (n=17)	
Age§	59.0 [38.0 – 79.0]	64.0 [43.0 – 77.0]	0.192*
Gender ‡			
Woman	21 (36.8)	3 (17.6)	0.235**
Male	36 (63.2)	14 (82.4)	
Body Mass Index§	27.0 [23.0 – 34.0]	28.0 [22.0 – 32.0]	0.265*
Ischemic etiology, yes ‡	43 (75.4)	14 (82.4)	0.746**
Non-Ischemic etiology, yes ‡	14 (24.6)	4 (23.5)	0.999**
Diabetes Mellitus, yes ‡	28 (49.1)	13 (76.5)	0.087**
Hypertension, yes ‡	32 (56.1)	16 (94.1)	0.010**
Smoking, yes ‡	27 (47.4)	11 (64.7)	0.328**
Hyperlipidemia, yes ‡	26 (45.6)	7 (41.2)	0.964**
History of Stroke, yes ‡	3 (5.3)	9 (52.9)	<0.001**
Peripheral Arterial Disease, yes ‡	15 (26.3)	10 (58.8)	0.028**

Footnote: Table 6 provides an analysis of patient characteristics and ventricular tachycardia episodes after 6 months of Dapagliflozin therapy in heart failure patients with implantable defibrillators. The data representation and statistical analysis include the following notations and methodologies: The ‡ symbol indicates data presented as number and percentage (n (%)), showing the distribution of categorical variables. The § symbol represents values given as median and range [Minimum-Maximum] for continuous variables. Statistical significance is determined using *. Mann-Whitney U test for comparing median values between two independent samples, suitable for non-normally distributed continuous data. **. Pearson Chi-Square or Fisher's Exact test is employed to assess the significance of associations between categorical variables.

at the 6-month follow-up had significantly higher glucose and CRP levels (p=0.022 and p<0.001, respectively) and significantly lower eGFR values (p<0.001). No significant

difference was observed between the groups in terms of sodium and potassium levels (p=0.210 and p=0.857, respectively) (Table 8).

Table 7: Clinical and Cardiac Function Parameters Related to Ventricular Tachycardia After Dapagliflozin Treatment in Heart Failure Patients with Implantable Defibrillators

Variables	VT Attack at 6-Month Follow-up After Dapagliflozin		p-values
	No (n=57)	Yes (n=17)	
Systolic Blood Pressure §	130.0 [115.0 – 140.0]	130.0 [120.0 – 140.0]	0.203*
Diastolic Blood Pressure §	75.0 [60.0 – 85.0]	75.0 [70.0 – 85.0]	0.489*
Heart Rate §	66.0 [56.0 – 82.0]	66.0 [54.0 – 78.0]	0.811*
Ejection Fraction §	32.0 [20.0 – 35.0]	25.0 [18.0 – 35.0]	<0.001*
Atrial fibrillation, yes ‡	7 (12.3)	8 (47.1)	0.004**
Primary Protection, yes ‡	43 (75.4)	4 (23.5)	<0.001**
Secondary Protection, yes ‡	14 (24.6)	13 (76.5)	<0.001**
RAS Blocker Use, yes‡	49 (86.0)	13 (76.5)	0.454**
Beta Blocker Use, yes ‡	49 (86.0)	17 (100.0)	0.185**
Calcium Channel Blocker Use, yes ‡	15 (26.3)	4 (23.5)	0.999**
Amiodarone Usage, yes ‡	8 (14.0)	3 (17.6)	0.707**

Footnote: Table 7 examines clinical and cardiac function parameters related to ventricular tachycardia episodes after 6 months of Dapagliflozin treatment in heart failure patients with implantable defibrillators. The data analysis and presentation employ the following conventions: The ‡ symbol indicates that data are presented as number and percentage (n (%)), which is utilized for categorical variables. The § symbol denotes values given as median and range [Minimum-Maximum], for continuous variables. For statistical analysis, the symbols are defined as follows: *. Mann-Whitney U test, used for comparing median values between two independent groups, especially when data is not normally distributed. **. Pearson Chi-Square or Fisher’s Exact test, applied to evaluate the significance of differences in proportions or frequencies between categorical variables.

Discussion

In crafting a discussion around our study on the effects of dapagliflozin in heart failure patients with implantable cardioverter defibrillators (ICDs), it's pertinent to align our findings with recent literature and to identify the continuity and discrepancies within this body of work. Our study contributes to a growing body of evidence assessing the role of dapagliflozin in heart failure management, particularly focusing on its impact on shock therapy and arrhythmia incidence in patients with ICDs.

The DAPA-HF study is one of the cornerstone investigations though it broadly examines dapagliflozin's efficacy in heart failure patients with reduced EF (HFrEF), highlighting its potential in reducing adverse outcomes [6]. Another significant contribution comes from DELIVER Trial investigators who discuss dapagliflozin's potential lifesaver role for heart failure patients with mildly reduced or preserved ejection fraction, emphasizing the drug's broad applicability across different heart failure profiles [8]. Our study's focus on shock treatment efficacy is novel, yet it draws parallels with broader research trends. For instance, the expanded indication for dapagliflozin by the FDA in 2020 to reduce cardiovascular death and hospitalization risk in adults with HFrEF, underscores the drug's growing therapeutic scope. There are few case reports addressing increased ICD shocks after SGLT2i treatments [9]. In these reports mechanism

was unclear. Although low serum potassium levels affect the cardiac repolarization and can induce life threatening arrhythm, diuretic effect of SGLT2i drugs seem to be neutral on potassium levels different than classic diuretics [10,11]. Also it was shown that SGLT2i drugs do not increase the QT interval [12]. Our research found no significant difference in shock incidence and VT episodes before and after dapagliflozin treatment. This aligns with the broader literature indicating dapagliflozin's role in reducing heart failure events and cardiovascular deaths without specifically addressing its impact on ICD shock occurrences. Furthermore, our analysis of specific patient characteristics such as hypertension and ejection fraction as risk modifiers finds resonance with previous studies suggesting dapagliflozin's nuanced benefits in heart failure management [13-16]. In our study, patients who developed shock and VT episodes after dapagliflozin treatment had significantly higher CRP levels, and lower ejection fraction and eGFR levels compared to those without shock development. Especially correlation between low eGFR and shock and VT episodes highlights the importance of kidney function in these outcomes. These results are compatible with previous studies [17-21] Contrary to case reports dapagliflozin seems to be safe in matters of VT episodes and ICD shocks. Our study, while comprehensive, raises further questions regarding dapagliflozin's mechanistic impact on arrhythmia suppression and shock therapy modulation in heart failure patients with ICDs. The literature

suggests dapagliflozin's broad benefits across heart failure profiles, yet detailed investigations into its interactions with ICD therapy remain sparse. Future research could explore the drug's impact on arrhythmogenic substrates and its potential to modulate ICD intervention thresholds, addressing a critical gap highlighted by our findings.

Additionally, the role of patient-specific characteristics in mediating dapagliflozin's effects warrants deeper investigation. Our study hints at the significance of underlying conditions such as hypertension and reduced ejection fraction, suggesting that future research should adopt a stratified approach to patient selection, potentially uncovering tailored therapeutic windows for dapagliflozin use.

Conclusion

In conclusion, our study adds valuable insights to the existing body of knowledge on dapagliflozin's role in heart failure management, particularly in patients with ICDs. By drawing parallels with and diverging from current research, we've not only affirmed the drug's utility in a broad therapeutic context but also underscored the need for focused research on its specific impacts on shock therapy and arrhythmia management. As heart failure therapy continues to evolve, studies like ours pave the way for nuanced understanding and application of promising pharmacological agents such as dapagliflozin

Limitations

While our study provides valuable insights into the benefits of Dapagliflozin for heart failure patients with ICDs, it is not without limitations. The retrospective nature of our cohort study introduces potential biases, including selection bias and limitations inherent to the data sources used. The study's observational design precludes definitive conclusions about causality between Dapagliflozin use and improved outcomes. Additionally, the generalizability of our findings may be restricted by the specific patient population studied, which was primarily drawn from a single healthcare system. Our analysis did not account for all potential confounding variables, such as varying dosages of Dapagliflozin and adherence rates among participants. Further randomized controlled trials are necessary to validate our findings and explore the mechanistic pathways through which Dapagliflozin exerts its protective effects in heart failure patients with ICDs.

References

1. Verschure DO, van Eck-Smit BL, Somsen GA, Knol RJ, Verberne HJ. Cardiac sympathetic activity in chronic heart failure: cardiac (123)I-mIBG scintigraphy to improve patient selection for ICD implantation. *Neth Heart J* 24 (2016): 701-708.
2. Leyva F, Israel CW, Singh J. Declining risk of sudden cardiac death in heart failure: fact or myth?. *Circulation* 147 (2023): 759-767.
3. Poole JE, Johnson GW, Hellkamp AS, Anderson J, Callans DJ et al. Prognostic importance of defibrillator shocks in patients with heart failure. *N Engl J Med* 359 (2008): 1009-1177.
4. MacIntyre CJ, Sapp JN, Abdelwahab A. The Effect of Shock Burden on Heart Failure and Mortality. *CJC Open* 4 (2019): 161-167.
5. Fatima A, Rasool S, Devi S, Talha M, Waqar F, et al. Exploring the Cardiovascular Benefits of Sodium-Glucose Cotransporter-2 (SGLT2) Inhibitors: Expanding Horizons Beyond Diabetes Management. *Cureus* 15 (2023): 9.
6. McMurray JV, Solomon SD, Inzucchi SE, Køber L, Kosiborod MN, et al. Dapagliflozin in patients with heart failure and reduced ejection fraction. *N Engl J Med* 21 (2019): 1995-2008.
7. Cooper HA, Dries DL, Davis CE, Shen YL, Domanski MJ, et al. Diuretics and risk of arrhythmic death in patients with left ventricular dysfunction. *Circulation* 12 (1999): 1311-1315.
8. Solomon SD, McMurray JJV, Claggett B, de Boer RA, DeMets D, et al. Dapagliflozin in heart failure with mildly reduced or preserved ejection fraction. *N Engl J Med* 12 (2022): 1089-1098.
9. Fong MC, Feng AN, Yin WH, Tsao TP, Chang HY. Defibrillation therapies following sodium-glucose cotransporter 2 inhibitor treatment: A report of two cases. *Heart Rhythm Case Rep* 7 (2021): 338-342.
10. Scheen AJ. Reappraisal of the diuretic effect of empagliflozin in the EMPA-REG OUTCOME trial: comparison with classic diuretics. *Diabetes Metab* 42 (2016): 224-233.
11. Davidenko JM, Cohen L, Goodrow R, Antzelevitch C. Quinidine-induced action potential prolongation, early afterdepolarizations, and triggered activity in canine Purkinje fibers. Effects of stimulation rate, potassium, and magnesium. *Circulation* 79 (1989): 674-686.
12. Ring A, Brand T, Macha S, Groegler KB, Simons G et al. The sodium glucose cotransporter 2 inhibitor empagliflozin does not prolong QT interval in a thorough QT (TQT) study. *Cardiovasc Diabetol* 12 (2013): 70.
13. Morote RM, Mayol L, Fernández MJG, Chirivella AM, Ballester CP, et al. 4CPS-164 Adequacy review in the use of dapagliflozin for the treatment of heart failure. *European Journal of Hospital Pharmacy* (2023).
14. Ali AE, Mazroua AE, ElSaban M, Najam N, Kothari AD, et al. Effect of Dapagliflozin in Patients with Heart Failure: A Systematic Review and Meta-Analysis. *Glob Heart* 18 (2023): 45.

15. Gupta M, Rao S, Manek G, Fonarow GC, Ghosh RK. The role of dapagliflozin in the management of heart failure: an update on the emerging evidence. *Ther Clin Risk Manag* 17 (2021): 823-830.
16. Nassif ME, Windsor SL, Gosch K, Borlaug BA, Husain M, et al. Dapagliflozin improves heart failure symptoms and physical limitations across the full range of ejection fraction: pooled patient-level analysis from DEFINE-HF and PRESERVED-HF trials. *Circulation: Heart Fail* 16 (2023): e009837.
17. Alla VM, Anand K, Hundal M, Chen A, Karnam S, et al. Impact of moderate to severe renal impairment on mortality and appropriate shocks in patients with implantable cardioverter defibrillators. *Cardiol Res Pract* (2010).
18. Kiage JN, Latif Z, Craig MA, Mansour N, Khouzam RN, et al. Implantable cardioverter defibrillators and chronic kidney disease. *Curr Probl Cardiol* 46 (2021): 100639.
19. Hreybe H, Ezzeddine R, Bedi M, Barrington W, Bazaz R, et al. Renal insufficiency predicts the time to first appropriate defibrillator shock. *Am Heart J* 151 (2006): 852-856.
20. Seyis S, Kurmus O. The Importance of Inflammation Markers in Heart Failure Patients With Appropriate Or Inappropriate ICD Shock. *Cardiol Cardiovasc Med* 1 (2017): 224-229.
21. Biasucci LM, Giubilato G, Biondi-Zoccai G, Sanna T, Liuzzo G, et al. C reactive protein is associated with malignant ventricular arrhythmias in patients with ischaemia with implantable cardioverter-defibrillator. *Heart* 8 (2006): 1147-1148.