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Role of sodium glucose cotransporter-2 (SGLT2) inhibitors in the modulation of QTc interval and ventricular arrhythmia in patients with diabetes mellitus combined with hypertension and coronary artery disease

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Abstract: **Background**: Patients with diabetes mellitus combined with hypertension and coronary artery disease (DM-HTN-CAD) are prone to QTc interval prolongation and ventricular arrhythmia. Although sodium glucose cotransporter-2 (SGLT2) inhibitors have hypoglycemic and cardioprotective effects, their regulatory effects on relevant indicators in such patients still need to be clarified. **Objectives**: This study aimed to analyze the impact of SGLT2 inhibitor on QTc interval and ventricular arrhythmia in patients with DM-HTN-CAD. **Methods**: From January 2023 to January 2025, 150 patients with DM-HTN-CAD were selected in the Hospital. Patients were divided into conventional treatment and SGLT2 inhibitor groups depending on the treatment regimen. The SGLT2 inhibitors group received SGLT2 inhibitor treatment in addition to the conventional treatment group. Compression of the main indicators [including QTc interval, changes in echocardiographic parameters (left and right ventricular diameter, left and right atrial diameter and ejection fraction), blood pressure and glucose indicators] and secondary indicators (including quality of life score, incidence of complications and incidence of adverse reactions) before and after treatment was done among both groups. **Results**: No differences were observed in the basic characteristics between the two groups ($P>0.05$). After treatment, all parameters between the two groups illustrated a remarkable discrepancy compared with pre-treatment ($P<0.05$). In addition, patients in the SGLT2 inhibitors group exhibited lower QTc intervals, left and right atrial diameters, left and right ventricular diameters, systolic blood pressure, diastolic blood pressure and fasting blood glucose levels as compared to the conventional therapy group; The left ventricular ejection fractions, quality of life scores and overall clinical response rates were higher ($P<0.05$). The complications and adverse reaction incidences were lower in the SGLT2 inhibitors group compared to the conventional treatment group ($P<0.05$). **Conclusion**: SGLT2 inhibitors effectively shorten QTc interval, reduce ventricular arrhythmia and cardiovascular risks in DM-HTN-CAD patients and show favorable safety for clinical reference.

Keywords: Coronary artery disease; Diabetes; Hypertension; QTc interval; Sodium glucose cotransporter 2 inhibitor; Ventricular arrhythmia

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INTRODUCTION

Diabetes, hypertension and coronary artery disease, as being chronic diseases with high incidence in the world, are intertwined in the pathophysiological mechanism, forming the "cardiovascular metabolic triad", which has become the main driver of the global cardiovascular disease burden (Yen *et al.*, 2022). Diabetes is centred on persistent hyperglycaemia resulting from insufficient insulin secretion or insulin resistance. Long term metabolic disorder can lead to microvascular and macrovascular diseases, damage the integrity of vascular endothelium and accelerate the process of atherosclerosis (Lu *et al.*, 2024). Hypertension exacerbates cardiac afterload, induces left ventricular hypertrophy and myocardial remodeling and further damages the endothelial barrier of blood vessels, creating conditions for lipid deposition (Lussier *et al.*, 2024). Coronary artery disease, as the end stage of cardiac manifestation of atherosclerosis, primarily involves myocardial ischemia and hypoxia caused by coronary artery stenosis or occlusion and can lead to myocardial infarction and heart failure in severe cases (Tomii *et al.*, 2024).

Diabetes mellitus combined with hypertension and coronary artery disease (DM-HTN-CAD) presents insidious and complex clinical manifestations. In the early stage, they often show nonspecific fatigue, chest tightness and decreased activity tolerance. As the disease progresses, typical angina pectoris, nocturnal paroxysmal dyspnea, dizziness, headache and other symptoms may appear. Some patients even have sudden cardiac death as the first manifestation (Jyotsna *et al.*, 2023; Mir *et al.*, 2024). This type of patient is prone to physiological abnormalities such as QTc interval prolongation and ventricular arrhythmia due to multiple pathological factors, including myocardial

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metabolic disorders, ion homeostasis imbalance and myocardial remodeling (Lin *et al.*, 2017). The prolongation of QTc interval, as an important marker of abnormal myocardial repolarization, can increase the risk of malignant arrhythmias such as apical torsion ventricular tachycardia, while arrhythmias such as premature ventricular contractions and ventricular tachycardia further exacerbate myocardial ischemia, forming a vicious cycle of "arrhythmia myocardial ischemia" (Ye *et al.*, 2021). In addition, this type of patient is often accompanied by multiple organ complications such as renal dysfunction and peripheral vascular disease, which further worsen the prognosis and form a cross-system disease chain reaction (Wilk-Sledziewska *et al.*, 2025).

At present, the clinical treatment for patients with DM-HTN-CAD focuses on multi-target drug combination treatment, which mainly includes four methods: hypoglycemic, hypotensive, antiplatelet and lipid-lowering treatment (Piechocki *et al.*, 2024). Hypoglycemic treatment is based on metformin, combined with insulin or sulfonylurea drugs to control blood glucose levels. Some patients choose GLP-1 receptor agonists to balance blood glucose management and cardiovascular protection (Gebrie *et al.*, 2021). Blood pressure lowering therapy often uses ACEI/ARB drugs combined with calcium channel blockers or diuretics to reduce myocardial remodeling while lowering blood pressure (Chatzipieris *et al.*, 2025). Antiplatelet therapy mainly uses aspirin or clopidogrel to prevent coronary artery thrombosis (Solomon *et al.*, 2023). Lipid-lowering therapy centres on statins, aiming to reduce low-density lipoprotein cholesterol levels and delay progression of atherosclerosis (Pedro-Botet *et al.*, 2025). However, existing treatment plans still have significant limitations: firstly, although they can improve basic indicators such as blood glucose and blood pressure, their regulatory effect on myocardial electrophysiological abnormalities is limited and the control rate of QTc interval prolongation and ventricular arrhythmia is less than 40%; secondly, the combined use of multiple drugs increases the risk of drug interactions and some antiarrhythmic drugs may even prolong the QTc interval, leading to treatment contradictions; thirdly, for patients with poor blood sugar control, the improvement effect of traditional treatment plans on cardiovascular metabolic indicators is significantly weakened, making it difficult to meet the treatment needs of high-risk populations. In addition, existing treatments have not fully taken into account key aspects such as myocardial ion homeostasis regulation and mitochondrial function protection and cannot fundamentally block the mechanism of arrhythmia occurrence.

Sodium glucose cotransporter-2 (SGLT2) inhibitors, as novel oral hypoglycaemic agents, exert their blood glucose-lowering actions by specifically inhibiting glucose reabsorption in the proximal renal tubules and increasing urinary glucose excretion. Their unique cardiovascular protective effects have become a research focus (Natale *et al.*, 2024). Numerous clinical studies confirmed that SGLT2 inhibitors not only reduce weight and improve insulin resistance with no increased hypoglycaemia risk, but also exert cardiovascular protective effects through mechanisms independent of hypoglycemic effects, such as reducing hospitalization rates for heart failure, cardiovascular mortality risk and delaying the progression of chronic kidney disease (Janež and Fioretto, 2021). In recent years, further research has found that SGLT2 inhibitors can exert potential antiarrhythmic effects by regulating myocardial ion homeostasis, inhibiting myocardial fibrosis and reducing oxidative stress. For example, it is found that SGLT2 inhibitors can shorten the QTc interval and reduce the incidence of ventricular premature beats in patients with heart failure (Özen *et al.*, 2024). It is also found that SGLT2 inhibitors can reduce the risk of malignant arrhythmias in patients with coronary heart disease by improving myocardial energy metabolism (Jaiswal *et al.*, 2025). However, the current research on SGLT2 inhibitors mostly focuses on single disease or atrial fibrillation and other arrhythmia types. Direct evidence for QTc interval and ventricular arrhythmia populations with DM-HTN-CAD is still scarce.

Based on the above research background, the core hypothesis of this study is that in patients with DM-HTN-CAD, SGLT2 inhibitors can shorten QTc interval and reduce the incidence of ventricular arrhythmia by improving myocardial ion homeostasis and reducing myocardial remodeling. The expected outcome is that after treatment, the treatment group with SGLT2 inhibitors will remarkably shorten the QTc interval and reduce the incidence of ventricular arrhythmias compared to the conventional treatment group, especially in the subgroup with poor blood glucose control, with more significant benefits and good safety. The potential application value of the results of this study is significant, which can provide direct clinical evidence for SGLT2 inhibitors to regulate myocardial electrophysiology in high-risk patients and clarify their positioning in QTc interval and ventricular arrhythmia management. In addition, it can provide diabetes patients with multiple cardiovascular diseases who have poor blood glucose control with an optimized plan that breaks through the limitations of traditional treatment, provide new ideas for comprehensive prevention and management of cardiovascular diseases, promote the standardized application of SGLT2 inhibitors in high-risk cardiovascular populations and help reduce the risks of cardiac sudden death.

MATERIALS AND METHODS

Study design

This study is a retrospective clinical controlled experiment to explore the regulatory effect of SGLT2 inhibitors on QTc interval and ventricular arrhythmia in patients with DM-HTN-CAD. The study subjects were selected from patients

with DM-HTN-CAD who had seen a doctor in the Hospital from January 2023 to January 2025 and were divided into the conventional treatment group and the SGLT2 inhibitors group according to the clinical treatment regimen accepted by the patients. The conventional treatment group received basic treatment of reducing blood sugar, blood pressure, antiplatelet and lipid. The SGLT2 inhibitors group added SGLT2 inhibitors to the routine basic treatment regimen. The study retrospectively collected patient data that met the inclusion criteria through hospital electronic medical record systems, medical record management systems, etc. A total of 165 patient information were initially obtained. After screening according to predetermined exclusion criteria, 158 patients were included in the study queue. All included patients were followed up in a standardized manner and a total of 8 cases were lost to follow-up during the follow-up period. Finally, complete data collection and statistical analysis were completed for 150 patients. This study primarily aims to compare and analyse the clinical efficacy of 'conventional treatment + SGLT2 inhibitors' versus simplified conventional treatment in patients with the aforementioned comorbidities, thereby providing evidence based on medical practice for clinical assessment of arrhythmias in these patients. The patient selection and follow-up process is illustrated in fig. 1.

Inclusion and exclusion criteria

Inclusion criteria: (1) Conform to the diagnostic criteria for type 2 diabetes in the Guidelines for the Prevention and Treatment of Type 2 diabetes in China (Li *et al.*, 2023), as well as the diagnostic criteria for hypertension in the Guidelines for the Prevention and Treatment of Hypertension in China and the diagnostic criteria for coronary artery disease in the Guidelines for the Diagnosis and Treatment of Coronary Artery Disease (Bhatt *et al.*, 2022; Yin *et al.*, 2022); (2) Age range: 40-75 years old, gender not limited; (3) Have not used SGLT2 inhibitors drugs within the first 3 months of enrollment; (4) The patient has good compliance and can cooperate to complete a 6-month follow-up and various indicator tests; (5) There is no history of definite adverse drug reactions (such as severe gastrointestinal reactions, allergic reactions, muscle soreness, urinary and reproductive tract infections, etc.) due to the use of SGLT2 inhibitors within the first 3 months of enrollment; (6) Being able to clearly express one's own symptoms and cooperate in completing the quality of life rating scale.

Exclusion criteria: (1) Patients with type 1 diabetes, gestational diabetes or secondary diabetes; (2) Individuals allergic to SGLT2 inhibitors (dapagliflozin) or conventional therapeutic drugs (such as metformin, ACEI/ARB drugs); (3) Patients with severe heart failure, acute myocardial infarction, or malignant arrhythmia; (4) Patients with severe liver and kidney failure, end-stage renal disease, or requiring dialysis treatment; (5) Patients with combined malignant tumors, hematological diseases, autoimmune diseases, or active infections; (6) Patients who have participated in other clinical drug trials before enrollment; (7) Patients with severe cognitive impairment, mental illness, or inability to cooperate with follow-up; (8) Patients with a history of ketoacidosis or high-risk factors; (9) Patients who plan to interrupt treatment, relocate from the study area, or have a high expected follow-up loss rate due to personal reasons; (10) □ther clear diseases/conditions that may interfere with observation indicators or affect the safety of the study, as assessed by the physician, such as a history of severe gastrointestinal bleeding or drug abuse.

Ethical statement

This study was conducted in accordance with the Helsinki Declaration and ethical guidelines of the hospital and was approved by the hospital ethics committee.

Treatment measures

Both groups of patients received unified basic treatment: including diabetes, hypertension and coronary artery disease related health education (once a month for group education), personalized diet treatment (nutritionists develop daily calorie and nutrient distribution plans), exercise guidance (moderate intensity aerobic exercise, 150 minutes per week) and regular work and rest management (sleep 7-8 hours per day) (Llego and Bustillo, 2025).

The conventional treatment group was treated with conventional combination therapy on this basis: amlodipine tablets (Jiangsu Hengrui Pharmaceutical Co., Ltd., 5 mg × 7 tablets, national drug approval number H20203486) once a day, 5 mg each time. They were taken orally on an empty stomach in the morning. Metformin hydrochloride sustained-release tablets (Shandong Mingren Furuida Pharmaceutical Co., Ltd., 0.5 g × 30 tablets, National Medical Products Approval No. H20052118) were administered once daily, 1.0 g per dose, 30 minutes after dinner. Alternatively, the dosage could be adjusted to twice daily, 0.5 g per dose, 30 minutes after breakfast and dinner, based on patient tolerance, with the maximum daily dose not exceeding 2.0 g. Aspirin enteric coated tablets (Bayer Healthineers Co., Ltd., 100 mg × 30 tablets, National Medical Products Approval J20171021) should be taken once a day, 100 mg each time, orally after dinner. Rosuvastatin calcium tablets (AstraZeneca Pharmaceutical Co., Ltd., 10 mg × 7 tablets, National Medical Products Approval No. J20170008) should be taken orally once a day, 10 mg each time, before bedtime.

The SGLT2 inhibitors group received SGLT2 inhibitors: dapagliflozin tablets (Jiangsu Haosen Pharmaceutical Group Co., Ltd., 10 mg × 14 tablets, national drug approval number H20233761) in addition to the conventional treatment regimen, once a day, 10mg each time, orally taken 30 minutes after breakfast.

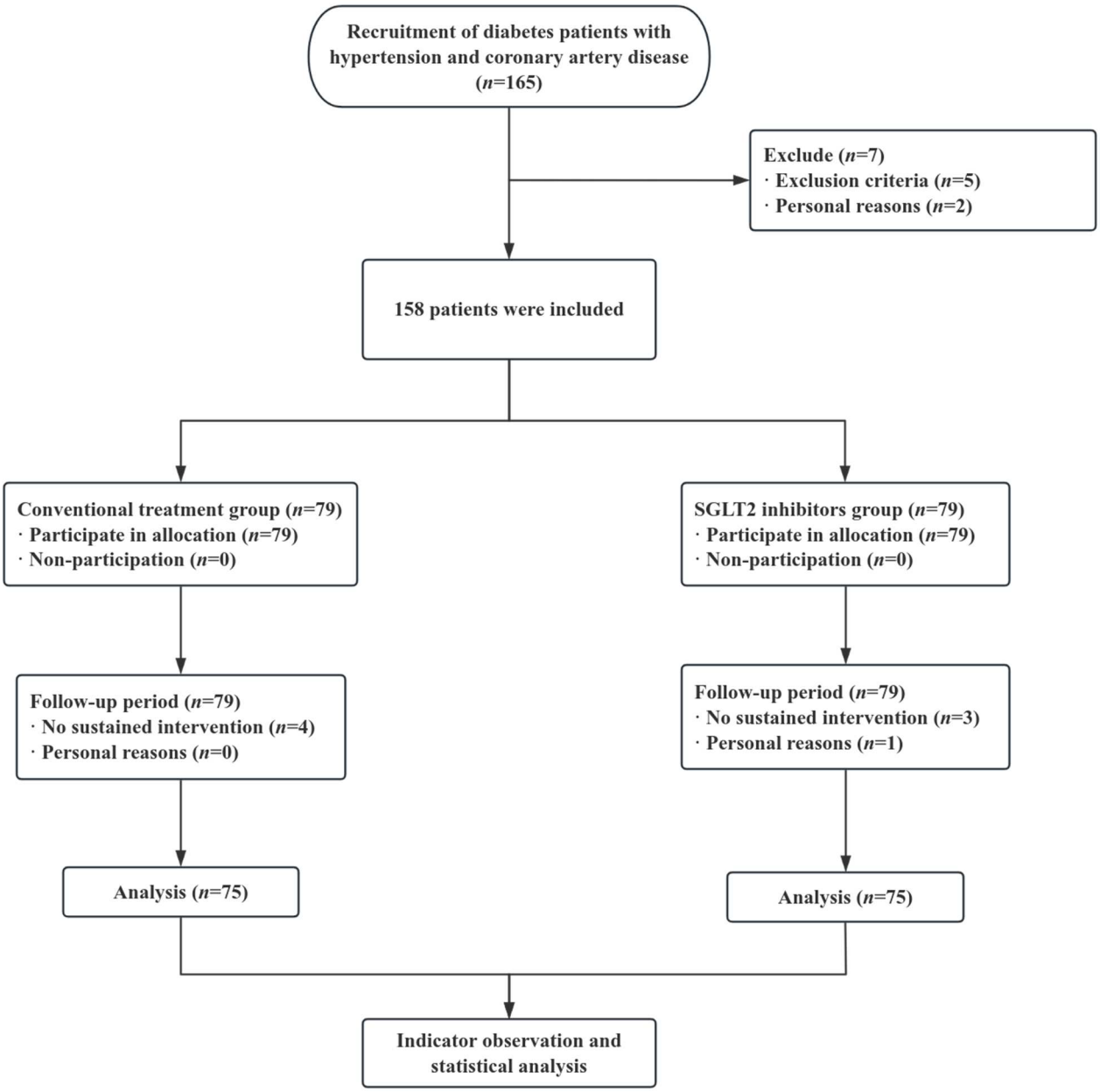

Fig. 1: Flow chart

Both groups received continuous treatment for 3 months, with monthly follow-up to monitor blood pressure, blood glucose and adverse reactions. The attending physician may follow a standardized stepwise adjustment plan based on monthly follow-up blood pressure (target < 130/80 mmHg) and blood glucose (target <7.0% glycated hemoglobin) control, with amlodipine starting at a dose of 5 mg/day. If blood pressure does not meet the standard for two consecutive follow-up visits, the maximum dose can be increased to 10 mg/day. Metformin is administered at a starting dose of 0.5 g/time and 3 times/day, gradually increasing when blood glucose levels are not met, with a maximum dose not exceeding 2.0 g/day. The dosage of other drugs remains stable throughout the entire process.

Observation indicators

Main indicators

QTc interval

QTc interval measurement should follow standardized procedures (Luzza *et al.*, 2023). Specifically, a 12 lead electrocardiogram machine (CM1200B, Shenzhen Koman Medical Equipment Co., Ltd., Guangdong Medical Equipment Approval 20192070677) that has been calibrated annually is used. All patients were asked to collect electrocardiograms on an empty stomach from 8:00 to 10:00 in the morning. Before measurement, patients were allowed to rest quietly for 5-10 minutes to eliminate interference factors such as exercise and emotions. The patient is placed in a supine position to maintain stable

breathing and electrocardiograms of at least 3-5 complete cardiac cycles are collected at a paper speed of 25 mm/s and a gain of 10 mm/mV. Use a vernier caliper to measure the QT interval: the starting point is the intersection of the QRS complex and the TP segment and the endpoint is the descending edge of the T wave (or at the moment of returning to baseline, excluding U wave interference). Measure continuously for three normal cardiac cycles and take the average value. The heart rate correction adopts the Bazett formula ($QTc=QT/RR^{0.5}$, both QT and RR are in seconds, RR=60/heart rate) and the Fridericia formula ($QTc=QT/RR^{0.33}$) is used when the heart rate is less than 60 beats per minute or greater than 100 beats per minute. The heart rate determination is based on the automatic measurement value of the electrocardiogram machine. If the difference between manual review and automatic measurement value is greater than 5 beats per minute, the average of 3 manual measurements shall be taken as the final heart rate. During measurement, abnormal cycles such as premature beats and conduction block should be excluded. If the QT interval difference measured for three consecutive cardiac cycles is greater than 20ms, an electrocardiogram should be re collected after a 5-minute interval. A total of three measurements should be taken and the median of the three measurements should be taken as the final QT interval value to ensure accuracy.

Changes in echocardiographic parameters

Using a color Doppler ultrasound diagnostic instrument (EPIQ7C, Philips Ultrasound Co., Ltd., USA) (C Gao *et al.*, 2021). The patient is placed in a left lateral position, breathing calmly and holding their breath while cooperating, using a 2.5-3.5 MHz phased array probe for exploration. Display the standard parasternal long axis view of the left ventricle and measure the left and right ventricular diameters, inner diameters and left ventricular ejection fraction using M-mode ultrasound technology. All measurements are taken as the average of three complete cardiac cycles to reduce errors.

Blood pressure and blood glucose indicators

The diastolic blood pressure, systolic blood pressure and fasting blood glucose indicators of both groups of patients were measured using standardized methods. The blood pressure measurement is performed using a calibrated electronic blood pressure monitor (HEM-7211, □mron Health Medical Co., Ltd., Japan). The patient rests quietly for 5 minutes before measurement, empties the bladder, sits with the elbow level with the heart and measures continuously for 3 times (with an interval of 1 minute). The average of the last 2 measurements is taken as the recorded systolic and diastolic blood pressure. Fasting blood glucose measurement requires patients to fast for 8-12 hours overnight (no sugary drinks, can drink a small amount of water). The next morning, 3mL of elbow vein blood is collected and detected using a fully automated biochemical analyzer (AU5800, Beckman Coulter Biomedical Co., Ltd., Japan) using glucose oxidase method. Fasting blood glucose values are recorded (Dai *et al.*, 2020). All indicators were measured once before treatment (baseline) and once after treatment (study endpoint) to ensure dynamic continuity and comparability of the data.

Clinical efficacy

Based on the observation indicators of this study, clinical efficacy is divided into three levels: significant efficacy, effective efficacy and ineffective efficacy. *Obvious effect*: QTc interval shortened by ≥ 30 ms or returned to normal range compared to before treatment, left ventricular ejection fraction increased by ≥ 5% compared to before treatment, left ventricular diameter decreased by ≥ 10% compared to before treatment, systolic/diastolic blood pressure decreased by ≥ 20/10 mmHg compared to before treatment and fasting blood glucose decreased by ≥ 1.0 mmol/L. *Effective*: QTc interval shortened by 10-29 ms compared to before treatment, left ventricular ejection fraction increased by 2-4%, left ventricular diameter decreased by 5-9%, systolic/diastolic blood pressure decreased by 10-19/5-9 mmHg and fasting blood glucose decreased by 0.5-0.9 mmol/L. *Ineffective*: QTc interval is not shortened or prolonged, echocardiographic parameters, blood pressure and fasting blood glucose are not improved or even worsened, or the frequency of ventricular arrhythmias is not reduced.

Secondary indicators

Quality of life score

The quality of life score was measured using the "36 item Brief Health Status Survey Questionnaire (SF-36 Scale)" (Wu *et al.*, 2023). The specific process is as follows: the scale includes 36 items in 8 dimensions: physiological function, physical pain, general health status, energy, social function, emotional function and mental health. During the measurement, trained researchers will provide one-on-one explanations and instructions to patients to ensure that they understand the meaning of each item. Patients will independently fill out the instructions in a quiet environment. If there are visual impairments or limited educational levels, researchers will read out the content of the items without induction and record the answers based on the patient's oral narration. After filling out the form, the researchers checked the completeness of the items (no omissions or errors) and then converted the original scores of each dimension according to the SF-36 standard scoring rules and converted the original scores into standard scores ranging from 0 to 100 (the higher the standard score, the better the quality of life for that dimension). Finally, the quality of life level of the patients was comprehensively evaluated through the standard scores, which were measured once before treatment (baseline) and once after treatment (study endpoint) to compare the changes in quality of life before and after treatment.

Complications

The complications monitored in this study mainly include sudden cardiac death, hospitalization for heart failure, acute myocardial infarction, stroke and severe arrhythmia (such as apical torsion ventricular tachycardia). The monitoring method is to evaluate the patient's occurrence of the above-mentioned complications and symptoms through monthly outpatient follow-up, telephone follow-up and medical record review during the treatment period. At the same time, electrocardiogram and cardiac ultrasound should be rechecked every 2 months. If the patient shows the above symptoms or abnormal examination results, further examinations (such as coronary CT angiography and head CT) should be arranged immediately to confirm the diagnosis. The determination of complications needs to be jointly confirmed by two attending cardiologists based on standards such as the "Chinese Guidelines for Diagnosis and Treatment of Heart Failure 2022" and the time, type and severity of complications should be recorded. If there is a difference in judgment, it shall be reviewed and determined by personnel with the title of deputy chief physician or above in the department and the incidence of complications during the treatment period of both groups of patients shall be finally calculated.

Adverse reactions

The adverse reactions that need to be monitored in this study mainly target the drugs used, including blood volume deficiency related to SGLT2 inhibitors (such as dizziness and orthostatic hypotension), urinary and reproductive tract infections (such as urinary frequency and urgency), as well as gastrointestinal reactions related to conventional drugs (such as nausea and diarrhea), liver dysfunction and muscle pain. The monitoring method is as follows: during monthly follow-up during the treatment period, researchers use a unified adverse reaction assessment form to ask patients one by one whether they have the above symptoms. If patients experience suspected adverse reaction symptoms, relevant examinations should be promptly completed (such as urine culture screening for urinary and reproductive tract infections). Calculate the incidence of adverse reactions during the treatment period for two groups of patients.

Follow-up visits

Based on the follow-up data after treatment in the clinical diagnosis and treatment records, the focus was on extracting the follow-up information three months after the start of treatment (at the end of treatment) to dynamically evaluate the regulatory effect of SGLT2 inhibitors on QTc interval and ventricular arrhythmia in patients with DM-HTN-CAD. These follow-up nodes mainly focus on the occurrence of drug-related adverse reactions (such as insufficient blood volume, urinary and reproductive tract infections) and cardiovascular complications (such as hospitalization for heart failure, acute myocardial infarction). Although the integrity of follow-up data in retrospective studies is limited by the original records, this study still uses standardized data extraction standards (such as explicitly including cases with complete time point follow-up records) to ensure the validity of information as much as possible, providing a basis for analyzing the continuity and safety of SGLT2 inhibitors regulatory effects.

Sample size calculation

Perform power analysis using G*Power 3.0 computer software to calculate the sample size required for detecting statistically significant differences. Based on the main results of clinical efficacy and previous studies (Najar *et al.*, 2022) and considering the efficacy of alpha levels of 0.05 and 85%, it was determined that a sample size of 59 patients is required for each group. Considering potential uncertainties, the sample size selected for this study is 75 cases per group, which is well justified and sufficient to provide reliable conclusions.

Statistical analysis

Data analysis was conducted using SPSS statistical software version 28.0. Lucidchart is used to draw flowcharts. The data in this study were subjected to a normal distribution test. The baseline features are described as the number of people and variables (represented by $\bar{x}\pm s$). The QTc interval, changes in echocardiographic parameters, blood pressure and blood glucose indicators and quality of life scores in the results are all expressed as $\bar{x}\pm s$. An independent sample *t*-test was used to compare both groups. At the same time, Cohen's d-value was added to quantify the magnitude of inter group differences and a 95% CI was reported to reflect the reliability of the results. The clinical efficacy, incidence of complications and adverse reactions in the results are expressed as percentages (%). The comparison between groups was conducted using the chi-square test, supplemented with RR and 95% CI to clarify the strength of the association. All statistically different tests were two-tailed, with $P<0.05$ representing statistical significance.

RESULTS

Basic information

150 patients with DM-HTN-CAD from January 2023 to January 2025 were included in this study. According to the treatment plan, they were divided into the conventional treatment group and the SGLT2 inhibitors group to explore the regulatory effect of SGLT2 inhibitors on QTc interval and ventricular arrhythmia in these patients. Prior to the initiation of the study, detailed baseline demographic characteristics such as age, gender, body mass index and other key information were collected and recorded for two groups of patients. The results are shown in table 1. In the statistical analysis stage, independent sample t-test is used for continuous variables (such as age) and chi-square test

is used for categorical variables (such as gender). Results indicated that no significant differences were observed among baseline characteristics between both groups (P>0.05). This ensures effective control of demographic and clinical confounding factors during the research process, reduces potential interference with research conclusions and lays a reliable foundation for accurately evaluating the regulatory effect of SGLT2 inhibitors, ensuring the scientific validity and clinical reference value of the research results.

Main outcome

QTc interval

The results of this study (Table 2) illustrated that the QTc interval levels of patients in the conventional treatment group and SGLT2 inhibitors group before treatment were (440.64 ± 18.90) ms and (441.91 ± 19.19) ms, respectively, with no statistically significant differences (P>0.05), indicating that the baseline myocardial repolarization function of both groups was balanced and comparable. After treatment with different regimens, the QTc interval between both groups was markedly reduced versus pre-treatment (P<0.05), with the conventional treatment group decreasing to (423.29 ± 12.73) ms and the SI group decreasing to (412.83 ± 11.85) ms and the differences among the groups after treatment was significant (P<0.05). This indicates that both treatment options can improve the myocardial repolarization status of patients and the SGLT2 inhibitors group has a better effect on shortening the QTc interval.

Changes in echocardiographic parameters

The monitoring of echocardiographic parameters in this study is shown in table 3. There were no significant differences in left atrial diameter, left ventricular diameter, right atrial diameter, right ventricular diameter and left ventricular ejection fraction among the conventional treatment group and the SGLT2 inhibitors group pre-treatment (P>0.05), indicating that the baseline cardiac structure and systolic function levels of both groups were balanced and comparable. After treatment with different regimens, both groups illustrated improvement in the above indicators compared to pre-treatment and the difference among the groups was significant (P<0.05 for both groups). The left atrial diameter, left ventricular diameter, right atrial diameter, right ventricular diameter and left ventricular ejection fraction in the conventional treatment group were (35.84 ± 1.03) mm, (48.85 ± 1.56) mm, (33.30 ± 2.03) mm, (24.73 ± 1.37) mm and (56.35 ± 1.60)%, respectively. The corresponding indicators in the SGLT2 inhibitors group were (32.94 ± 1.05) mm, (47.13 ± 1.86) mm, (31.87 ± 1.97) mm, (22.57 ± 1.05) mm and (59.03 ± 1.65)%, respectively. These results indicate that both treatment regimens can improve cardiac structural remodeling and systolic function in patients and the SGLT2 inhibitors group has a better improvement effect.

Blood pressure and blood glucose indicators

The monitoring results of blood pressure and blood glucose indicators in this study are shown in table 4. There were no significant differences (P>0.05) in diastolic blood pressure, systolic blood pressure and fasting blood glucose levels between the conventional treatment group and the SGLT2 inhibitors group before treatment, indicating that the baseline blood pressure and blood glucose control status of both groups were balanced and comparable. After treatment with different regimens, the above indicators between both groups were remarkably reduced compared to pre-treatment and the difference among the groups was significant (P<0.05 for both groups). The diastolic blood pressure, systolic blood pressure and fasting blood glucose in the conventional treatment group were (86.18 ± 2.17) mmHg, (136.42 ± 3.64) mmHg and (6.94 ± 0.96) mmol/L, respectively. The corresponding indicators in the SGLT2 inhibitors group were (81.49 ± 2.57) mmHg, (127.76 ± 4.07) mmHg and (5.79 ± 0.91) mmol/L, respectively. This indicates that both treatment regimens can effectively control patients' blood pressure and blood sugar and the SGLT2 inhibitors group has better antihypertensive and hypoglycemic effects.

Clinical efficacy

The clinical efficacy evaluation results of this study are shown in table 5. Among the 75 patients in the conventional treatment group, 62 were effectively treated, with a total clinical effectiveness rate of 82.67%. Among the 75 patients in the SGLT2 inhibitors group, 70 were effectively treated, with a total clinical effectiveness rate of 93.33%. The difference in the total clinical effective rate between the two groups was a significant difference (P<0.05), indicating that the comprehensive efficacy of the SGLT2 inhibitors group was remarkably better than that of the conventional treatment group in improving the overall condition with DM-HTN-CAD.

Secondary outcome

Quality of life score

The results of the quality of life score (based on the SF-36 scale) in this study are shown in table 6. There were no significant differences in scores among the conventional treatment group and the SGLT2 inhibitors group pre-treatment [(81.34 ± 4.06) scores vs. (81.30 ± 3.77) scores, P>0.05]. The baseline quality of life levels of both groups are balanced and comparable. After treatment with different regimens, both groups illustrated significant improvement in scores compared to before treatment (P<0.05) and the difference among the groups was significant *(P<0.05)*. The score of the conventional treatment group increased to (90.38 ± 3.94) scores and the score of the SGLT2 inhibitors group increased to (94.06 ± 2.82) scores, indicating that both treatment regimens can improve the quality of life and the improvement effect of the SGLT2 inhibitors group is better.

Table 1: Baseline disease characteristics ($\bar{x}$±s)

Parameter		Conventional treatment group (*n*=75)	SGLT2 Inhibitors group (*n*=75)	t/x^2	*P*	Cohen's d (95% CI) / Relative risk (95% CI)
Age (*year*)		63.51±6.82	63.85±6.56	0.311	0.756	Cohen's d=0.05 (95% CI: -0.32~0.42)
Gender (*Male/female*)		40/35	38/37	0.080	0.777	RR=1.08 (95% CI: 0.76~1.53)
Height (*year*)		158.94±4.55	158.33±4.69	-0.808	0.420	Cohen's d=0.13 (95% CI: -0.24~0.50)
Weight (*kg*)		64.81±3.89	64.29±3.68	-0.841	0.402	Cohen's d=0.14 (95% CI: -0.23~0.51)
Body mass index (kg/m^2)		23.19±1.40	23.22±1.22	0.140	0.889	Cohen's d=0.02 (95% CI: -0.35~0.39)
Course of diabetes (*year*)		6.97±1.89	7.14±1.84	0.558	0.578	Cohen's d=0.09 (95% CI: -0.28~0.46)
Hypertension course (*year*)		7.13±1.93	7.03±1.83	-0.326	0.745	Cohen's d=0.05 (95% CI: -0.32~0.42)
Classification of coronary artery disease	*Grade Ⅰ*	28/75	30/75	0.190	0.663	RR=0.93 (95% CI: 0.62~1.40)
	Grade Ⅱ	35/75	34/75	0.081	0.777	RR=1.03 (95% CI: 0.72~1.47)
	Grade Ⅲ	12/75	11/75	0.038	0.845	RR=1.09 (95% CI: 0.52~2.29)
Drinking alcohol (*yes/no*)		57/18	55/20	0.237	0.626	RR=1.08 (95% CI: 0.86~1.35)
Smoking (*yes/no*)		58/17	56/19	0.110	0.741	RR=1.07 (95% CI: 0.84~1.36)
Temperature (℃)		36.33±0.39	36.36±0.39	0.471	0.638	Cohen's d=0.08 (95% CI: -0.29~0.45)
Breathing (*breaths/min*)		17.64±1.75	17.48±2.21	-0.492	0.624	Cohen's d=0.08 (95% CI: -0.29~0.45)

Table 2: QTc interval ($\bar{x}$±s, ms)

Time	Conventional treatment group (*n*=75)	SGLT2 inhibitors group (*n*=75)	*t*	*P*	Cohen's d (95% CI)
Pre-treatment	440.64±18.90	441.91±19.19	0.408	0.684	Cohen's d=0.06 (95% CI: -0.31~0.43)
Post-treatment	423.29±12.73	412.83±11.85	-5.209	<0.001	Cohen's d=0.73 (95% CI: 0.35~1.11)
t	-6.594	22.774			
P	<0.001	<0.001			
Cohen's d (95% CI)	Cohen's d=1.10 (95% CI: 0.70~1.50)	Cohen's d= 1.76 (95% CI: 1.32~2.20)			

Complications

The monitoring results of complications in this study are shown in Table 7. Among the 75 patients in the SGLT2 inhibitors group, 4 cases developed complications, with a total incidence rate of 5.33%. Among the 75 patients in the conventional treatment group, 11 cases developed complications, with a total incidence rate of 14.67%. The difference in the total incidence rate of complications between the two groups was significant (P<0.05). It shows that in the treatment of patients with DM-HTN-CAD, the risk of complications in the conventional treatment group is higher than that in the SGLT2 inhibitors group.

Adverse reactions

The adverse reaction monitoring results of this study are shown in Table 8. Among the 75 patients in the SGLT2 inhibitors group, 7 cases had adverse reactions, with a total incidence rate of 9.33%. Among the 75 patients in the conventional treatment group, 15 cases had adverse reactions, with a total incidence rate of 20.00%.

Table 3: Changes in echocardiographic parameters

Parameter	Time	Conventional treatment group (*n*=75)	SGLT2 inhibitors group (*n*=75)	*t*	*P*	Cohen's d (95% CI)
Left atrial diameter (mm)	Pre-treatment	37.07±2.78	36.87±2.70	-0.447	0.656	Cohen's d=0.07 (95% CI: -0.30~0.44)
	Post-treatment	35.84±1.03*	32.94±1.05*	-17.075	<0.001	Cohen's d=2.71 (95% CI: 2.23~3.19)
Left ventricular diameter (mm)	Pre-treatment	50.23±3.87	50.05±3.67	-0.292	0.771	Cohen's d=0.05 (95% CI: -0.32~0.42)
	Post-treatment	48.85±1.56*	47.13±1.86*	-6.136	<0.001	Cohen's d=0.97 (95% CI: 0.58~1.36)
Right atrial diameter (mm)	Pre-treatment	34.88±1.90	34.82±2.14	-0.182	0.856	Cohen's d=0.03 (95% CI: -0.34~0.40)
	Post-treatment	33.30±2.03*	31.87±1.97*	-4.378	<0.001	Cohen's d=0.70 (95% CI: 0.32~1.08)
Right ventricular diameter (mm)	Pre-treatment	26.20±1.90	25.63±1.91	-1.832	0.069	Cohen's d=0.29 (95% CI: -0.01~0.59)
	Post-treatment	24.73±1.37*	22.57±1.05*	-10.837	<0.001	Cohen's d=1.72 (95% CI: 1.31~2.13)
Left ventricular ejection fraction (%)	Pre-treatment	53.64±1.89	53.52±2.04	-0.374	0.709	Cohen's d=0.06 (95% CI: -0.31~0.43)
	Post-treatment	56.35±1.60*	59.03±1.65*	10.098	<0.001	Cohen's d=1.61 (95% CI: 1.21~2.01)

Note: "*" represents marked discrepancy compared with pre-treatment, *P*<0.05.

Table 4: Blood pressure and blood glucose indicators

Parameter	Time	Conventional treatment group (*n*=75)	SGLT2 inhibitors group (*n*=75)	*t*	*P*	Cohen's d (95% CI)
Diastolic blood pressure (mmHg)	Pre-treatment	94.15±5.41	93.95±4.30	0.331	0.741	Cohen's d=0.04 (95% CI: -0.33~0.41)
	Post-treatment	86.18±2.17*	81.49±2.57*	-12.075	<0.001	Cohen's d=1.92 (95% CI: 1.50~2.34)
Systolic blood pressure (mmHg)	Pre-treatment	168.18±3.61	167.91±3.53	-0.463	0.644	Cohen's d=0.07 (95% CI: -0.30~0.44)
	Post-treatment	136.42±3.64*	127.76±4.07*	-13.735	<0.001	Cohen's d=2.19 (95% CI: 1.75~2.63)
Fasting blood glucose (mmol/L)	Pre-treatment	9.21±1.92	9.02±2.04	-0.587	0.558	Cohen's d=0.09 (95% CI: -0.28~0.46)
	Post-treatment	6.94±0.96*	5.79±0.91*	-7.529	<0.001	Cohen's d=1.20 (95% CI: 0.80~1.60)

Note: "*" represents marked discrepancy compared with pre-treatment, *P*<0.05.

Table 5: Clinical efficacy analysis [*n*(%)]

Group	□bvious effect (*n*)	Effective (*n*)	Ineffective (*n*)	Total effective rate (*n*, %)
Conventional treatment group (*n*=75)	30	32	13	62 (82.67)
SGLT2 inhibitors group (*n*=75)	34	36	5	70 (93.33)
x^2	4.735			
P	<0.05			
Relative risk (95% CI)	RR=1.13 (95% CI: 1.00~1.28)			

Table 6: Quality of life score ($\bar{x}$±s, score)

Time	Conventional treatment group (*n*=75)	SGLT2 inhibitors group (*n*=75)	*t*	*P*	Cohen's d (95% CI)
Pre-treatment	81.34±4.06	81.30±3.77	-0.063	0.950	Cohen's d=0.01 (95% CI: -0.36~0.38)
Post-treatment	90.38±3.94	94.06±2.82	6.578	<0.001	Cohen's d=1.05 (95% CI: 0.66~1.44)
t	13.838	23.472			
P	<0.001	<0.001			
Cohen's d (95% CI)	Cohen's d=2.68 (95% CI: 2.18~3.18)	Cohen's d=4.37 (95% CI: 3.65~5.09)			

Table 7: Complications [*n*(%)]

	Conventional treatment group (*n*=75)	SGLT2 inhibitors group (*n*=75)	x^2	*P*	Relative risk (95% CI)
Sudden cardiac death	2 (2.67)	1 (1.33)	1.020	0.312	RR=2.00 (95% CI: 0.20~20.03)
Heart failure	3 (4.00)	1 (1.33)	1.846	0.174	RR=3.00 (95% CI: 0.33~27.27)
Acute myocardial infarction	2 (2.67)	1 (1.33)	1.020	0.312	RR=2.00 (95% CI: 0.20~20.03)
Stroke	2 (2.67)	0 (0.00)	3.046	0.081	RR=5.00 (95% CI: 0.25~99.98)
Severe arrhythmia	2 (2.67)	1 (1.33)	1.020	0.312	RR=2.00 (95% CI: 0.20~20.03)
□verall incidence rate	11 (14.67)	4 (5.33)	5.556	<0.05	RR=2.75 (95% CI: 0.95~7.95)

Table 8: Adverse reactions [n (%)]

	Conventional treatment group (*n*=75)	SGLT2 inhibitors group (*n*=75)	x^2	*P*	Relative risk (95% CI)
Dizziness	2 (6.67)	1 (1.33)	1.020	0.312	RR=5.00 (95% CI: 0.55~45.55)
□rthostatic hypotension	2 (6.67)	1 (1.33)	1.020	0.312	RR=5.00 (95% CI: 0.55~45.55)
Frequent urination	2 (6.67)	1 (1.33)	1.020	0.312	RR=5.00 (95% CI: 0.55~45.55)
Urinary urgency	1 (3.33)	1 (1.33)	0.000	1.000	RR=2.50 (95% CI: 0.16~38.96)
Nausea	2 (2.67)	0 (0.00)	3.046	0.081	RR=5.00 (95% CI: 0.25~99.98)
Diarrhea	2 (6.67)	1 (1.33)	1.020	0.312	RR=5.00 (95% CI: 0.55~45.55)
Abnormal liver function	2 (6.67)	1 (1.33)	1.020	0.312	RR=5.00 (95% CI: 0.55~45.55)
Muscle pain	2 (6.67)	1 (1.33)	1.020	0.312	RR=5.00 (95% CI: 0.55~45.55)
□verall incidence rate	15 (20.00)	7 (9.33)	4.880	<0.05	RR=2.14 (95% CI: 0.90~5.10)

The difference in the total incidence rate of adverse reactions between the both groups was significant differences (P<0.05). It shows that the risk of adverse reactions in the SGLT2 inhibitors group is lower than that in the conventional treatment group in the treatment of patients with DM-HTN-CAD.

DISCUSSION

The DM-HTN-CAD remarkably increased the risk of abnormal myocardial repolarization and ventricular arrhythmia. Hypertension mediated left ventricular hypertrophy and myocardial ischemia caused by coronary artery disease can promote late stage sodium current enhancement in myocardial cells by activating the calcium/calmodulin dependent protein kinase II pathway, leading to abnormal increase in sodium ion influx and intracellular calcium overload, thereby prolonging QTc interval and reducing ventricular fibrillation threshold (Frak *et al.*, 2022). At the same time, the oxidative stress and inflammatory response exacerbated by hyperglycemia can further deteriorate myocardial electrophysiological stability by inducing myocardial fibrosis, damaging endothelial function and disrupting energy metabolism, leading to an increased incidence of malignant arrhythmia in patients with this condition compared to those with a single disease. Moreover, prolonged QTc interval is positively correlated with cardiovascular mortality risk (Balogh *et al.*, 2023).

At present, the combination therapy used in clinical practice focuses on controlling blood pressure, blood glucose and antiplatelet aggregation. Although it can reduce the risk of macroscopic cardiovascular events, it lacks targeted regulation of myocardial electrophysiological disorders. In traditional protocols, some antihypertensive and hypoglycemic drugs may exacerbate QTc interval prolongation by affecting ion channels, while the use of antiarrhythmic drugs is limited by contraindications such as cardiac dysfunction (Valentin *et al.*, 2022). Although recent studies suggest that SGLT2 inhibitors can play a potential antiarrhythmic role by inhibiting the activity of sodium/hydrogen exchanger 1, improving myocardial ion homeostasis and reducing fibrosis and can shorten the QTc interval in patients with non-diabetes cardiomyopathy, such evidence mostly comes from people with heart failure or a single disease. Special studies on patients with DM-HTN-CAD are scarce and the dose effect relationship of its regulation of QTc interval and the synergistic mechanism with traditional drugs have not been clear (De Pascalis *et al.*, 2021; Wichaiyo and Saengklub, 2022). Therefore, targeted research is urgently needed to elucidate the electrophysiological regulatory effects of SGLT2 inhibitors in this comorbid population, providing a basis for optimizing treatment plans.

The baseline data of this study illustrated that there were no significant differences in basic information between the both groups ($P>0.05$), which ensured the comparability of both groups and eliminated the interference of baseline confounding factors on treatment efficacy, laying a reliable foundation for the subsequent evaluation of the differences between the SGLT2 inhibitors group and the conventional treatment group. From the perspective of core efficacy indicators, both groups illustrated a significant reduction in QTc interval after treatment and the SGLT2 inhibitors group had a shorter QTc interval, indicating that the SGLT2 inhibitors group had more advantages in improving myocardial electrophysiological stability and reducing the risk of malignant arrhythmia. This is consistent with the conclusion of a previous study on patients with diabetes and coronary heart disease. This study found that the regimen containing SGLT2 inhibitors can achieve targeted shortening of QTc interval by inhibiting the late sodium current of myocardial cells and reducing calcium overload (Yan and Su, 2023). At the same time, this study found that SGLT2 inhibitors not only have a direct ion channel regulatory effect in this comorbid population, but also can alleviate multiple pathological stresses by synergistically controlling glucose and blood pressure and their QTc interval shortening effect is more significant. It should be noted that this study did not validate the relevant pathways through basic experiments. The following mechanistic explanations are reasonable speculations based on existing literature and require further research to confirm.

In terms of improvement in cardiac structure and function, the SGLT2 inhibitors group had lower left atrial diameter, left ventricular diameter, right atrial diameter and right ventricular diameter after treatment compared to the conventional treatment group and had a higher left ventricular ejection fraction. The reduction in left ventricular diameter and reversal of left atrial remodeling indicate a decrease in myocardial load and ventricular wall stress, while an increase in left ventricular ejection fraction directly reflects enhanced myocardial contractile function (Riccardi *et al.*, 2023). These changes collectively suggest that the SGLT2 inhibitor regimen is more effective in reversing cardiac remodeling and protecting cardiac function. It is speculated that the mechanism may be related to the unique action of SGLT2 inhibitors in this protocol: these drugs can achieve dual protection of cardiac structure and function by inhibiting the activity of sodium/hydrogen exchanger 1, reducing myocardial fibrosis and improving myocardial energy metabolism (replacing glucose with ketone bodies for energy supply, reducing oxygen consumption) (Chung *et al.*, 2023).

From the perspective of metabolic control and overall benefits, the SGLT2 inhibitors group had lower average blood pressure (systolic and diastolic) and fasting blood glucose levels after treatment compared to the conventional treatment group and the clinical total effective rate (93.33% vs. 82.67%) and quality of life score (94.06±2.82 points vs. 90.38±3.94 points) were remarkably better. The effective control of blood pressure and glucose is the core to delay the progress of DM-HTN-CAD (Geng *et al.*, 2024), while the synergistic effect of SGLT2 inhibitors group regimen in reducing blood sugar (by promoting urinary glucose excretion) and reducing blood pressure (by diuresis, improving vascular endothelial function) not only directly reduces the risk of macro cardiovascular events, but also improves the quality of life

by reducing physical discomfort (such as dizziness and fatigue) and reducing disease related concerns. The core value of this result lies in breaking through the clinical limitations of "single indicator control": traditional treatments often focus on achieving single indicators such as blood pressure and blood glucose, but ignore the linkage effect of "metabolic control, organ protection, quality of life". However, this study confirms that the SGLT2 inhibitor group regimen can not only achieve deep metabolic indicators, but also alleviate myocardial ischemia, improve physical fitness and enhance patients' quality of life. This is consistent with the findings reported. in the systematic review and meta-analysis of SGLT2 inhibitors, functional capacity and quality of life in heart failure patients, which indicated that regimens containing SGLT2 inhibitors can remarkably improve functional capacity and quality of life in heart failure patients (M Gao *et al.*, 2024). These results further support the concept of comprehensive benefits centered on patients, rather than simply pursuing improvements in laboratory indicators.

It is worth noting that the overall incidence of complications and adverse reactions in the SGLT2 inhibitors group was lower than that in the conventional treatment group, which is different from the traditional understanding that "potent treatment regimens often come with higher safety risks. The critical significance of this discovery lies in revealing the optimizable space for the "efficacy safety balance": previous studies have expressed concerns that SGLT2 inhibitors may increase the risk of urinary and reproductive tract infections, insufficient blood volume and other conditions (Yang *et al.*, 2024). However, in this study, the safety indicators of the SGLT2 inhibitors group were better, possibly due to targeted monitoring (such as regular urine routine examination) and treatment (such as guiding drinking water and paying attention to personal hygiene) implemented in the SGLT2 inhibitors group, which reduced the risk of adverse reaction progression. The synergistic effect of SGLT2 inhibitors with other drugs in the SGLT2 inhibitors regimen (such as reducing myocardial ischemia) may also indirectly reduce complications caused by poor disease control (such as worsening angina). This result provides important safety basis for the clinical promotion of SGLT2 inhibitor regimen and also suggests that the "efficacy safety balance" can be optimized through refined management.

This study has several limitations. First, the 3-month short-term follow-up is insufficient to verify the long-term effects of SGLT2 inhibitors on myocardial electrophysiological homeostasis, cardiac remodeling reversal and blood pressure-glucose control in patients with chronic progressive DM-HTN-CAD. Second, the single-center sample causes selection bias in geographic distribution, disease severity and medication history, restricting the extrapolation of results to broader populations. Third, the retrospective non-randomized design leads to inherent confounding factors such as baseline imbalance and inconsistent concomitant medications. Fourth, the lack of multi-dose SGLT2 inhibitor groups and head-to-head comparisons between different SGLT2 inhibitors hinders the determination of optimal dosage and comprehensive evaluation of clinical advantages. Finally, this study did not conduct basic experiments to verify the relevant mechanisms and all mechanistic explanations are based on speculation from existing literature, which is also a direction that needs to be addressed in future research. Subsequent studies can extend the follow-up period to 1-2 years, with a focus on exploring the effects of SGLT2 inhibitor regimen on long-term QTc interval stability, cardiovascular event incidence and quality of life in patients. Expand the sample sources to multiple centers, including patients from different regions and with varying degrees of underlying disease severity, to enhance the extrapolation of results. Simultaneously setting up a multi dose SGLT2 inhibitor treatment group and a comparison group of different drug types to determine the optimal medication regimen, providing more comprehensive evidence-based support for individualized clinical treatment.

CONCLUSION

This study compared conventional therapy and SGLT2 inhibitor-based treatment in DM-HTN-CAD patients to optimize clinical regimens. Results showed that SGLT2 inhibitors conferred superior benefits in QTc interval regulation, cardiac structural improvement, blood pressure-glucose control, clinical efficacy and quality of life, with comparable safety profiles in complications and adverse reactions. However, limitations include a short observation period, single-center sample, insufficient exploration of SGLT2 inhibitors' underlying mechanisms and undetermined optimal dosage. Future multi-center, large-sample, long-term follow-up studies combined with molecular biology assays are needed to validate efficacy across populations, clarify mechanisms and refine treatment strategies.

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None

Authors' contribution
Jia Liu: Developed and planned the study, performed experiments and interpreted results. Edited and refined the manuscript with a focus on critical intellectual contributions; Yinglin Shi, Yuan Zhang: Participated in collecting, assessing and interpreting the data. Made significant contributions to data interpretation and manuscript preparation; Xin Wang, Xiaoming Zhu: Provided substantial intellectual input during the drafting and revision of the manuscript.

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Data availability statement

The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

Ethical approval

This study was approved by Beijing Chaoyang Hospital, Capital Medical University Ethics Committee (N□. 2022--127-1).

Conflicts of interest

The authors declare that they have no conflict of interest.

Consent to participate

Signed informed consent forms were obtained from every participant.

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