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Sodium-Glucose Cotransporter 2 Inhibitors Significantly Lower the Cardiac Electrophysiological Balance Index in Type 2 Diabetes Patients

Tip 2 Diyabet Hastalarında SGLT2 İnhibitörlerinin Kardiyak Elektrofizyolojik Denge İndeksi Üzerine Etkileri

ABSTRACT

Objective: Sodium-glucose cotransporter 2 (SGLT2) inhibitors, a novel group of oral antidiabetic drugs, have demonstrated cardioprotective benefits and positive metabolic effects in patients with diabetes mellitus (DM). The cardiac electrophysiological balance index (ICEB) is an eletrocardiographic ratio that provides information about the equilibrium between left ventricular depolarization and repolarization duration, offering valuable insights into the predisposition to ventricular arrhythmias. The aim of this study is to analyze the potential impact of SGLT2 inhibitors on ICEB.

Method: Patients were prospectively selected from a pool of 2,789 consecutive type 2 DM patients. After exclusions, 174 patients formed the monotherapy group, and 143 age- and sex-matched patients who were switched to SGLT2 inhibitor combination therapy constituted the combination therapy group. All treatment changes were supervised by endocrinologists blinded to the patient groups. Baseline and six-month electrocardiogram (ECG) data of both groups were analyzed. ICEB was defined as QT/QRS, and ICEBc as QTc/QRS.

Results: Although there was no statistically significant difference between the monotherapy and combination therapy groups in terms of baseline ECG parameters, QT (385.05 ± 13.21 vs. 372.32 ± 4.32; P < 0.001), QTc (409.24 ± 8.17 vs. 383.72 ± 7.24; P < 0.001), ICEB (4.15 ± 0.51 vs. 4.03 ± 0.54; P = 0.004), and ICEBc (4.40 ± 0.75 vs. 4.16 ± 0.61; P < 0.0001) values at the six-month mark were significantly lower in the SGLT2 inhibitor group.

Conclusion: SGLT2 inhibitors significantly lower ICEB and ICEBc, potentially reducing ventricular susceptibility to arrhythmias as early as six months into treatment for diabetic patients.

Keywords: Arrhythmia, diabetes mellitus, index of cardiac electrophysiological balance sodium-glucose cotransporter 2

ÖZET

Amaç: Sodyum-glukoz kotransporter 2 (SGLT2) inhibitörleri, yeni bir oral antidiyabetik ilaç grubu olup diyabetes mellitus (DM) hastalarında kardiyoprotektif yararlar ve olumlu metabolik etkiler göstermiştir. Kardiyak elektrofizyolojik denge indeksi (ICEB), sol ventrikül depolarizasyonu ve repolarizasyonu süreleri arasındaki denge hakkında bilgi sağlayan ve ventriküler aritmi yatkınlığına dair değerli ipuçları sunan bir elektrokardiyografik orandır. Bu çalışmanın amacı, SGLT2 inhibitörlerinin ICEB üzerindeki potansiyel etkisini analiz etmektir.

Yöntem: Hastalar, 2.789 ardışık tip 2 DM hastası arasından prospektif olarak seçildi. Dışlamalar sonrasında 174 hasta monoterapi grubunu, 143 yaş ve cinsiyet açısından eşleştirilmiş ve SGLT2 inhibitörü kombinasyon tedavisine geçirilen hasta ise kombinasyon tedavi grubunu oluşturdu. Tüm tedavi değişiklikleri, hasta gruplarından habersiz endokrinologlar tarafından denetlendi. Her iki grubun bazal ve altı aylık elektrokardiyogram (EKG) verileri analiz edildi. ICEB, QT/QRS ve ICEBc ise QTc/QRS olarak tanımlandı.

Bulgular: Monoterapi ve kombinasyon tedavisi grupları arasında bazal EKG parametreleri açısından istatistiksel olarak anlamlı bir fark bulunmamakla birlikte, altı aylık takipte QT (385,05 ± 13,21 vs. 372,32 ± 4,32; P < 0,001), QTc (409,24 ± 8,17 vs. 383,72 ± 7,24; P < 0,001), ICEB (4,15 ± 0,51 vs. 4,03 ± 0,54; P = 0,004) ve ICEBc (4,40 ± 0,75 vs. 4,16 ± 0,61; P < 0,0001) değerleri SGLT2 inhibitörü grubunda anlamlı derecede daha düşüktü.

Sonuç: SGLT2 inhibitörleri, ICEB ve ICEBc'yi anlamlı derecede düşürerek diyabetik hastalarda tedavinin altıncı ayından itibaren ventriküler aritmilere karşı duyarlılığı azaltabilir.

Anahtar Kelimeler: Aritmi, diyabetes mellitus, kardiyak elektrofizyolojik denge indeksi, sodyum-glukoz kotransporter 2

ORIGINAL ARTICLE
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Diabetes mellitus (DM) is one of the most common endocrine disorders worldwide. Due to DM-related oxidative stress, endothelial dysfunction, and vascular remodeling, there is a well-established relationship between DM and increased cardiovascular mortality and morbidity.[1] Furthermore, various studies have demonstrated that DM elevates susceptibility to ventricular arrhythmias through a range of underlying mechanisms.[2] Despite advancements in medicine and technology, sudden cardiac death (SCD) remains a major public health concern. While the exact cause cannot always be determined in SCD cases, a substantial portion is attributable to ventricular arrhythmias.[3] Early, simple, and effective detection of ventricular arrhythmias is therefore critical. Numerous noninvasive electrocardiographic (ECG) parameters can be utilized to predict ventricular arrhythmias. One such parameter is the Cardiac Electrophysiological Balance Index (ICEB), defined as the ratio of the QT interval to QRS duration (QT/QRS). ICEB provides valuable information about the equilibrium between the durations of ventricular depolarization and repolarization. ICEB is also regarded as the noninvasive equivalent of the cardiac wavelength,[3] which is invasively measured during electrophysiological studies and is strongly associated with the occurrence of ventricular arrhythmias.[4]

Sodium-glucose cotransporter 2 (SGLT2) inhibitors are a relatively new class of oral antidiabetic drugs that exert beneficial effects on both the heart and the vascular systems. The international EMPA-REG OUTCOME study (Empagliflozin Cardiovascular Outcome Event Trial in Type 2 Diabetes Mellitus Patients) revealed that, in patients with a history of cardiovascular diseases, the use of empagliflozin significantly reduces rates of hospitalization due to heart failure, cardiovascular mortality, and all-cause mortality.[5,6] Although the underlying mechanisms remain unclear, the most plausible explanations involve the direct effects of reduced inflammation on the heart,[7] decreased oxidative stress,[8] and improved ionic homeostasis.[9] SGLT2 inhibitors also have a positive impact on various types of arrhythmias. Duran et al.[10] demonstrated that SGLT2 inhibitors decrease ventricular repolarization indexes, which are predictive of ventricular arrhythmias. Moreover, a post hoc analysis of recently published DAPA-HF study (Dapagliflozin and Prevention of Adverse Outcomes in Heart Failure) data revealed that SGLT2 inhibitors significantly reduced the composite outcome of resuscitated cardiac arrest, life-threatening ventricular arrhythmia, or sudden cardiac death in patients with heart failure and reduced ejection fraction.[11]

While there are studies examining the effects of SGLT2 inhibitors on various ventricular arrhythmia predictors, no study to date has specifically evaluated their impact on ICEB. In the present study, we investigated the effects of SGLT2 inhibitors on ICEB.

ABBREVIATIONS

ANOVA	One-way analysis of variance
APD	Action potential duration
BUN	Blood urea nitrogen
CBC	Complete blood count
DAPA-HF study	Dapagliflozin and Prevention of Adverse Outcomes in Heart Failure
DM	Diabetes mellitus
ECG	Electrocardiogram
EMPA-REG OUTCOME study	Empagliflozin Cardiovascular Outcome Event Trial in Type 2 Diabetes Mellitus Patients
HbA1c	Glycated hemoglobin
HDL	High-density lipoprotein
HR	Heart rate
ICEB	Cardiac Electrophysiological Balance Index
LDL	Low-density lipoprotein
QT/QRS	Ratio of the QT interval to the QRS duration
SCD	Sudden cardiac death
SGLT2	Sodium-glucose cotransporter 2
TGs	Triglycerides

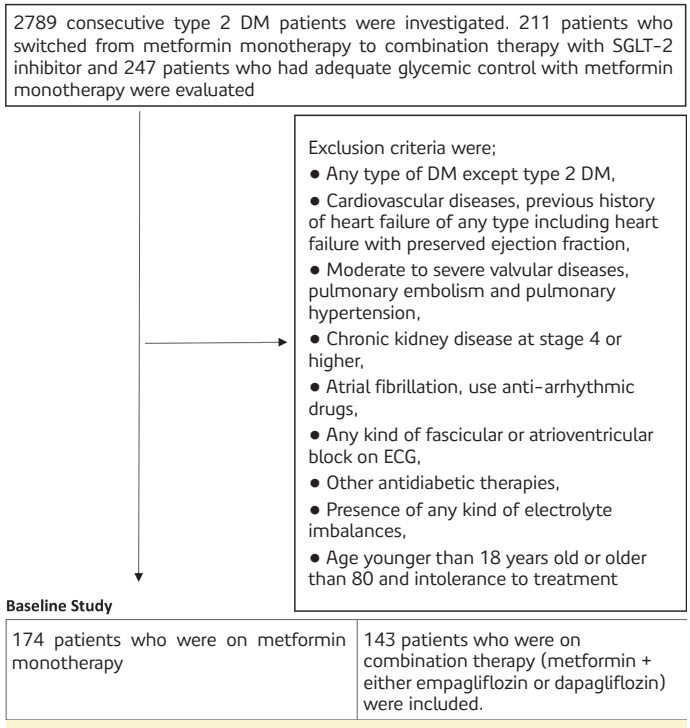

Figure 1. Flow chart of the study design.

DM, Diabetes Mellitus; SGLT-2, Sodium Glucose Cotransporter 2.

Materials and Methods

Study Population and Design

This was a prospectively designed cross-sectional investigation. A total of 2,789 consecutive type 2 DM patients were evaluated. Of these, 211 patients who switched from metformin monotherapy to combination therapy with an SGLT2 inhibitor and 247 patients who achieved adequate glycemic control with metformin monotherapy were included in the study. Endocrinologists, blinded to the study design, initiated and supervised all pharmacological therapies. Exclusion criteria included the presence of any type of DM except type 2 DM, cardiovascular diseases, previous history of heart failure of any type, including heart failure with preserved ejection fraction, moderate to severe valvular diseases, pulmonary embolism, pulmonary hypertension, chronic kidney disease at stage 4 or higher, atrial fibrillation, use of antiarrhythmic drugs, any type of fascicular or atrioventricular block on ECG, other antidiabetic therapies, presence of any electrolyte imbalances, age younger than 18 years or older than 80, and intolerance to

Table 1. Baseline Demographical, Clinical, Biochemical and ECG Data of Metformin Monotherapy and Combination Therapy Groups Before Switching to the Combination Therapy are Given

Variables	Monotherapy group (n = 174)	Combination therapy group (n = 143)	P
Demographical data			
Age (years)	42.25 ± 6.21	43.52 ± 5.83	0.125
Gender (male n/%)	85/48.85	68/47.55	0.693
BMI (kg/m^2)	27.11 ± 2.64	29.51 ± 4.37	0.032
Hyperlipidemia (n/%)	69/39.65	60/41.95	0.097
Smoking (n/%)	51/29.31	38/26.57	0.108
Family history (n/%)	49/28.16	38/26.57	**0.382**
Biochemical data			
Fasting blood glucose (mg/dl)	137.11 ± 23.32	141.65 ± 21.76	**0.042**
Total cholesterol (mg/dl)	184.63 ± 10.13	186.06 ± 8.65	0.359
LDL (mg/dl)	75.11 ± 8.93	77.23 ± 7.74	0.632
HDL (mg/dl)	44.26 ± 6.11	46.38 ± 7.95	0.716
Triglyceride (mg/dl)	165 (86-476)	163 (91-489)	0.564
BUN (mg/dl)	25.71 ± 2.54	24.98 ± 4.16	0.963
Creatinine (mg/dl)	0.77 (0.68-1.43)	0.78 (0.65-1.36)	0.153
Sodium (mEq/L)	135.29 ± 2.47	137.58 ± 2.38	0.871
Potasium (mEq/L)	4.41 ± 0.43	4.35 ± 0.42	0.295
AST (mg/dl)	21.54 ± 3.67	22.14 ± 4.21	0.643
ALT (mg/dl)	23 (7-45)	22 (7-51)	0.872
HBA1c (%)	6.58 ± 0.87	7.84 ± 0.72	<**0.001**
Hemoglobin (g/dl)	13.78 ± 1.52	13.67 ± 1.24	0.857
WBC (10^9/l)	8.8 (4.5-12.4)	7.5 (5.1-11.8)	0.193
PLT (10^9/l)	271.58 ± 17.35	279.69 ± 21.12	0.356

ECG, Electrocardiogram; BMI, Body Mass Index; LDL, Low-Density Lipoprotein; HDL, High-Density Lipoprotein; BUN, Blood Urea Nitrogen; AST, Aspartate Aminotransferase; ALT, Alanine Aminotransferase; WBC, White Blood Cell; PLT, Platelet; ICEB, The Index of Cardiac Electrophysiological Balance.

treatment. After applying these exclusion criteria, 174 patients on metformin monotherapy and 143 patients on combination therapy (metformin + either empagliflozin or dapagliflozin) were included in the study (Figure 1).

Study Protocol

Demographic and clinical data for all included patients were recorded. Standard 12-lead ECGs were performed for all patients before switching to combination therapy and six months after the treatment. Venous blood samples were drawn after overnight fasting to measure complete blood count (CBC), plasma glucose, glycated hemoglobin (HbA1c), blood urea nitrogen (BUN), creatinine, total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), triglycerides (TGs), sodium, and potassium levels. Informed consent was obtained from all patients included in the study. Ethics committee approval was obtained from Biruni University Non-Interventional Clinical Research Ethics Committee (Approval Number: 2024/86-70, Date: 24.01.2024), and conducted in accordance with the Declaration of Helsinki.

Electrocardiographic Analysis

All 12-lead ECGs were recorded in the supine position after 15 minutes of rest at room temperature, using a paper speed of 50 mm/s and calibration of 1 mV/10 mm with a BeneHeart R12 ECG machine (Schiller AT-102, Doral, Florida, USA). A minimum of 10 analyzable leads was considered acceptable; otherwise, the ECG was repeated. Cardiologists who were blinded to patient group assignment (monotherapy or combination therapy) analyzed the ECGs. The Bazett formula was used to adjust the QT interval for heart rate (HR). The QT interval, defined as the duration between the beginning of the Q wave and the conclusion of the T wave was calculated as follows: QTc = QT / (R-R) 1/2. ICEB was calculated as the ratio of the QT interval to the QRS duration (QT/QRS), and ICEBc was calculated as QTc/QRS. Each measurement was repeated three times and averaged.

Statistical Analysis

Statistical analyses were conducted using a commercially available software program (SPSS version 16.0, SPSS, Chicago, IL, USA). Continuous data were presented as mean ± standard deviation (SD), while categorical data were expressed as counts and percentages. The Kolmogorov-Smirnov test was used to assess the normality of data distribution. Cohen's Kappa test was used to evaluate the degree of agreement between the two cardiologists analyzing the ECG parameters. A Kappa coefficient (κ) < 0.40 was considered weak, 0.41-0.60 intermediate, 0.61-0.80 substantial, and > 0.80 near-complete agreement. Analysis of continuous variables was performed using either

Table 2. ECG Data of Metformin Monotherapy and Combination Therapy Groups are Given

Variables	Monotherapy group (n = 174)	Combination therapy group (n = 143)	P
ECG data of both groups before switching to the combination therapy			
QT (ms)	386.05 ± 15.54	385.13 ± 12.47	0.582
QTc (ms)	409.32 ± 10.43	408.27 ± 11.93	0.671
QRS (ms)	93.89 ± 3.48	93.09 ± 4.52	0.372
ICEB	4.15 ± 0.32	4.13 ± 0.62	0.267
ICEBc	4.35 ± 0.83	4.33 ± 0.38	0.769
ECG data of both groups after 6 month of combination therapy			
QT (ms)	385.05 ± 13.21	372.32 ± 4.32	<**0.001**
QTc (ms)	409.24 ± 8.17	383.72 ± 7.24	<**0.001**
QRS (ms)	92.83 ± 4.83	92.12 ± 3.46	0.793
ICEB	4.15 ± 0.51	4.03 ± 0.54	**0.004**
ICEBc	4.40 ± 0.75	4.16 ± 0.61	<**0.0001**

ECG, Electrocardiogram; ICEB, The Index of Cardiac Electrophysiological Balance.

Table 3. 6th Month ECG Data of 3 Groups are Given

Variables	Monotherapy group (n = 174)	Empag subgroup (n = 63) (metformin+empagliflozin)	Dapag subgroup (n = 80) (metformin+dapagliflozin)	P
QT (ms)	385.05 ± 13.21	373.54 ± 10.73	372.43 ± 3.89	**0.003***
QTc (ms)	409.24 ± 8.17	385.34 ± 9.83	383.02 ± 5.46	**0.003***
QRS (ms)	92.83 ± 4.83	92.91 ± 2.16	92.25 ± 2.60	0.813
ICEB	4.15 ± 0.51	4.03 ± 0.27	4.02 ± 0.45	**0.002***
ICEBc	4.40 ± 0.75	4.16 ± 0.37	4.15 ± 0.35	<**0.001***

*Empag subgroup vs. Dapag subgroup P = NS. ECG, Electrocardiogram, ICEB, The Index of Cardiac Electrophysiological Balance; NS, Non Significant.

the independent samples t-test or the Mann-Whitney U test. Analysis of categorical variables before switching to combination therapy and at the sixth month of treatment was conducted using the Chi-square test or Fisher's exact test. Dependent samples t-tests and Wilcoxon signed-rank tests were utilized for repeated measures of ECG parameters. Variations between continuous variables were examined using Friedman tests or one-way analysis of variance (ANOVA) with repeated measures. To evaluate the molecular impact of SGLT2 inhibitors on ECG parameters, Friedman tests or two-way ANOVA with repeated measures were employed. Post hoc analyses were conducted using dependent samples t-tests or Wilcoxon tests. A p value < 0.05 was considered statistically significant.

Results

A total of 317 patients participated in this study. Of these, 174 patients (91 female, 85 male) were in the metformin monotherapy group, and 143 patients (75 female, 68 male) were in the combination therapy group. Table 1 summarizes the clinical, demographic, and biochemical data of both groups before switching to combination therapy. No statistically significant differences were observed between the groups in terms of age, gender, mean metformin doses, biochemical parameters, or the incidence of hyperlipidemia, family history of atherosclerosis, hypertension, and smoking. However, fasting blood glucose (137.11 ± 23.32 vs. 141.65 ± 21.76; P = 0.042), body mass index (BMI) (27.11 ± 2.64 vs. 29.51 ± 4.37; P = 0.032), and HbA1c (6.58 ± 0.87 vs. 7.84 ± 0.72; P < 0.001) levels were significantly higher in the combination therapy group compared to the monotherapy group.

Comparison of Electrocardiographic Data

Two independent cardiologists, blinded to the patient data, analyzed the ECGs. There was near-complete concordance between the two cardiologists for QT, QTc, QRS, ICEB, and ICEBc measurements (QT: $\kappa = 0.92$, P < 0.0001; QTc: $\kappa = 0.90$, P < 0.0001; QRS: $\kappa = 0.94$, P < 0.0001; ICEB: $\kappa = 0.93$; ICEBc: $\kappa = 0.92$, P < 0.0001). Before switching to combination therapy, there were no significant differences between the groups in QT, QTc, QRS, ICEB, and ICEBc measurements.

At the six-month mark, while the statistical significance in fasting blood glucose levels between the groups disappeared (135.23 ± 18.27 vs. 137.12 ± 15.43; P = 0.089), the significant difference in BMI persisted (27.25 ± 2.45 vs. 29.48 ± 3.72; P = 0.038). The ECG data at the sixth month revealed significant reductions in QT (385.05 ± 13.21 vs. 372.32 ± 4.32; P < 0.001), QTc (409.24 ± 8.17 vs. 383.72 ± 7.24; P < 0.001), ICEB (4.15 ± 0.51 vs. 4.03 ± 0.54; P = 0.004), and ICEBc (4.40 ± 0.75 vs. 4.16 ± 0.61; P < 0.0001) in the combination therapy group compared to the monotherapy group (Table 2, Figure 2). To further assess the selective molecular effects of SGLT2 inhibitors on ECG parameters, patients were grouped based on the specific subtype of SGLT2 inhibitor used. Sixty-three patients formed the Empag subgroup (metformin + empagliflozin), and 80 patients formed

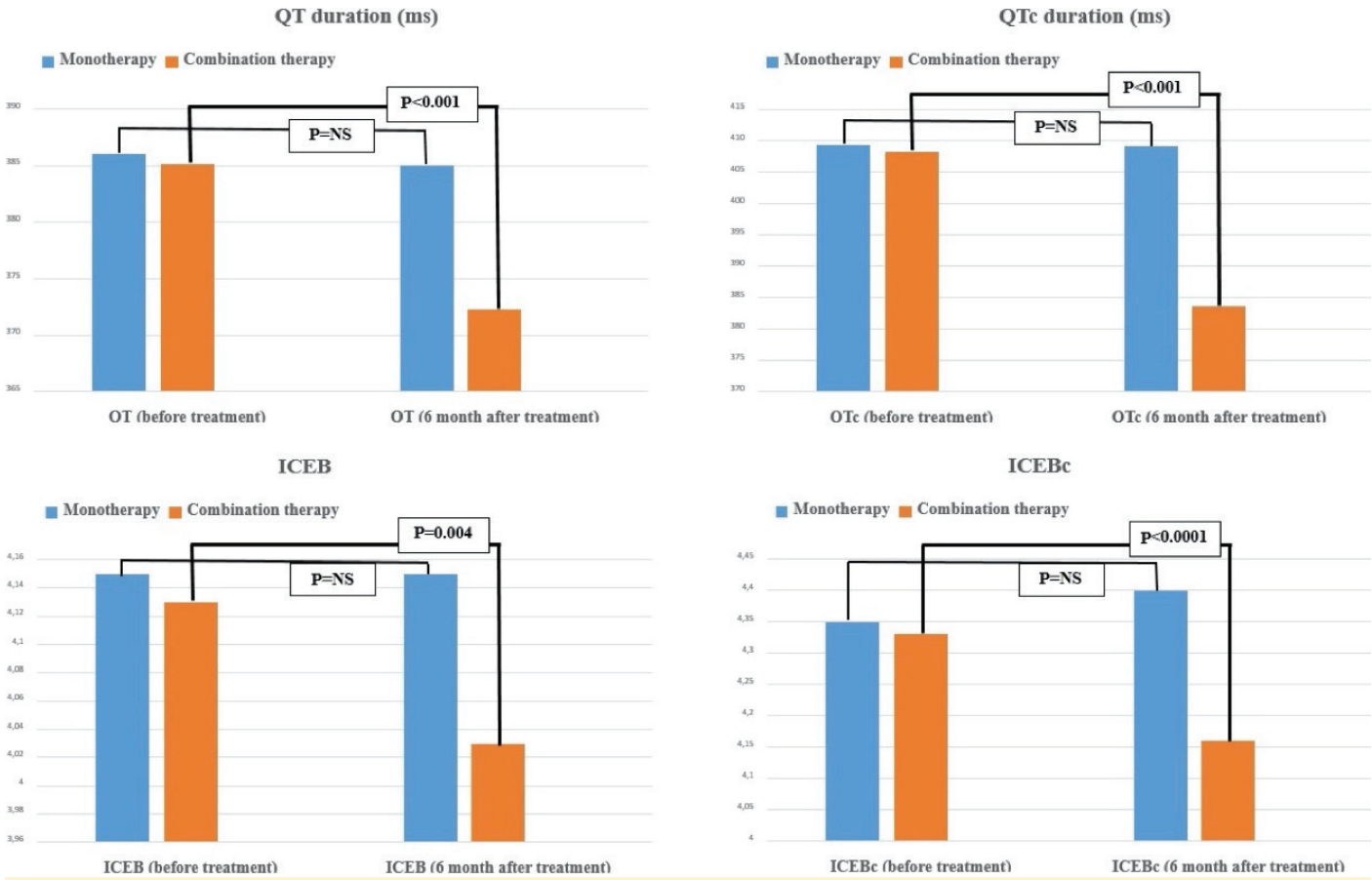

Figure 2. QT, QTc, index of cardiac electrophysiological balance (ICEB), and ICEBc values before switching to combination therapy and six months after combination therapy.

the Dapag subgroup (metformin + dapagliflozin). Significant decreases in QT, QTc, ICEB, and ICEBc values were observed at the sixth month compared to baseline in both subgroups where different SGLT2 inhibitors were used. However, no significant differences were detected between the SGLT2 inhibitor subtype groups. Detailed data for the Empag and Dapag subgroups are presented in Table 3.

Discussion

This study aimed to analyze the impact of adding SGLT2 inhibitors to metformin on the ICEB in patients with type 2 DM. The primary finding is that the addition of SGLT2 inhibitors to metformin monotherapy significantly reduces ICEB in type 2 DM patients after six months of combination therapy. Furthermore, the consistent effects observed between the Empag and Dapag subgroups suggest that these outcomes reflect a class effect of SGLT2 inhibitors rather than a molecule-specific effect.

The impaired glycemic control and prolonged hyperglycemia associated with DM exert deleterious effects on the cardiovascular system. This not only damages the vascular endothelium and contributes to atherosclerosis but also adversely affects various components of the conduction system, leading to arrhythmias associated with DM.[12] While the relationship between DM and cardiac rhythm disturbances is well-established, the precise mechanism underlying this association is not fully understood. Potential contributing factors include chronic inflammation, myocardial fibrosis, fluctuations in blood glucose levels, structural or electrophysiological remodeling of the heart, autonomic dysfunction, and alterations in mitochondrial enzymatic mechanisms.[13] Although many arrhythmias are not immediately life-threatening, prolonged rhythm disturbances can increase the risk of heart failure, cerebrovascular accidents, and cardiac arrest. The relationship between DM and atrial fibrillation has been extensively studied and well-established.[14-16]

Furthermore, due to similar underlying mechanisms, numerous studies provide evidence of an association between diabetes mellitus and ventricular arrhythmias.[17] It is well-recognized that myocardial electrical heterogeneity contributes to cardiac arrhythmias.[18] In addition to their favorable effects on cardiovascular mortality, studies have demonstrated the beneficial role of SGLT2 inhibitors in reducing cardiac rhythm disturbances. Sodium channels, which are highly expressed in cardiomyocytes, play a critical role in triggering the initial depolarization phase. Drugs that affect sodium channels can suppress fast inward sodium currents and stabilize membrane potential.[19] Hence, SGLT2 inhibitors are recommended for the potential prevention of ventricular arrhythmias.[20] Furthermore, Kusaka et al.[21] demonstrated that empagliflozin, the first clinically available member of SGLT2 inhibitors, significantly reduced interstitial fibrosis and macrophage infiltration in cardiomyocytes

while also decreasing the size of the cardiomyocytes. Reduction in cardiac fibrosis attenuates the pro-fibrotic signaling pathway, decreases glucocorticoid-regulated kinase-1 activity, and lowers epithelial sodium channel expression.[22] As a result, the electrical heterogeneity of the myocardium diminishes, stabilizing membrane action potentials and reducing cardiac arrhythmias.[21]

Previous studies have also highlighted the positive effects of SGLT2 inhibitors on various cardiac arrhythmia predictors. A recently published analysis of 68 trials, including data from 63,166 patients, revealed that SGLT2 inhibitors significantly reduced the incidence of SCD.[23] Notably, in the aforementioned trial, no significant difference in the incidence of ventricular arrhythmias was observed between the SGLT2 inhibitor group and the placebo group. However, it is worth mentioning that not all ventricular arrhythmias were reported, and the total number of recorded cases was very low (220 ventricular arrhythmia events in 49,963 patients, less than 1%).

The ICEB is a relatively new ECG parameter used to predict ventricular arrhythmias. It is considered the noninvasive counterpart of the cardiac wavelength and reflects the balance between total ventricular action potential duration (APD) and the ventricular repolarization phase. Under normal conditions, there is a close relationship between APD and the refractory period, allowing them to be used as proxies for each other. This close relationship between repolarization and recovery of excitability can be disrupted in various conditions affecting myocardial depolarization.[24] As a result, the ventricular myocardium becomes more susceptible to malignant ventricular arrhythmias.[25]

The effects of various conditions on ICEB have been explored in different studies, yielding contradictory results. In one study, Alsancak et al.[26] showed no significant correlation between ICEB and coronary collateral circulation in patients with chronic total occlusions. In another study, although Tp-e intervals, Tp-e/QT ratio, and ICEB values were higher in patients with coronary ectasia, ICEB values did not reach statistical significance.[27] Conversely, in a separate study, Alsancak et al.[28] demonstrated that ICEB significantly decreased after thrombolytic therapy in patients with acute pulmonary embolism. Despite these findings, there is limited evidence in the literature investigating the impact of SGLT-2 inhibitors on ICEB. In a previous study, Gökalp et al.[29] suggested that SGLT2 inhibitors significantly reduce ICEB in diabetic patients with heart failure with preserved ejection fraction. However, the present study is the first in the literature to demonstrate the favorable effects of SGLT2 inhibitors on ICEB in patients with diabetes mellitus who do not have any form of heart failure.

Study Limitations

Our study has several limitations that warrant consideration. Although we demonstrated a decrease in ICEB and discussed its close association with ventricular arrhythmias, due to financial constraints, we were unable to analyze ventricular arrhythmias in both groups using ambulatory rhythm monitoring. Second, this single-center trial included a limited number of patients. Studies with larger sample sizes could potentially yield more statistically significant results and additional insights. Finally, we relied on patients' medical records to exclude cardiovascular diseases. Due to ethical concerns, we did not perform coronary angiography.

Conclusion

SGLT2 inhibitors appear to improve ventricular susceptibility to arrhythmias by lowering ICEB in patients with type 2 DM. Furthermore, no significant differences in ICEB were observed between subtypes of SGLT2 inhibitors. This finding may suggest a class effect rather than a molecule-specific effect.

Ethics Committee Approval: Ethics committee approval was obtained from Biruni University Non-Interventional Clinical Research Ethics Committee (Approval Number: 2024/86-70, Date: 24.01.2024).

Informed Consent: Informed consent was obtained from all patients included in the study.

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