Original Article

Empagliflozin Effects on Supraventricular Arrhythmias in Heart Failure Patients With Implantable Cardioverter-Defibrillator

Majid Shohrati[1], PhD; Morteza Khodaparast[2], PhD; Mahdi Bagheri[1], PhD; Mohammad Tayyebi[3*], PhD

ABSTRACT

Background: Empagliflozin, a sodium-glucose cotransporter-2 inhibitor (SGLT2i), is a primary pharmacological therapy for chronic heart failure (CHF). Notably, it has demonstrated anti-arrhythmic properties in some experimental and human studies. This clinical trial aimed to evaluate the effect of empagliflozin on supraventricular arrhythmias in patients with CHF and an implantable cardioverter-defibrillator (ICD).

Methods: In a before-and-after clinical trial conducted in Tehran, Iran, 62 patients were administered empagliflozin 10 mg/d for 12 weeks. The frequency and proportion of supraventricular arrhythmias, including atrial fibrillation (AF), atrial flutter (AFL), and inappropriate ICD therapies during the 12-week treatment period were compared with the 12 weeks before enrollment. Hospitalizations due to CHF, blood glucose levels, lipid profiles, and vital signs were also assessed as secondary outcomes.

Results: Empagliflozin significantly reduced the frequency of supraventricular tachycardia and AF/AFL per hour ($P = 0.028$ and $P = 0.038$, respectively). However, the frequency of inappropriate therapies and the proportion of patients with supraventricular arrhythmias or inappropriate ICD therapies did not change significantly. Empagliflozin also reduced hospitalizations due to CHF ($P = 0.008$). Furthermore, fasting blood sugar, HbA1c, triglycerides, systolic blood pressure, diastolic blood pressure, heart rate, and high-density lipoprotein levels improved after 12 weeks ($P < 0.001$, $P < 0.003$, $P < 0.013$, $P < 0.001$, $P < 0.032$, $P < 0.009$, and $P < 0.008$, respectively).

Conclusions: Empagliflozin exhibits anti-arrhythmic properties for AF/AFL in individuals with CHF and an ICD. These anti-arrhythmic effects may be attributed to its positive impact on hyperglycemia, hypertension, dyslipidemia, and hospitalizations due to CHF. ***(Iranian Heart Journal 2025; 26(2): 66-76)***

KEYWORDS: Arrhythmia, Atrial fibrillation, Empagliflozin, Implantable cardioverter-defibrillator, SGLT2 inhibitor

[1] Department of Clinical Pharmacy, Faculty of Pharmacy, Baqiyatallah University of Medical Sciences, Tehran, IR Iran.
[2] Atherosclerosis Research Center, Clinical Sciences Institute, Baqiyatallah University of Medical Sciences, Tehran, IR Iran.
[3] Department of Cardiovascular Diseases, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, IR Iran.

***Corresponding Author:** Mohammad Tayyebi, PhD; Department of Cardiovascular Diseases, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, IR Iran.
Email: tayyebim@mums.ac.ir **Tel:** +989153032232

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Supraventricular arrhythmias, such as atrial flutter (AFL) and atrial fibrillation (AF), are associated with increased mortality and morbidity. [1] AF is one of the most significant arrhythmias and is characterized by an irregular and rapid rate of the atrial chambers, which can lead to blood coagulation in the heart, chronic heart failure (CHF), stroke, and myocardial infarction. [2] CHF may also predispose patients to develop AF. As a result, CHF and AF are often reciprocal and coexist. [3] A large proportion of CHF patients have implantable cardioverter-defibrillators (ICDs) to treat dangerous and potentially fatal cardiac arrhythmias. An ICD is an electrical device implanted under the skin, consisting of a small battery and wires directed into the heart chambers. It senses irregular heartbeats and delivers ICD therapies, such as anti-tachycardia pacing or electric shocks, when indicated. [4] It has been demonstrated that supraventricular arrhythmias may trigger inappropriate ICD shocks, making the treatment of AF and AFL in these patients critically important. [5]

The primary approach to managing AF involves rate control, rhythm control with antiarrhythmic medications, and coagulation prevention with anticoagulants. In medically intractable cases, catheter ablation and electrical isolation of the pulmonary vein are utilized. [6, 7] Nonetheless, both medical and surgical approaches fall short of being ideal in terms of efficacy, side effects, and patient compliance. Therefore, investigating new and effective treatment options is necessary. [8] Sodium-glucose cotransporter-2 inhibitors (SGLT2is), such as empagliflozin, ertugliflozin, dapagliflozin, and canagliflozin, were initially approved for treating type 2 diabetes mellitus. They work by blocking SGLT2 receptors in the proximal section of the nephrons, reducing the reabsorption of sodium and glucose. This action leads to natriuresis and glycosuria, thereby lowering plasma glucose levels. [9] Recently, gliflozins have been approved as first-line treatments for CHF patients, regardless of the presence of diabetes, as large clinical trials have demonstrated significant cardiovascular benefits, particularly in reducing hospitalizations due to CHF and cardiovascular mortality. [10, 11]

Recent experimental and clinical studies suggest the antiarrhythmic potential of SGLT2is against supraventricular arrhythmias, particularly AF. [12,13] Administering empagliflozin 3 days before coronary artery bypass grafting and during the first 3 postoperative days reduced the incidence of postoperative atrial fibrillation and ventricular arrhythmias (P = 0.09 and P = 0.02, respectively). [14] Two recent randomized controlled clinical trials in Japan and Iran demonstrated that empagliflozin significantly decreased the number of ventricular arrhythmias recorded by the ICD. [15,16] Nevertheless, no prospective clinical trial has evaluated the role of gliflozins in supraventricular arrhythmias as a pre-specified outcome.

For the first time, in this prospective clinical trial, we evaluated the impact of empagliflozin, an SGLT2i, on the frequency and proportion of supraventricular arrhythmias and inappropriate ICD interventions, including ATP and shock, in CHF patients with an ICD. Both diabetic and nondiabetic patients were enrolled. Additionally, the association of empagliflozin with improvements in arrhythmia risk factors, such as blood glucose, lipid profile, hypertension, and other vital signs, was assessed.

METHODS

Study Design

This prospective, before-and-after clinical trial was conducted from January 2024 through August 2024 in Tehran, Iran. Patients were recruited from individuals referred to the hospital clinic for routine ICD

setting checks and programming. The study was approved by the Research Ethics Committee of Baqiyatallah University of Medical Sciences (ethical approval number: IR.BMSU.BAQ.REC.1402.089) and registered with the Iranian Clinical Trials Registry (registration code: IRCT20240116060704N1).

Patient Selection

Inclusion Criteria:

Subjects were included based on the following criteria:

1. Provision of signed and informed written consent;
2. Adults aged ≥ 18;
3. Diagnosis of CHF based on clinical evaluation and echocardiography parameters; or
4. Implantation of an ICD at least 12 weeks prior to enrollment in the trial.

Exclusion Criteria:

Subjects were excluded if they met any of the following criteria:

1. Previous use of any form of gliflozins;
2. CHF classified as New York Heart Association (NYHA) functional class IV;
3. Renal impairment (creatinine clearance < 20 mL/min/1.73 m²);
4. Liver impairment (alanine aminotransferase or aspartate aminotransferase > 120 U/L);
5. Pregnancy or lactation;
6. Body mass index (BMI) < 18.5 kg/m²;
7. Occurrence of any of the following events within 12 weeks before or after starting the study:
    - Change in the dose or type of antiarrhythmic drug (eg, β-blockers, digoxin, mexiletine, amiodarone, or sotalol);
    - Catheter ablation for supraventricular arrhythmias.
    - Percutaneous coronary intervention or coronary artery bypass graft surgery; and
    - Development of coronary heart disease, ischemic or hemorrhagic stroke, or epilepsy;
8. Use of single-chamber ICDs or ICDs incapable of recording supraventricular arrhythmias;
9. Comorbidities such as infections, type 1 diabetes mellitus, primary or secondary Addison's disease, malnutrition, malignancy, or major surgery; or
10. Unwillingness or inability to continue participation in the trial.

Intervention group and measurements

The study group consisted of CHF patients with an ICD who used empagliflozin at home for 12 weeks. Initially, patient characteristics and vital signs were recorded. Subjects then underwent laboratory tests, including a complete blood count (CBC), electrolytes, plasma glucose, lipid profile, and hepatic, renal, and thyroid function tests, at a reference laboratory. Patients who met the inclusion and exclusion criteria were assessed for the history of the proportion and frequency of supraventricular arrhythmias, including AF and AFL, as well as inappropriate ICD therapies during the 12 weeks prior to enrollment. The need for hospitalization due to CHF over the past 12 weeks was also documented. Patients were then prescribed empagliflozin 10 mg/d tablets to be taken in the morning, with or without food, for 12 weeks, in addition to their standard CHF treatment regimen. After 12 weeks, patients' ICD data were re-evaluated for the proportion and frequency of supraventricular arrhythmias, hospitalizations due to CHF, blood glucose levels, lipid profiles, and vital signs.

Primary Outcomes:

The primary outcomes were the frequency and proportion of supraventricular arrhythmias, including AF and AFL, during the 12 weeks after treatment compared with

the 12 weeks prior. Inappropriate ICD interventions (ATP and shock) were also measured as primary outcomes.

Secondary Outcomes:

Secondary outcomes included fasting blood sugar (FBS), hemoglobin A1c (HbA1c), lipid profile (total cholesterol, low-density lipoprotein [LDL], high-density lipoprotein [HDL], and triglyceride [TG]), systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate (HR), and oxygen saturation (SaO_2). These parameters were measured at baseline and 12 weeks after treatment. Additionally, the need for hospitalization due to CHF during the 12 weeks before and after the intervention was evaluated as a secondary outcome (Fig. 1).

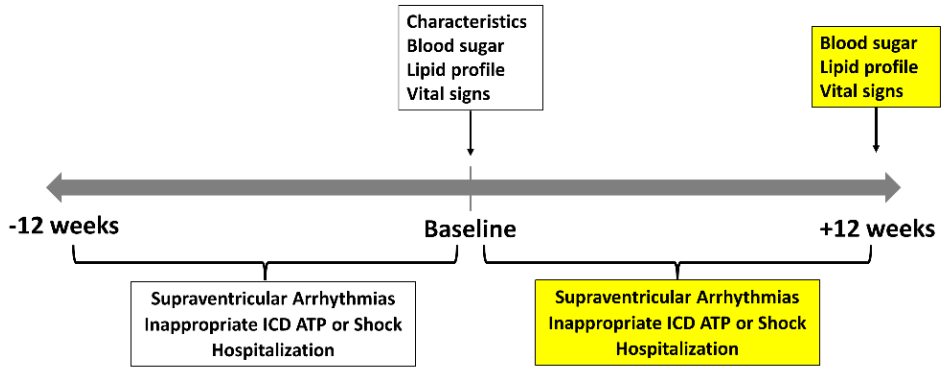

Figure 1. The image presents this study's outline.

Statistical Analysis

Based on previous ICD records of our patients, approximately 60% of the subjects experienced at least 1 episode of supraventricular arrhythmias within a 3-month period. Using the following formula, with a power of 90% and a type I error of 5%, the required sample size to detect at least a 30% reduction in the proportion of subjects with supraventricular tachycardia was calculated to be 59 patients. Accounting for an estimated 20% loss to follow-up, the adjusted sample size was increased to 70 subjects.

$$\varphi = \frac{\pi_A(1-\pi_B)}{\pi_B(1-\pi_A)}$$

$$\pi_{Discordant} = \pi_A(1-\pi_B) + \pi_B(1-\pi_A)$$

$$n_{pair} \geq \frac{\left(Z_{1-\alpha/2}(\varphi+1) + Z_{1-\beta}\sqrt{(\varphi+1)^2 - (\varphi-1)^2\pi_{Discordant}}\right)^2}{(\varphi-1)^2\pi_{Discordant}}$$

The data collected at the end of the study follow-up were initially described using measures of central tendency and dispersion. The Shapiro-Wilk test was used to assess the normality of quantitative variables. Qualitative data were reported as numbers (percentages), and quantitative data were expressed as mean ± standard deviation (SD). A paired *t*-test (or the Wilcoxon test for non-parametric variables) was employed to compare quantitative data before and after the intervention. Additionally, the McNemar test was employed to compare qualitative variables before and after the intervention. A significance level < 0.05 was used for all analyses. All statistical analyses were performed using SPSS, version 26.

RESULTS

Patients' baseline characteristics

Ninety-three patients were evaluated for the study. Of these, 69 patients met the eligibility criteria. Seven subjects were lost to follow-up, resulting in a total of 62 patients who completed the study. The mean

age was 60.77 ± 11.30 years, and 82.3% of the participants were male. Additionally, 27.4% of the patients had type 2 diabetes mellitus. Other baseline characteristics, including job status, education level, laboratory data, medication history, social history, and past medical history, are presented in Table 1.

Table 1. Patients' baseline demographic characteristics

Variables	Total Population (N=62)	Variables	Total Population (N=62)
Appearance		*Medication History*	
Age, y	60.77±11.30	Antiplatelet	44 (70.9%)
Male sex	51 (82.3%)	Anticoagulant	16 (25.8%)
BMI, kg/m^2	26.01±4.65	Statin	37 (59.6%)
Job Status		ACEi	24 (38.7%)
Retired	31 (50.0%)	ARB	21 (33.8%)
Housewife	13 (21.0%)	ARNI	2 (3.2%)
Employee	3 (4.8%)	β-blocker	52 (83.8%)
Self-employed	15 (24.2%)	MRA	45 (72.5%)
Educational Level		HCTZ	3 (4.8%)
Uneducated	8 (12.9%)	Furosemide	28 (45.1%)
Under diploma	25 (40.3%)	CCB	3 (4.8%)
Diploma	20 (32.3%)	Nitrate	22 (35.4%)
Associate Degree	3 (4.8%)	Digoxin	6 (9.6%)
Bachelor's	4 (6.5%)	Sotalol	1 (1.6%)
Master's	2 (3.2%)	Amiodarone	14 (22.5%)
Doctorate	0 (0.0%)	Mexiletine	3 (4.8%)
Laboratory Data		*Social history*	
WBC, 103/µL	7.60±2.11	Smoking or Tobacco	10 (16.1%)
Neutrophil, %	57.12±11.82	Alcohol	3 (4.8%)
Hemoglobin, g/dL	14.16±1.73	Opioid	9 (14.5%)
MCV, fL	87.87±5.45	*Past medical history*	
MCH, pg	29.12±2.47	DM2	17 (27.4%)
Platelet, 103/µL	207.51±56.37	Hypertension	35 (56.5%)
AST, U/L	25.30±11.54	IHD	42 (67.7%)
ALT, U/L	25.56±16.26	PCI	17 (27.4%)
Urea, mg/dL	35.55±14.06	CABG	15 (24.2%)
Creatinine, mg/dL	1.16±0.22	DCM	8 (12.9%)
Sodium, mEq/dL	138.72±3.08	HF-function class I	17 (27.4%)
Potassium, mEq/dL	4.29±0.41	HF-function class II	30 (48.4%)
Calcium, mg/dL	9.24±0.48	HF-function class III	15 (24.2%)
TSH, µU/mL	2.59±2.14	LVEF (%)	24.42±7.51

ACEi: angiotensin-converting enzyme inhibitor, ALT: alanine aminotransferase, ARB: angiotensin receptor blocker, ARNI: angiotensin receptor/neprilysin inhibitor, AST: aspartate aminotransferase, BMI: body mass index, CABG: coronary artery bypass graft, CCB: calcium channel blocker, DCM: dilated cardiomyopathy, DM2: type 2 diabetes mellitus, HCTZ: hydrochlorothiazide, HF: heart failure, IHD: ischemic heart disease, LVEF: left ventricular ejection fraction, MCH: mean corpuscular hemoglobin; MCV: mean corpuscular volume, MRA: mineralocorticoid receptor antagonist, PCI: percutaneous coronary intervention, TG: triglyceride, TSH: thyroid stimulating hormone, WBC: white blood cell

Table 2 provides information on ICD type, indication, and settings. Additionally, it displays zone rates among individuals categorized as primary prevention without prior VT/VF, primary prevention with prior VT/VF, and secondary prevention.

Table 2. ICD information

Variables	Total Population (N=62)
ICD-type	
Dual chamber	42 (67.7%)
Triple chamber	20 (32.3%)
ICD-indication	

Ischemic cardiomyopathy	42 (67.7%)
Non-ischemic cardiomyopathy	20 (32.3%)
ICD-setting	
Primary prevention without prior VT/VF	20 (32.3%)
VT1 zone rate, bpm	146.88±7.10
VT2 zone rate, bpm	181.84±4.43
VF zone rate, bpm	205.20±12.25
Primary prevention with prior VT/VF	11 (17.7%)
VT1 zone rate, bpm	147.63±10.40
VT2 zone rate, bpm	177.50±11.55
VF zone rate, bpm	205.09±13.18
Secondary prevention	31 (50.0%)
VT1 zone rate, bpm	139.51±9.57
VT2 zone rate, bpm	165.72±14.31
VF zone rate, bpm	204.70±9.01

ICD: implantable cardioverter-defibrillator, VF: ventricular fibrillation, VT: ventricular tachycardia

Comparison of supraventricular arrhythmias and inappropriate ICD intervention frequencies and proportions before and after treatment

After 12 weeks of treatment with empagliflozin, the frequency of supraventricular tachycardia per hour and AF/AFL per hour significantly decreased (P = 0.028 and P = 0.038, respectively). Inappropriate ICD therapies (ATP/shock) also decreased, but the difference was not statistically significant (P = 0.141). These findings are presented in Table 3.

After 12 weeks of treatment with empagliflozin, the proportions of patients with at least 1 episode of supraventricular tachycardia, AF/AFL, and inappropriate ICD therapies (ATP/shock) were 8.10%, 6.4%, and 3.3% lower, respectively. However, these differences were not statistically significant (P = 0.180, P = 0.219, and P = 0.687, respectively). The results are presented in Figure 2.

Comparison of hospitalization due to HF between the 2 groups

As shown in Table 4, after 12 weeks of treatment with empagliflozin, hospitalization due to CHF was significantly reduced (P = 0.008).

Comparison of blood glucose, lipid profile, and vital signs between the 2 groups

After 12 weeks of treatment with empagliflozin, FBS, HbA1c, TG, SBP, DBP, and HR significantly decreased (P < P < 0.001, P < 0.003, P < 0.013, P < 0.001, P < 0.032, and P < 0.009, respectively). Conversely, HDL levels significantly increased (P = 0.008). The effects on total cholesterol, LDL, and SaO_2 were not statistically significant (P = 0.897, P = 0.452, and P = 0.494, respectively). These results are presented in Table 5.

Table 3. Frequencies of supraventricular arrhythmias and ICD therapies before and after treatment

Parameters	12 Weeks Before Initiation (N=62)	12 Weeks After Initiation (N=62)	*P*
Supraventricular tachycardia per hour	121.68±566.35	99.49±498.60	0.028#
AF/AFL per hour	119.85±566.70	98.59±498.77	0.038#
Inappropriate ICD ATP/shock	1.09±5.82	0.06±0.30	0.141#

Wilcoxon test
ATP: anti-tachycardia pacing, ICD: implantable cardioverter-defibrillator

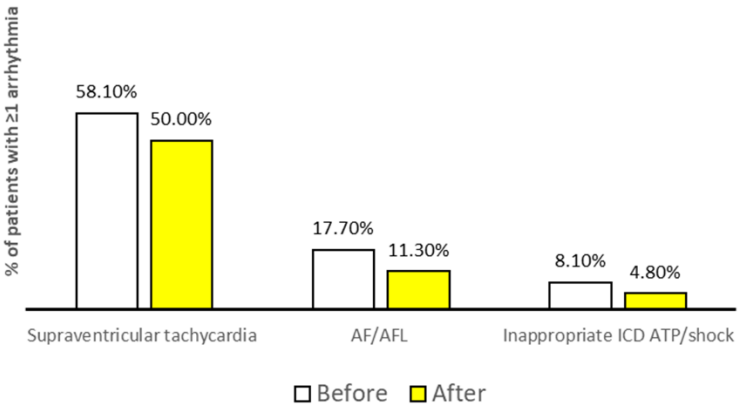

Figure 2. The image presents the proportions of supraventricular arrhythmias and inappropriate ICD interventions before and after treatment.

ICD: implantable cardioverter-defibrillator

Table 4. Hospitalization due to heart failure before and after treatment

Parameter	12 weeks Before Initiation (N=62)	12 Weeks After Initiation (N=62)	*P*
Hospitalization	0.27±0.54	0.11±0.31	0.008#

Wilcoxon test

Table 5. Blood sugar, lipid profile, and vital signs at baseline and 3 months after intervention

Parameters	Baseline (N=62)	12 Weeks After Initiation (N=62)	*P*
FBS, mg/dL	124.37±62.33	113.44±51.10	<0.001#
HbA1C, %	6.30±2.25	6.04±1.88	0.003#
Total cholesterol, mg/dL	164.98±39.90	161.03±39.19	0.897#
LDL, mg/dL	90.07±29.64	92.13±28.99	0.452†
HDL, mg/dL	41.59±8.73	43.77±9.52	0.008†
TG, mg/dL	144.92±78.78	131.21±64.66	0.013#
SBP, mm Hg	133.41±20.22	124.80±17.05	<0.001†
DBP, mm Hg	78.22±10.84	75.22±11.62	0.032†
HR, bpm	76.75±12.99	74.41±14.34	0.009#
SaO_2 (%)	94.50±2.36	94.67±2.67	0.494#

Wilcoxon test
† Paired *t*-test
DBP: diastolic blood pressure, FBS: fasting blood sugar, HbA1C: hemoglobin A1c, HDL: high-density lipoprotein, HR: heart rate, LDL: low-density lipoprotein; SaO_2: O_2 saturation, SBP: systolic blood pressure, TG: triglyceride

Subgroup analysis of individuals using antiarrhythmic medications

A subgroup analysis of 22 patients who were taking at least 1 antiarrhythmic medication (amiodarone, sotalol, mexiletine, or digoxin) showed that the frequency of supraventricular tachycardia and AF/AFL per hour tended to decrease (P = 0.052 and P = 0.068, respectively). Further, the proportion of patients with supraventricular tachycardia decreased from 63.6% (14 patients) to 40.9% (9 patients), although the difference was not statistically significant (P = 0.063). In contrast, a subgroup analysis of 40 patients who were not taking any antiarrhythmic medications showed no

significant effects on the frequency or proportions of supraventricular arrhythmias or inappropriate ICD therapies.

DISCUSSION

In this clinical trial, we evaluated the effect of empagliflozin, an SGLT2i, on supraventricular arrhythmias and inappropriate ICD therapies (ATP and shock) in CHF patients. Empagliflozin significantly reduced the frequency of supraventricular tachycardia and AF/AFL per hour (P = 0.028 and P = 0.038, respectively). Nonetheless, the frequency of inappropriate ATP/shocks and the proportion of patients with supraventricular arrhythmias or inappropriate ICD therapies did not change significantly.

A subgroup analysis of patients using antiarrhythmic medications revealed that only those already on antiarrhythmic medications tended to have a lower frequency of supraventricular tachycardia and AF/AFL per hour (P = 0.052 and P = 0.068, respectively). In addition, the proportion of patients with supraventricular tachycardia tended to be lower in this subgroup (P = 0.063). This may be because individuals not on antiarrhythmic medications had fewer or no supraventricular arrhythmias and inappropriate ICD therapies at baseline, making the antiarrhythmic effects of empagliflozin less apparent in this subgroup.

Gliflozins were initially developed for treating type 2 diabetes mellitus. Subsequently, large human trials evaluating cardiovascular safety demonstrated their cardiorenal protective effects, including reductions in morbidity, hospitalization, and mortality due to CHF. Interestingly, SGLT2is are now repurposed for use in individuals with or without diabetes who have CHF. [10, 11]

In our study, the use of empagliflozin for 12 weeks reduced hospitalizations due to CHF (P = 0.008). Furthermore, recent data from experimental studies, observational studies, and post-hoc analyses of randomized controlled trials suggest significant beneficial effects of SGLT2is on supraventricular arrhythmias. A recent study revealed that scaled-dose dapagliflozin directly blocks peak sodium currents, thereby reducing the excitability of atrial cardiomyocytes isolated from patients undergoing open-heart surgery. [17] An observational analysis from a global health research network revealed that ischemic stroke and mortality rates were lower in patients receiving SGLT2is after 3 years of follow-up. [18] Another observational study from the National Taiwan University historical cohort demonstrated that SGLT2i users had a 20% lower risk of stroke after 5 years of follow-up. [19] A randomized controlled trial involving 17,160 subjects with type 2 diabetes mellitus who had or were at risk of atherosclerotic cardiovascular events showed that dapagliflozin reduced the risk of AF and AFL by 19% over a 4.2-year follow-up period. [20] Additionally, a recent meta-analysis of 6 randomized controlled trials, including 9467 CHF patients, demonstrated that SGLT2i use was associated with a significant reduction in the risk of AF (relative risk [RR] 0.62, 95% confidence interval [CI] 0.44 to 0.86; P = 0.005) and AF/AFL (RR 0.64, 95% CI 0.47 to 0.87; P = 0.004). [21] Currently, an updated secondary analysis of more than 80,000 patients from 33 placebo-controlled randomized clinical trials demonstrated that SGLT2is were associated with a lower risk of AF and AF/AFL (risk ratio: 0.88, 95% CI 0.78 to 1.00; P = 0.04 and risk ratio: 0.86, 95% CI 0.77 to 0.96; P = 0.01, respectively).[22]

The exact mechanism underlying the antiarrhythmic effects of gliflozins remains unclear, but these drugs appear to favorably

influence pathophysiologic mechanisms involved in supraventricular arrhythmias. [13] Experimental studies suggest that gliflozins directly reduce oxidative stress, inflammation, fibrosis, and electrophysiological remodeling, thereby improving endothelial function, cellular metabolism, and homeostasis in the myocardium and circulation. [12]

Gliflozins inhibit inflammation and electrical remodeling by modulating the Na+/H+ exchanger and late sodium current channels, regulating adenosine triphosphate, ryanodine receptor 2 phosphorylation, Ca2+/calmodulin-dependent protein kinase type-II activity, and inhibiting nucleotide-binding oligomerization domain-like receptor 3 (NLRP3). Gliflozins also reduce cardiac load and inhibit sympathetic tone, improving cardiac autonomic imbalance. [23,24] Additionally, SGLT2is can improve high blood glucose, hypertension, and dyslipidemia, which are recognized risk factors for arrhythmias. [25-27]

In our study, FBS, HbA1c, TG, SBP, DBP, and HR were significantly lower after 12 weeks ($P < 0.001$, $P < 0.003$, $P < 0.013$, $P < 0.001$, $P < 0.032$, and $P < 0.009$, respectively), while HDL was significantly higher ($P = 0.008$). These findings align with the known pharmacological effects of empagliflozin. [28, 29] Thus, the control of these risk factors with SGLT2is may have contributed to the positive effects of empagliflozin in reducing the frequency of supraventricular tachycardia and AF/AFL episodes.

In this study, for the first time, the impact of empagliflozin, an SGLT2i, on supraventricular arrhythmias in CHF patients with an ICD was prospectively evaluated and pre-specified. Both diabetic and non-diabetic patients were included. The ICD's capability for remote telemonitoring of supraventricular tachycardia, AF/AFL episodes, and inappropriate ICD therapies allowed for precise documentation of the antiarrhythmic effects of gliflozins.

However, our study has several limitations. First, it was not a placebo-controlled trial. Since eligible patients had CHF and gliflozins are now considered first-line treatment for CHF, it was not ethical to deprive this group of standard care. Second, many eligible patients had already started gliflozins for CHF or diabetes at the time of enrollment, making them ineligible for inclusion. This limited the number of patients who could be enrolled in the study. Third, the follow-up duration for this trial was only 12 weeks, whereas a longer period may be necessary to fully reveal the benefits of SGLT2is on supraventricular arrhythmias. According to a recent meta-analysis, the effects of SGLT2is on AF/AFL are more pronounced in follow-ups exceeding one year. [22]

In conclusion, future studies with a larger sample size, longer follow-up duration, and a randomized controlled trial design in patients with ICDs but without CHF are warranted to more comprehensively compare the antiarrhythmic effects of gliflozins against a placebo.

CONCLUSIONS

Empagliflozin reduces the frequency of supraventricular tachycardia and AF/AFL episodes in CHF patients with an ICD after 12 weeks. It also improves high blood glucose, hypertension, and dyslipidemia while reducing hospitalizations due to CHF in these patients. Thus, the positive effects on supraventricular arrhythmias may be attributed to these beneficial outcomes. Further clinical trials with larger sample sizes and long-term follow-up are needed to evaluate and fully determine the potential benefits of gliflozins.

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Conflict of Interest: The authors report no conflicts of interest.

Ethical Approval: The study protocol was approved by the local Ethics Committee of Baqiyatallah University of Medical Sciences (reference number: IR.BMSU.BAQ.REC.1402.089) and registered on the Iranian Registry of Clinical Trials as IRCT20240116060704N1 (approval date: 2024-01-22). All participants were informed about the study protocol and provided written consent.

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