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Effects of SGLT2 Inhibition on Metabolic Parameters and Cardiac Function in Patients with Type 2 Diabetes Mellitus and Coronary Heart Disease

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ABSTRACT

Objective: To investigate the efficacy and safety of SGLT2 inhibitors in patients with type 2 diabetes mellitus complicated by coronary atherosclerotic heart disease.

Methods: Seventy-six patients diagnosed with coronary heart disease (CHD) and type 2 diabetes mellitus (T2DM) were included in this study conducted at the Department of Cardiology, First Affiliated Hospital of Kunming Medical University, between January 2022 and August 2023. The patients were stratified into two cohorts based on their treatment regimen, the observation group (n=40) and the control group (n=36). The control group received alternative glucose-lowering medications, excluding dapagliflozin, while the observation group was administered dapagliflozin either as monotherapy or in combination with other glucose-lowering agents. Both groups underwent standard secondary prevention therapy for CHD for a duration of 6 months. Comparisons were made between the two groups in terms of TC, TG, LDL-C, HDL-C, FBG, HbA1c, SUA, CRP, BNP, BMI, BW, LVEDD, LVEF, IVST and safety evaluation.

Results: The findings revealed that in the observation group, there were significant reductions in FBG, HbA1c, BMI, BW, SUA, CRP, LDL-C, TC, TG, BNP, LVEDD, and IVST post-treatment compared to pre-treatment levels. Additionally, HDL-C and LVEF exhibited significant increases. While there were no statistically significant differences in LVEDD within the cohort ($P > .05$), all other intra-group comparisons displayed statistically significant variances ($P < .05$). Following treatment, the control group exhibited reductions in FBG, HbA1c, BMI, BW, LDL, TC, TG, BNP, LVEDD, and LVEF compared to baseline levels, while HDL, SUA, CRP, and IVST increased. However, these intragroup differences did not reach statistical significance ($P > .05$). Intergroup analysis following treatment showed statistically significant differences in FBG, HbA1c, CRP, LDL-c, TC, TG, LVEF, and IVST ($P < .05$). Conversely, no significant intergroup differences were found SUA, BW, BMI, HDL-C, LVEF, LVEDD and BNP ($P > 0.05$).

Conclusion: dapagliflozin provides cardiovascular benefits by reducing inflammatory responses and improving cardiovascular risk factors through multiple pathways, including lowering blood glucose, regulating blood lipids, reducing inflammatory markers, and inhibiting ventricular remodeling.

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Keywords: Type 2 Diabetes Mellitus, Coronary Atherosclerotic Heart Disease, Dapagliflozin, Metabolic Parameters, Cardiac Function

Abbreviation List
SGLT2i: Sodium-Glucose Transporter 2 Inhibitors
CHD: Coronary Heart Disease
T2DM: 2 Diabetes Mellitus
MACE: Major Adverse Cardiovascular Events
TC: Total Cholesterol
TG: Triglycerides
LDL-C: Low-Density Lipoprotein
HDL-C: High-Density Lipoprotein
FBG: Fasting Blood Glucose
HbA1c: Glycated Hemoglobin
UA: Serum Uric Acid
CRP: C-Reactive Protein
BNP: B-Type Natriuretic Peptide;
BMI: Body Mass Index;
BW: Body Weight
LVEDD: Left Ventricular End-Diastolic Diameter
LVEF: Left Ventricular Ejection Fraction
IVST: Interventricular Septal Thickness

Introduction

Globally, diabetes mellitus (DM) and coronary artery disease (CAD) are highly prevalent chronic non-communicable diseases exhibiting a sustained increase in both incidence and prevalence. According to statistics, the global number of adults with diabetes mellitus reached 415 million in 2015, and is projected to increase to 642 million by 2024 [1]. Meanwhile, as the leading cause of death worldwide, coronary artery disease affects approximately 126 million people globally, accounting for about 1.72% of the world's population, and is responsible for nearly 9 million deaths

annually. It is estimated that by 2030, the current prevalence of CAD, which stands at 1,655 per 100,000 population, is expected to rise to over 1,845 per 100,000 [2,3]. Furthermore, diabetes mellitus is recognized as an independent risk factor for coronary artery disease [4]. Sustained hyperglycemia promotes the progression of atherosclerosis via multiple interrelated pathophysiological pathways, including insulin resistance, endothelial dysfunction, oxidative stress, chronic inflammation, and disordered lipid metabolism [5]. Studies have shown that the risk of cardiovascular disease in patients with diabetes is 2-4 times higher than that in non-diabetic individuals [6]. Moreover, the coexistence of diabetes and coronary artery disease is often associated with more extensive diffuse coronary artery lesions, multi-vessel involvement, and consequently, poorer clinical prognosis [7,8]. Patients exhibited a significantly higher incidence of major adverse cardiovascular events (MACE), such as myocardial infarction and heart failure [8,9]. According to epidemiological data, the global direct medical costs attributed to diabetes were estimated at approximately USD 760 billion in 2019. This expenditure is projected to rise to USD 825 billion by 2030 and USD 845 billion by 2045 [10]. Such substantial costs not only significantly compromise the quality of life of affected individuals but also impose a persistent and profound socioeconomic burden, driven by elevated healthcare expenses and associated losses in productivity [11].

Current antidiabetic strategies predominantly rely on conventional therapies such as biguanides, thiazolidinediones, sulfonylureas, and insulin [12]. While these pharmacological interventions can partially improve insulin resistance, they are often limited in addressing multiple risk factors comprehensively, including weight gain and hypoglycemia [13]. Moreover, their modest cardiovascular benefits further restrict long-term clinical applicability. Emerging evidence suggests that thiazolidinediones, including rosiglitazone, may be associated with an increased risk of cardiotoxicity [14]. Consequently, for patients with type 2 diabetes mellitus and concomitant coronary artery disease, antidiabetic medications with proven cardiovascular protective effects, along with complementary benefits such as lipid modulation, anti-inflammatory properties, and overall metabolic improvement, should be considered as preferred therapeutic options.

Sodium-glucose cotransporter 2 inhibitors (SGLT2i) are a newer class of oral glucose-lowering agents that function independently of insulin. By competitively antagonizing the binding of glucose to SGLT2 receptors, they inhibit approximately 90% of glucose reabsorption in the proximal renal tubules. This promotes urinary glucose excretion, reduces plasma glucose levels, and consequently contributes to glycemic control, weight loss, and overall metabolic improvement [15,16]. This study retrospectively analyzed echocardiographic indicators and clinical data from patients with type 2 diabetes mellitus and coronary artery disease treated with dapagliflozin, aiming to systematically evaluate its therapeutic efficacy in real-world clinical practice and to provide new evidence-based insights for optimizing treatment strategies in this comorbid population.

Materials and Methods

Research Subjects A retrospective analysis was performed on 76 patients diagnosed with coronary heart disease and type 2 diabetes mellitus, who were admitted to the Cardiology Department at the First Affiliated Hospital of Kunming Medical University between January 2022 and August 2023. The patients, with an age range of 35 to 87 years and a mean age of 62.64 ± 11.19 years, comprised 61 males (80.3%) and 15 females (19.7%). Approval for this study was obtained from the Medical Ethics Committee of the First Affiliated Hospital of Kunming Medical University.

Inclusion criteria (1) Meeting the diagnostic criteria for type 2 diabetes mellitus [17]. (2) the patient fulfills the diagnostic criteria for coronary heart disease [18]. (3) being at least 18 years old, (4) having complete clinical data available.

Exclusion criteria (1) Severe acute diabetic complications within the past month, including diabetic ketoacidosis or hyperosmolar hyperglycemic state. (2) Episode of hypoglycemic coma within the preceding month. (3) Presence of concurrent multi-organ failure. (4) Diagnosis of malignant arrhythmias. (5) Comorbid severe gastrointestinal bleeding, autoimmune diseases, hematologic disorders, malignant tumors, or other chronic debilitating diseases. (6) Pregnancy or lactation. (7) Known intolerance to SGLT2 inhibitors. (8) Psychiatric disorders resulting in inability to cooperate with the study. (9) History of recurrent urinary tract infections. (10) Acute phase of infectious disease.

Group Allocation According to the use of dapagliflozin, patients were categorized into an observation group (n=40) and a control group (n=36). The observation group comprised patients aged 35–79 years (mean age: 59.45 ± 9.49), including 32 males (80%), 25 smokers (62.5%), 21 patients with hypertension (52.5%), and 13 with hyperlipidemia (32.5%). The control group consisted of individuals aged 48–87 years (mean age: 66.19 ± 11.97), including 29 males (80.6%), 19 smokers (52.8%), 16 patients with hypertension (44.4%), and 17 with hyperlipidemia (47.2%). No statistically significant differences were identified in baseline characteristics between the two groups ($P > 0.05$), demonstrating their comparability.

Treatment Protocol Patients in the observation group were administered dapagliflozin tablets (10 mg once daily) as either monotherapy or combination therapy with other glucose-lowering agents, including biguanides, insulin, sulfonylureas, glinides, α-glucosidase inhibitors, or DPP-4 inhibitors. The control group received alternative glucose-lowering regimens excluding SGLT2 inhibitors. All patients in both cohorts received standard management for coronary heart disease in accordance with clinical guidelines, which comprised antiplatelet therapy (aspirin plus clopidogrel or ticagrelor), statins, antihypertensive and lipid-lowering treatments, alongside dietary counseling and regular physical activity. The intervention was maintained consistently for a period of 6 months.

Observation Indicators

- Laboratory Assessments: After a 10-hour overnight fast, venous blood samples (5 mL) were collected from all patients before and after the treatment period. The following parameters were measured: TC, TG, LDL-C, HDL-C, FBG, HbA1c, SUA, CRP, BNP.
- Measurements and Calculations: Body mass index (BMI) was calculated from body weight and height, which were measured before and after the treatment period, using the formula: weight (kg) / height $(m)^2$.
- Echocardiographic parameters: Including LVEDD, LVEF and IVST were obtained from all patients before and after treatment.
- Safety evaluation: The incidence of adverse events, including nausea, hypoglycemia, headache, urinary tract infection, ketoacidosis, and fracture, was compared between the two groups during the treatment period.

Statistical analysis Statistical analyses were conducted using SPSS version 27.0 (IBM Corp., Armonk, NY, USA). Continuous variables conforming to a normal distribution were summarized as mean ± standard deviation and compared between groups with the independent samples t-test. Within-group comparisons before and after intervention were performed using the paired t-test. For continuous data that violated normality assumptions, nonparametric tests were applied, and results were reported as median with interquartile range [M (Q1, Q3)]. Categorical variables were expressed as frequencies and percentages [n (%)] and analyzed by the chi-square test. A two-tailed P-value less than 0.05 was deemed indicative of statistical significance.

Results

Comparison of Baseline Clinical Characteristics between the Two Groups

A comparative assessment of baseline demographic and clinical parameters revealed no statistically significant differences between the observation and control groups. The variables analyzed included age, sex, smoking status, comorbid conditions (hypertension and hyperlipidemia), lipid profiles (TC, TG, LDL-C, HDL-C), glycemic indices (FBG, HbA1c), SUA, CRP, BNP, BMI, BW, as well as echocardiographic parameters such as LVEDD, LVEF, IVST (all $P > 0.05$). These findings confirm the baseline comparability of the two groups, thereby supporting the validity of subsequent comparative analyses. Detailed data are summarized in Table 1.

Table 1: Comparison of General Clinical Data between Two Groups of Patients

Clinical variables	Obs group (40)	Ctrl group (36)	t / χ^2	P
age(Y, χ±s)	59.45±9.49	66.19±11.97	-2.702	0.09
Male [n(%)]	32 (80)	29 (80.6)	0.004	0.952
Smoking [n(%)]	25 (62.5)	19 (52.8)	0.735	0.391
HTN [n(%)]	21(52.5)	16 (44.4)	0.492	0.483
HLD [n(%)]	13(32.5)	17 (47.2)	1.719	0.190
TC	4.08±1.30	4.11±1.21	-0.117	0.907
TG	2.04±1.34	1.75±0.74	1.140	0.258
LDL-C	2.41±1.23	2 .50±1.27	-0.358	0.721
HDL-C	0.94±0.22	0.99±0.24	-1.028	0.307
FBG	8.23±3.44	8.45±3.19	-0.288	0.774
HbA1c	7.6 (7.13, 8.4)	7.2 (6.73, 8.03)	-1.885	0.059
BMI	24.82±2.87	24.97±3.57	-0.203	0.839
SUA	403.25± 130.29	355.23±105.28	1.755	0.083
CRP	5.55 (2.23, 12.29)	2.64 (0.76, 9.89)	-1.692	0.091
IVST	11.90±1.82	12.28±1.58	-0.961	0.340
LVEDD	48.03±7.55	47.89±5.54	0.089	0.930
LVEF	60.08±13.41	59.78±10.38	0.107	0.915
BNP	234.41 (79.70,541.68)	115.39 (18.51,455.88)	-1.176	0.240

Note: Obs group: Observation group; Ctrl group: Control group; Y: year; TC: total cholesterol; TG: triglycerides; LDL-C: low-density lipoprotein; HDL-C: high-density lipoprotein; FBG: fasting blood glucose; HbA1c: glycated hemoglobin; SUA: serum uric acid; CRP: C-reactive protein; BNP: B-type natriuretic peptide; BMI: body mass index; BW: body weight; LVEDD: left ventricular end-diastolic diameter; LVEF: left ventricular ejection fraction; IVST: interventricular septal thickness; HLD: hyperlipidemia; HTN: Hypertension

Comparative Analysis of Metabolic and Inflammatory Parameter Changes between the Two Groups

Following the intervention, significant improvements in metabolic and inflammatory parameters were observed in the observation group. Specifically, FBG, HbA1c, SUA, CRP, BMI, and BW demonstrated statistically significant reductions relative to baseline ($P < 0.05$). In the control group, modest decreases were noted in FBG, HbA1c, BMI, and BW, whereas SUA and CRP levels exhibited mild elevation compared to pretreatment values; however, these changes did not reach statistical significance ($P > 0.05$). Between-group analyses post-treatment revealed that the observation group achieved significantly greater improvements in FBG, HbA1c and CRP levels compared to the control group ($P < 0.05$). In contrast, no statistically significant differences were detected between the two groups in terms of SUA, BMI, and BW ($P > 0.05$). Detailed data are summarized in Table 2 and Table 3.

Table 2: Comparison of Blood Glucose and SUA between the Two Patient Groups

Group	Time	FBG	HbA1c	SUA
Obs group	Pre-Tx	8.23±3.44	7.60 (7.13, 8.40)	403.25±130.29
n=40	Post-Tx	6.19±2.54	6.80 (6.43, 7.40)	354.20±103.52
Ctrl group	Pre-Tx	8.45±3.19	7.45 (6.78, 8.68)	355.23±105.28
n=36	Post-Tx	7.69±2.23	7.50 (6.73, 8.10)	369.99±107.30
T or Z/P Obs group (In-group)		3.654/0.001	-5.055/<0,001	2.526/0.016

T or Z/P Ctrl group (In-group)	1.869/0.07	-1.331/0.183	-0.477/0.637
T or Z/P Intergroup	-2.725/0.008	-2.718/0.007	-0.381/0.704

Note: Pre-Tx: Before Treatment; Post-Tx: Post-Treatment; Obs group: Observation group; Ctrl group: Control group; In-group: Intra-group comparison before and after treatment; Intergroup: Comparison between groups after treatment; FBG: fasting blood glucose; HbA1c: glycated hemoglobin; SUA: serum uric acid.

Table 3: Comparison of CRP, BMI, and BW between the Two Patient Groups

Group	Time	CRP	BW	BMI
Obs group	Pre-Tx	5.55 (2.23, 12.29)	68.79±8.51	24.82±2.87
n=40	Post-Tx	1.15 (0.40, 2.60)	66.05±8.32	23.82±2.77
Ctrl group	Pre-Tx	2.64 (0.76, 9.89)	69.17±11.47	24.97±3.57
n=36	Post-Tx	3.90 (1.08, 16.08)	68.74±11.09	24.82±3.40
T or Z/P Obs group (In-group)		-4.382/<0.001	6.257/<0.001	6.261/<0.001
T or Z/P Ctrl group (In-group)		-1.671/0.095	1.046/0.303	0.993/0.327
T or Z/P Intergroup		-3.669/<0.001	-1.211/0.230	-1.417/0.161

Note: Pre-Tx: Before Treatment; Post-Tx: Post-Treatment; Obs group: Observation group; Ctrl group: Control group; In-group: Intra-group comparison before and after treatment; Intergroup: Comparison between groups after treatment; CRP: C-reactive protein; BMI: body mass index; BW: body weight;

Comparison of Cardiac Indicators between the Two Patient Groups

Post-intervention analysis revealed a distinct metabolic improvement in the observation group, characterized by statistically significant reductions in LDL-C, TC, and TG. accompanied by a significant elevation in HDL-C compared to baseline ($P < 0.05$). Conversely, the control group exhibited modest decreases in LDL-C, TC, and TG, as well as a slight increase in HDL-C; however, these changes failed to achieve statistical significance ($P > 0.05$). Intergroup comparative analysis demonstrated that the observation group achieved superior improvements in LDL-C, TC, and TG levels relative to the control group, with between-group differences reaching statistical significance ($P < 0.05$). In contrast, no statistically significant difference was observed in HDL between the groups ($P > 0.05$). Detailed data are summarized in Table 4.

Table 4: Comparison of Blood Lipid Profiles between the Two Patient Groups

Group	Time	HDL	LDL	TC	TG
Obs group	Pre-Tx	0.94±0.22	2.4±1.12	4.08±1.30	2.04±1.34
n=40	Post-Tx	1.07 ±0.24	1.60±0.93	3.16±1.08	1.21±0.71
Ctrl group	Pre-Tx	0.99±0.24	2.5±1.13	4.1±1.21	1.75±0.74
n=36	Post-Tx	1.07±0.30	2.13±0.92	3.83±0.96	1.58±0.77
T or Z/P Obs group (In-group)		-3.738/0.001	3.731/0.001	3.54/0.001	4.775/<0.001
T or Z/P Ctrl group (In-group)		-1.732/0.092	2.00/0.053	1.94/0.120	1.355/0.184
T or Z/P Intergroup		0.064/0.949	-2.526/0.014	-2.821/0.006	-2.182/0.032

Note: Pre-Tx: Before Treatment; Post-Tx: Post-Treatment; Obs group: Observation group; Ctrl group: Control group; In-group: Intra-group comparison before and after treatment; Intergroup: Comparison between groups after treatment; TC: total cholesterol; TG: triglycerides; LDL-C: low-density lipoprotein; HDL-C: high-density lipoprotein;

Comparative Analysis of Cardiac Parameters between the Two Groups

Following the treatment, the observation group demonstrated reductions in LVEDD, LVEF, BNP and IVST compared to baseline. Among these changes, the decreases in LVEF and IVST were statistically significant ($P < 0.05$), while the reduction in LVEDD and BNP did not reach statistical significance ($P > 0.05$). In the control group, post-treatment assessment showed decreases in LVEDD, BNP and LVEF, along with an increase in IVST relative to pretreatment values; however, none of these changes were statistically significant (all $P > 0.05$). Between-group comparative analysis revealed statistically significant differences in LVEF and IVST ($P < 0.05$), whereas no significant intergroup difference was observed in LVEDD and BNP ($P > 0.05$). Detailed data are summarized in Table 5

Table 5: Comparison of Cardiac Parameters between the Two Patient Groups

Group	Time	IVST	LVEDD	LVEF	BNP
Obs group	Pre-Tx	11.90±1.82	48.03±7.55	60.08±13.41	234.41(79.70,541.68)
n=40	Post-Tx	11.13±1.28	46.68±8.44	65.13±13.60	148.20(18.86,335.95)
Ctrl group	Pre-Tx	12.28±1.58	47.89±5.54	59.78±10.38	115.39(18.51,455.86)
n=36	Post-Tx	12.61±1.23	47.47±4.98	58.83±9.61	104.87(40.54,290.54)
T or Z/P Obs group (In-group)		3.857/<0.001	2.074/0.450	-5.123/<0.001	-2.527/0.012
T or Z/P Ctrl group (In-group)		-1.220/0.230	0.754/0.456	0.978/0.335	-1.196/0.232
T or Z/P Intergroup		-5.146/<0.001	0.507/0.614	2.306/0.024	-0.021/0.983

Note: Pre-Tx: Before Treatment; Post-Tx: Post-Treatment; Obs group: Observation group; Ctrl group: Control group; In-group: Intra-group comparison before and after treatment; Intergroup: Comparison between groups after treatment; LVEDD: left ventricular end-diastolic diameter; LVEF: left ventricular ejection fraction; IVST: interventricular septal thickness; BNP: B-type natriuretic peptide

Safety Outcomes and Adverse Event Analysis

The adverse event profiles were systematically evaluated during the treatment period. In the observation group, the following events were documented: nausea (n=2), urinary tract infection (n=2), hypoglycemia (n=1), and headache (n=1). No cases of ketoacidosis or fracture were observed. The control group exhibited a distinct adverse event pattern, with higher incidence of nausea (n=3) and hypoglycemia (n=3), along with urinary tract infection (n=1) and headache (n=1). Similarly, no ketoacidosis or fractures occurred in this group. Comparative statistical analysis demonstrated no significant difference in overall adverse event incidence between the intervention and control groups (15.00% vs. 22.22%; $\chi^2 = 0.658$, $P = 0.417$). Detailed data are summarized in Table 6.

Table 6: Comparison of Adverse Reactions between Two Groups

Group	n	nausea	UTI	Hypo	HA	DKA	fracture	ADR
Obs group	40	2 (5.00)	2 (5.00)	1 (2.50)	1 (2.50)	0	0	6 (15.00)
Ctrl group	36	3 (8.33)	1 (2.78)	3 (8.33)	1 (2.78)	0	0	8 (22.22)
Ctrl group				0.658				
P				0.417				

Note: n: Number; Pre-Tx: Before Treatment; Post-Tx: Post-Treatment; Obs group: Observation group; Ctrl group: Control group; UTI: urinary tract infection; Hypo: hypoglycemia; HA: headache; DKA: ketoacidosis; ADR: Adverse Drug Reaction.

Discussion

Coronary artery disease (CAD) is a prevalent clinical cardiovascular entity, with diabetes mellitus recognized as a significant risk factor [19]. These two disorders demonstrate a pathologically synergistic relationship, mediated through shared pathways such as metabolic syndrome and chronic inflammation. These mechanisms collectively contribute to the accelerated progression of atherosclerosis [5]. Insulin resistance contributes to hyperinsulinemia, which in turn drives vascular endothelial dysfunction, dyslipidemia, and ultimately atherosclerosis [5]. Simultaneously, pro-inflammatory mediators derived from adipose tissue and sustained oxidative stress exacerbate vascular damage, establishing a vicious cycle that mutually amplifies both diabetes and coronary artery disease [20]. Epidemiological studies have demonstrated that diabetes mellitus is associated with a significantly elevated risk of cardiovascular events and higher post-myocardial infarction mortality, substantially jeopardizing patient survival and long-term health [19,21]. These intertwined pathologies represent a serious threat to both individual survival and public health. Current therapeutic strategies for glycemic control remain constrained by their limited cardiovascular benefits and a well-documented spectrum of adverse effects [22]. Dapagliflozin, however, emerges as a compelling therapeutic alternative by virtue of its pleiotropic mechanisms, potentially addressing these unmet clinical needs [23].

Fasting blood glucose (FBG) is defined as the plasma glucose concentration measured after a minimum 8-hour fast, whereas glycated hemoglobin (HbA1c) provides an integrated measure of average glycemic exposure over the preceding 8 to 12 weeks [24]. These biomarkers are integral not only to the diagnosis of diabetes but also to the ongoing assessment of glycemic management [24,25]. The results of this investigation revealed that patients in the observation group achieved significantly greater reductions in both fasting blood glucose and glycated hemoglobin (HbA1c) compared to the control group following treatment, with the differences attaining statistical significance. These results corroborate the earlier findings of Clifford et al., affirming that adjunctive therapy comprising an SGLT2 inhibitor and metformin yields superior glycemic regulation, pronounced reductions in HbA1c, and a favorable safety profile, notably without an associated increase in hypoglycemic risk [26]. This effect is attributed to the ability of SGLT2 inhibitors to reduce blood glucose levels by suppressing renal glucose reabsorption and promoting urinary glucose excretion [22]. Additionally, these agents significantly enhance glycemic control and ameliorate insulin resistance through multiple extra-renal mechanisms, including weight reduction, attenuation of hepatic steatosis, improved β-cell function, and enhanced insulin sensitivity in both hepatic and musculoskeletal tissues [27].

High-sensitivity C-reactive protein (CRP), synthesized predominantly by the liver under IL-6 stimulation, represents a key biomarker of systemic inflammation. Through its binding to NADPH oxidase, it amplifies reactive oxygen species (ROS) generation in endothelial cells, resulting in mitochondrial DNA impairment and functional deficits [28]. Concurrently, CRP activates the complement cascade, exacerbating inflammatory processes

and inducing vascular endothelial injury. These multifaceted mechanisms collectively underpin its critical involvement in the initiation and advancement of coronary atherosclerotic plaques [28,29]. Furthermore, emerging evidence implicates hs-CRP as a pivotal mediator in plaque destabilization and subsequent rupture [30]. Dyslipidemia-induced chronic inflammation serves as the central pathogenic driver of atherosclerosis [5]. Elevated circulating levels of low-density lipoprotein (LDL) infiltrate the compromised endothelial barrier, accumulate in the subendothelial space, and undergo oxidative modification, yielding highly pro-inflammatory and cytotoxic oxidized LDL (ox-LDL). This pivotal molecular trigger activates endothelial cells and recruits monocytes, which subsequently differentiate into macrophages [31]. These macrophages then relentlessly internalize ox-LDL via scavenger receptors, transforming into lipid-engorged foam cells-a hallmark initiating event and fundamental pathological feature of atherosclerotic plaque formation [31,32]. The findings of this investigation revealed that, following a 6-month dapagliflozin intervention, the observation group manifested a statistically significant decline in serum levels of CRP, LDL, TC, and TG relative to the control cohort. The observed metabolic benefits are principally attributable to the capacity of SGLT2 inhibitors to elicit a "pseudo-fasting" state via their distinctive promotion of glucosuria, thereby instigating a coordinated sequence of adaptive metabolic alterations. Central to this process is the substantial loss of urinary glucose, establishing a systemic negative energy balance. This catabolic state precipitates a pivotal endocrine transition marked by suppression of insulin release and concomitant augmentation of glucagon secretion [27]. The resultant hormonal configuration effectively antagonizes the suppression of hormone-sensitive lipase (HSL) within adipose tissue, potentiating robust lipolytic activity and facilitating the pronounced mobilization of free fatty acids (FFAs) from adipocyte stores [33]. Concurrently, the cellular energy sensor AMPK pathway is activated, further enhancing fatty acid oxidation and utilization [34]. Acting in concert, these adaptive responses not only intensify lipolytic flux but also orchestrate a broad-spectrum amelioration of the dyslipidemic profile, manifesting as substantive reductions in circulating triglycerides, total cholesterol, and low-density lipoprotein cholesterol. This multifaceted metabolic rewiring is postulated to underpin the cardiorenal protective benefits attributed to the intervention [35,36].

Chronic heart failure (CHF), the most severe complication of coronary artery disease (CAD), is primarily driven by a pathophysiological process characterized by the activation of the renin-angiotensin-aldosterone system (RAAS), cardiac hypertrophy, fibrosis, and ventricular remodeling. The interplay of these factors leads to a progressive decline in cardiac function, culminating in heart failure [37]. Consequently, alongside the treatment for CAD, therapeutic strategies for CHF must focus on improving hemodynamics and inhibiting ventricular remodeling. The findings of the present study revealed that the observation group exhibited a significantly higher left ventricular ejection fraction (LVEF) and a reduced interventricular septal thickness compared to the control group. These results suggest that SGLT2 inhibitors may confer additional cardioprotective benefits by further improving cardiac function. The beneficial effects are attributed to empagliflozin-induced activation of the tubuloglomerular feedback mechanism, which promotes selective constriction of the glomerular afferent arterioles, thereby reducing intraglomerular pressure and renal blood flow. This hemodynamic change elicits a mild hypoxic stimulus in the kidney, stimulating the production and release of erythropoietin (EPO), The rise in EPO levels enhances erythropoiesis, increasing oxygen-carrying capacity of the blood, which ultimately improves systemic oxygen supply and cardiac function [38]. Simultaneously, empagliflozin reprograms post-AMI myocardial energy metabolism by shifting the substrate utilization in cardiomyocytes from glucose oxidation toward endogenous ketone bodies. This metabolic adaptation promotes efficient energy generation via the tricarboxylic acid cycle and oxidative phosphorylation, thereby securing a stable and sufficient ATP supply [39]. Mechanistically, SGLT2 inhibitors mediate cardioprotection through pleiotropic actions. By suppressing the sodium-hydrogen exchanger (NHE) in cardiomyocytes, they attenuate intracellular sodium and calcium accumulation [40]. In parallel, these agents modulate immune-metabolic crosstalk by reprogramming adipose tissue macrophages from a pro-inflammatory M1 phenotype to an anti-inflammatory M2 state [35]. This dual intervention alleviates chronic low-grade inflammation driven by obesity and impedes myocardial fibrotic progression. Collectively, these effects converge to ameliorate key pathological features-including cardiac hypertrophy, fibrosis, maladaptive remodeling, and functional impairment-constituting a pivotal pathway underpinning their cardiovascular protection [41]. Results from the study by Ahmadieh et al. indicated that SGLT2 inhibitor therapy significantly improved serum uric acid levels, body weight, and body mass index (BMI) [42,43]. The discrepancy between their observations and the results of the current study may be attributable to the limited sample size and substantial interindividual heterogeneity within our study population, both of which might have contributed to the divergent outcomes. Furthermore, the results of this study indicated that there was no statistically significant difference in the incidence rates of nausea, urinary tract infection, hypoglycemia, headache, ketoacidosis, and fracture between the two groups ($P = 0.417$), which is consistent with the findings of Huang et al [44]. This further confirms the safety and feasibility of dapagliflozin.

Conclusion

In summary, dapagliflozin provides cardiovascular benefits by reducing inflammatory responses and improving cardiovascular risk factors through multiple pathways, including lowering blood glucose, regulating blood lipids, reducing inflammatory markers, and inhibiting ventricular remodeling. However, this study has several limitations, such as a relatively small sample size, a short follow-up period (only 6 months), and a retrospective design. Additionally, efficacy data were collected only for dapagliflozin without parallel comparison with other SGLT2 inhibitors. Therefore, future prospective, large-sample, long-term, high-quality clinical trials are warranted to compare the effects of different types of SGLT2 inhibitors on cardiovascular outcomes and further validate their cardioprotective effects.

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