

Article

Effects of SGLT-2 Inhibitors on Cardiac Function, Blood Glucose Levels, and Prognosis in Patients with Type 2 Diabetes Mellitus after Percutaneous Coronary Intervention: A Propensity Score Matching Study

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Abstract

Objective: To explore the effect of sodium–glucose cotransporter (SGLT-2) inhibitors on cardiac function, blood glucose level, and prognosis in patients with type 2 diabetes mellitus (T2DM) following percutaneous coronary intervention (PCI). **Methods:** A retrospective analysis was conducted on the clinical data of 195 patients with T2DM who underwent PCI in our hospital between September 2019 and August 2023. The patients were divided into control and observation groups on the basis of medical records. The general demographic information of all participants was collected. Propensity score matching (PSM) was employed to balance baseline data, allowing for the comparison of good cardiac function rates, cardiac function index levels, blood glucose levels, and adverse reactions after matching. **Results:** PSM matching was performed in a 1:1 ratio on the 84 patients enrolled in the two groups. The baseline data of the two groups were not statistically significantly different. Compared with those in the control group, the level of left ventricular ejection fraction had significantly increased and levels of left ventricular end-systolic diameter, glycosylated hemoglobin, fasting blood glucose, and 2 h postprandial blood glucose had significantly decreased in the observation group after treatment ($p < 0.05$). Left ventricular end-diastolic diameter and left ventricular posterior wall thickness ($p > 0.05$) showed no significant changes. The observation group had a higher rate of good cardiac function (95.24% vs. 80.95%) and lower total incidence of adverse reactions (11.90% vs. 30.95%) than the control group ($p < 0.05$). **Conclusions:** SGLT-2 inhibitors can significantly improve cardiac function and blood glucose levels in patients with T2DM after PCI with few adverse reactions and remarkable prognosis recovery effect. Therefore, they can be used in clinical practice.

Keywords

sodium–glucose cotransporter; percutaneous coronary intervention; type 2 diabetes mellitus; cardiac function

Introduction

Type 2 diabetes mellitus (T2DM) is mainly caused by hepatic insulin resistance, peripheral insulin resistance, and islet β cell dysfunction, resulting in uncontrolled hepatic glucose output and affecting peripheral glucose uptake. It is associated with various complications, such as cardiovascular disease and hyperlipidemia. Among these complications, acute myocardial infarction (AMI) is particularly severe [1–3]. Percutaneous coronary intervention (PCI) serves as an effective treatment for AMI by promoting cardiac function recovery and reducing revascularization needs. However, the incidence of postoperative stent restenosis is high, and patients often cannot effectively control blood glucose, resulting in cardiovascular endothelial cell damage, which prevents achieving the expected therapeutic effect and may increase the risk of death [4,5]. Therefore, choosing the appropriate and effective hypoglycemic measures for patients with T2DM combined with AMI is a difficult problem requiring solution in clinical work [6].

Sodium–glucose cotransporter (SGLT-2) inhibitors are a new type of drugs that can reduce glucose reabsorption in the kidney, control glucose secretion, promote glucose excretion, and finally continuously reduce blood glucose levels. Previous studies have shown that SGLT-2 can be used in patients with chronic heart failure to exert independent effects on endothelial function, improve cardiac function, and reduce hospitalization and mortality [7,8]. However, only few studies on the application of SGLT-2 in-

hibitors in patients with T2DM after PCI exist. Therefore, this study retrospectively analyzed the clinical data of 195 patients with T2DM who received PCI at our hospital between September 2019 and August 2023.

Materials and Methods

General Information

The clinical data of patients with T2DM treated with PCI in our hospital from September 2019 to August 2023 were retrospectively analyzed. This study included 114 cases in the control group and 81 cases in the observation group. It was reported to and approved by the ethics committee of Xuancheng People's Hospital (2023-lw011-01). Informed consent to participate in the study was obtained from all the participants. This study was conducted in accordance with the Declaration of Helsinki. The following general data were collected: age, T2DM duration, body mass index, gender, stent number, smoking history, drinking history, and insulin use.

Inclusion criteria: (1) patients after PCI; (2) patients aged 18–75 years and diagnosed with T2DM in accordance with the diagnostic criteria for T2DM based on the Chinese Guidelines for the Prevention and Treatment of Type 2 Diabetes (2020 edition) [9]; (3) receiving glucose-lowering management after PCI, including SGLT-2 inhibitors and other glucose-lowering therapies; (4) conscious persons; (5) nonpregnant or lactating patients; (6) patients who did not participate in other relevant studies in the past month; and (7) patients with complete medical records and related data.

Exclusion criteria: (1) patients with drug allergies; (2) patients with coagulation dysfunction; (3) patients with mental disorders; (4) patients with congenital heart disease; (5) patients suffering from serious infectious diseases; (6) patients with severe organ dysfunction; and (7) patients who had taken SGLT-2 inhibitors in the last 3 months.

Methods

Control Group

Patients in the control group were given metformin tablets after PCI (Specifications: 0.25 g, Shijiazhuang Yin-ing Pharmaceutical Co., Ltd., H20054790, Shijiazhuang, China) combined with other antidiabetic drugs (except SGLT-2 inhibitors) orally. The initial dose was 0.25 g taken once half an hour before meals, 2–3 times a day, after 7 days of treatment. In the absence of adverse reactions, the dose can be adjusted to 1–1.5 g daily but should not exceed 2 g.

Observation Group

Patients in the observation group were given metformin tablets (the same used in the control group) and SGLT-2 inhibitors (dapagliflozin tablets [specification: 10 mg, Astrazeneca Pharmaceuticals Co., Ltd., Sinopmedicine approval number HJ20170119, London, UK]) or canagliflozin tablets (specification: canagliflozin tablets) after PCI at a dose of 100 mg, (Changzhou Heng-bang Pharmaceutical Co., Ltd., Chinese Medicine approval number H20193392, Changzhou, China). Dapagliflozin tablets were administered at a dose of 10 mg once daily. Canagliflozin tablets were given at a dose of 100 mg before the first meal once a day. In the absence of adverse reactions after the patients had continuously taken the drug for 7 days, the dose of the drug can be adjusted to 300 mg once a day. Both groups were treated for 12 weeks. During treatment, blood glucose levels were detected regularly, and the drug dosage and hypoglycemic regimen were adjusted in accordance with the relevant guidelines and patient's tolerance [10].

Observation Indicators

(1) Left ventricular ejection fraction (LVEF), left ventricular end-diastolic diameter (LVEDD), left ventricular end-systolic diameter (LVESD), and left ventricular posterior wall thickness (LVPWT) were measured by using color Doppler ultrasound (Philips GE, E9, Philips Corporation, Amsterdam, Holland) before and 3 months after treatment. The “Chinese Adult Echocardiography Examination and Measurement Guidelines” (2016 edition) was used as a reference for the methods of image acquisition and cardiac structure measurement [11].

(2) The cardiac function recovery degree of the study subjects after PCI was compared in accordance with the New York Heart Association (NYHA) cardiac function classification standard [12]. The NYHA cardiac function classification is divided into four levels, as follows: Level I: Daily activities are not limited and do not cause angina, palpitations, or fatigue. Level II: Physical activity is mildly limited without obvious symptoms at rest, but general physical activity can cause palpitations, angina pectoris, and fatigue. Level III: Physical activity is remarkably limited without obvious symptoms at rest, but mild physical activity can cause palpitations, angina pectoris, shortness of breath, or fatigue. Level IV: Inability to perform physical activities and heart failure at rest. Good rate = (I + II)/total number of cases.

(3) The blood glucose levels of the subjects were evaluated before and 3 months after treatment. A total of 5 mL of venous blood was collected in the morning, and the serum was separated after centrifugation and sent for testing in a timely manner. Glycosylated hemoglobin (HbA1c) level was measured through high-performance liquid chromatography by using an MQ-6000 HbA1c analyzer (Shang-

Table 1. Comparison of the general data of the patients.

Indicators		Before matching				After matching			
		Observation group (n = 81)	Control group (n = 114)	χ^2/t	<i>p</i>	Observation group (n = 42)	Control group (n = 42)	χ^2/t	<i>p</i>
Age (years)		59.45 ± 9.45	58.93 ± 9.24	0.384	0.702	60.76 ± 8.22	61.14 ± 8.45	0.209	0.835
Gender (n, %)	Male	52 (64.20)	69 (60.53)	0.271	0.603	28 (66.67)	26 (61.90)	0.207	0.649
	Female	29 (35.80)	45 (39.47)			14 (33.33)	16 (38.10)		
T2DM duration (years)		8.46 ± 3.26	6.78 ± 2.23	4.274	<0.001	7.43 ± 2.65	7.74 ± 2.86	0.515	0.608
Body mass index (kg/m ²)		24.67 ± 4.25	26.38 ± 4.71	2.601	0.010	25.67 ± 2.61	25.82 ± 2.75	0.256	0.798
Stent number (pieces)		1.16 ± 0.51	1.35 ± 0.53	2.506	0.013	1.25 ± 0.52	1.36 ± 0.49	0.998	0.321
Smoking history (n, %)	Yes	21 (25.93)	33 (28.95)	0.216	0.642	15 (35.71)	10 (23.81)	1.424	0.233
	No	60 (74.07)	81 (71.05)			27 (64.29)	32 (76.19)		
Drinking history (n, %)	Yes	18 (22.22)	31 (27.19)	0.622	0.430	12 (28.57)	13 (30.95)	0.057	0.811
	No	63 (77.78)	83 (72.81)			30 (71.43)	29 (69.05)		
Insulin use (n, %)	Yes	23 (28.40)	35 (30.70)	0.121	0.728	14 (33.33)	11 (26.19)	0.513	0.474
	No	58 (71.60)	79 (69.30)			28 (66.67)	31 (73.81)		
SBP (mmHg)		128.23 ± 10.38	126.45 ± 11.15	1.130	0.260	127.15 ± 9.92	129.37 ± 10.22	1.010	0.315
DBP (mmHg)		87.09 ± 9.26	85.91 ± 10.85	0.795	0.428	85.24 ± 10.05	88.78 ± 9.34	1.672	0.098
Heart rate (time/min)		93.27 ± 10.35	91.23 ± 9.86	1.395	0.165	91.73 ± 9.92	90.82 ± 10.16	0.415	0.679
Complications	Hypertension (n, %)	37 (45.68)	53 (46.49)	2.319	0.198	19 (45.24)	20 (47.62)	0.048	0.826
	Dyslipidemia (n, %)	41 (50.62)	58 (50.87)	0.001	0.971	22 (52.38)	21 (50.00)	0.048	0.827
	Arrhythmia (n, %)	22 (27.16)	31 (29.82)	0.000	0.996	13 (30.95)	14 (33.33)	0.055	0.815
NHYA Level I+II (n, %)		63 (77.78)	82 (71.91)	0.849	0.357	32 (76.19)	31 (73.81)	0.063	0.801

Note: T2DM, diabetes mellitus type 2; SBP, systolic blood pressure; DBP, diastolic blood pressure; NHYA, New York Heart Association.

hai Huizhong Biotechnology Co., Ltd., Shanghai, China). The levels of fasting blood glucose (FBG) and 2 h postprandial blood glucose (2hPBC) were detected by employing an AU500 fasting blood glucose instrument (AU500, Yuyue Medical Equipment Co., Ltd., Danyang China). A glucose detection kit (hexokinase method) produced by Lidman Company (Beijing, China) was used.

(4) Patients were followed up regularly or in the outpatient clinic, and adverse reactions, including angina pectoris, hypotension, hypoglycemia, acute kidney injury, ketoacidosis, and malignant arrhythmia, were recorded. If multiple adverse reactions occurred, only the occurrence of adverse reaction symptoms was recorded, and the total incidence was calculated.

Statistical Processing

SPSS25.0 statistical software (version 25.0, IBM Corp, Armonk, NY, USA) was used to analyze data. Enumeration data (gender, smoking history, drinking history, insulin use, cardiac function recovery, and adverse reactions) were expressed as percentages, and χ^2 test was used. Measurement data (age, T2DM duration, body mass index, stent number, cardiac function index levels, and blood glucose index levels) were expressed in the form of ($\bar{x} \pm s$). $p < 0.05$ was considered statistically significant. Age, gender, T2DM duration, body mass index, stent number, smoking history, drinking history, and insulin use were selected as covariates with treatment methods as dependent variables and each covariate as an independent variable. Propensity scores were calculated through logistic regression. SPSS25.0 statistical software was used to match the control and observation groups in accordance with the nearest neighbor matching method in a 1:1 ratio, and the caliper value was 0.02.

Results

Comparison of the General Data of the Patients

T2DM duration, stent number, and body mass index differed between the two groups before matching ($p < 0.05$). After matching, each group contained 42 cases, and the general data, such as age, gender, T2DM duration, body mass index, stent number, smoking history, drinking history, and insulin use, of the two groups were basically the same ($p > 0.05$), as shown in Table 1.

Comparison of the Cardiac Function Index Levels of the Subjects

No statistically significant differences in the levels of LVEF, LVEDD, LVESD, and LVPWT were found before treatment ($p > 0.05$). Following treatment, the observation group exhibited a significant increase in LVEF level and

a significant decrease in LVESD level compared with the control group ($p < 0.05$). However, no notable change was observed in LVEDD and LVPWT levels ($p > 0.05$), as indicated by Table 2.

Comparison of the Cardiac Function Recovery of the Subjects

The observation group demonstrated a higher rate of favorable cardiac function than the control group (95.24% vs. 80.95%) ($p < 0.05$), as indicated by Table 3.

Comparison of the Blood Glucose Levels of the Subjects

Prior to treatment initiation, no noteworthy differences were detected in HbA1c, FBG, and 2hPBC levels between groups ($p > 0.05$). Nevertheless, after treatment, the observation group displayed significantly lower levels of HbA1c, FBG, and 2hPBC than the control group ($p < 0.05$), as presented in Table 4.

Comparison of Adverse Reactions among the Subjects

Comparing adverse reactions between groups revealed that the total incidence rate was lower in the observation group than in the control group (11.90% vs. 30.95%, $p < 0.05$), as shown in Table 5.

Discussion

At present, the incidence of diabetes in China has reached 11.6% and is increasing annually. Among different types of diabetes, T2DM accounts for the largest number of patients and usually coexists with cardiovascular diseases due to the influence of insulin resistance and hyperglycemia [13,14]. PCI, as the main treatment for patients with AMI, has shown good effects in reducing the incidence of adverse reactions [15]. However, due to the high blood glucose levels in patients with T2DM, blood glucose fluctuation adversely affects endothelial vascular healing. Therefore, the effective regulation of blood glucose levels and improvement of cardiac function in patients with T2DM undergoing PCI have gradually become the focus of clinical attention.

SGLT-2 Inhibitors are Beneficial for Ventricular Remodeling

Compared with those in the the control group, the LVEF level significantly increased and LVESD level significantly decreased ($p < 0.05$) in the observation group after treatment. LVEDD and LVPWT levels showed no significant changes ($p > 0.05$). The good rate of cardiac function in the observation group was higher than that in the control group ($p < 0.05$). SGLT-2 inhibitors can effectively improve cardiac function and ventricular remodeling in pa-

Table 2. Comparison of the levels of the cardiac function indicators of the study subjects ($\bar{x} \pm s$).

Group	n	LVEF (%)		LVEDD (mm)		LVESD (mm)		LVPWT (mm)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Observation group	42	50.86 $\pm$ 4.27	54.38 $\pm$ 3.26	55.14 $\pm$ 4.56	49.52 $\pm$ 3.83	42.36 $\pm$ 6.23	37.92 $\pm$ 3.14	9.71 $\pm$ 0.74	8.96 $\pm$ 0.75
Control group	42	51.12 $\pm$ 3.94	52.91 $\pm$ 3.14	54.86 $\pm$ 4.27	51.17 $\pm$ 4.12	42.90 $\pm$ 6.11	39.36 $\pm$ 3.28	9.52 $\pm$ 0.67	9.28 $\pm$ 0.84
<i>t</i>	-	0.290	2.105	0.291	1.901	0.401	2.055	1.234	1.842
<i>p</i>	-	0.773	0.038	0.772	0.061	0.689	0.043	0.221	0.069

LVEF, left ventricular ejection fraction; LVEDD, left ventricular end-diastolic diameter; LVESD, left ventricular end-systolic diameter; LVPWT, left ventricular posterior wall thickness.

Table 3. Comparison of the cardiac function recovery of the study subjects (n, %).

Group	n	Level I	Level II	Level III	Level IV	Good rate
Observation group	42	23 (54.76)	17 (40.48)	2 (4.76)	0 (0.00)	40 (95.24)
Control group	42	20 (47.62)	14 (33.33)	5 (11.90)	3 (7.14)	34 (80.95)
χ^2	-	-	-	-	-	4.086
<i>p</i>	-	-	-	-	-	0.043

Table 4. Comparison of the blood glucose levels of the study subjects ($\bar{x} \pm s$).

Group	n	HbA1c (%)		FBG (mmol/L)		2hPBC (mmol/L)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Observation group	42	8.67 $\pm$ 1.36	7.14 $\pm$ 0.75	8.53 $\pm$ 1.24	6.29 $\pm$ 0.91	12.35 $\pm$ 4.28	8.24 $\pm$ 1.27
Control group	42	8.21 $\pm$ 1.41	7.67 $\pm$ 0.85	8.95 $\pm$ 1.16	7.32 $\pm$ 0.86	11.84 $\pm$ 4.02	9.12 $\pm$ 1.43
<i>t</i>	-	1.522	3.030	1.603	5.331	0.563	2.982
<i>p</i>	-	0.132	0.003	0.113	<0.001	0.575	0.004

HbA1c, glycosylated hemoglobin; FBG, fasting blood glucose; 2hPBC, 2 h postprandial blood glucose.

Table 5. Comparison of adverse reactions among the subjects (n, %).

Group	n	Angina pectoris	Hypotension	Hypoglycemia	Acute kidney injury	Ketoacidosis	Malignant arrhythmia	Overall Incidence
Observation group	42	0 (0.00)	2 (4.76)	1 (2.38)	1 (2.38)	0 (0.00)	1 (2.38)	5 (11.90)
Control group	42	2 (2.38)	4 (9.52)	4 (9.52)	2 (4.76)	1 (2.38)	0 (0.00)	13 (30.95)
χ^2	-	-	-	-	-	-	-	4.525
<i>p</i>	-	-	-	-	-	-	-	0.033

tients with T2DM and AMI after PCI. LVEF is mainly used to evaluate the contractility of the heart, which has important value in guiding the treatment of cardiovascular diseases. Shi *et al.* [16] showed that after SGLT-2 inhibitor treatment, the left ventricular index levels of patients effectively improved. Among these indices, LVEF increased by 2.458%. Previous studies have demonstrated that SGLT-2 inhibitors are associated with improvement in cardiac function markers; such an improvement may reduce the burden and incidence of atrial fibrillation by promoting the recovery of autophagy, thereby benefiting the reversal of cardiac function [17]. The potential effect of SGLT-2 inhibitors on ventricular remodeling can be analyzed from the perspective of metabolic function. The hearts of patients with AMI are characterized by myocardial metabolic remodeling, which leads to increased myocardial oxygen demand and burden. SGLT-2 inhibitors can switch the mode of myocardial metabolism from glucose to ketone bodies. Given that ketone bodies are a more energy-saving fuel than glucose, SGLT-2 inhibitors can increase myocardial work efficiency and function, improve ventricular contractility, and play a positive role in left ventricular structural remodeling [18–20]. Therefore, SGLT-2 inhibitors can reduce ventricular filling pressure, improve cardiac diastolic and systolic function, and ultimately contribute to ventricular remodeling in patients with T2DM undergoing PCI [21,22].

SGLT-2 Inhibitors can Improve Cardiac Function by Regulating Glucose Metabolism in Vivo

Compared with those in the control group, the levels of HbA1c, FBG, and 2hPBC in the observation group had significantly decreased after treatment ($p < 0.05$). The total incidence of adverse reactions in the observation group was lower ($p < 0.05$) than that in the control group, indicating that SGLT-2 inhibitors could improve the blood glucose level of patients and prevent adverse events. Hong *et al.* [23] showed that HbA1c and FPG levels were controlled in patients with T2DM treated with SGLT-2 inhibitors. Current expert consensus and treatment guidelines generally believe that SGLT-2 inhibitors should not be used in patients with AMI to avoid adverse reactions, such as hypotension, acute kidney injury, malignant arrhythmia, and ketoacidosis [24,25]. However, the current data suggest that these adverse effects are less common in patients with AMI and T2DM treated with SGLT-2 inhibitors than in other patients. In fact, the factor affecting the aggravation of cardiovascular disease in patients is their high blood glucose level, which easily causes abnormal cardiac glucose metabolism and then affects cardiac lipid metabolism, leading to impaired cardiac function [26,27]. Previous studies have suggested that SGLT-2 inhibitors can maintain cardiac hemodynamics, enhance insulin resistance, inhibit oxidative stress, and improve cardiac function by changing myocardial metabolism, lowering blood glucose levels, and

promoting heart-mediated energy processes [28,29]. Therefore, SGLT-2 inhibitors can regulate glucose metabolism and accelerate cardiac function recovery in patients with T2DM after PCI.

First, this work is a Chinese population-based study, and the effect of SGLT-2 inhibitors on cardiac function has not been shown in other populations. Second, due to its small sample size and short selection time, this study had limited sample selection. Third, this study chose a retrospective cohort study design, which may be affected by information bias and confounding factors. However, our team collected the general data of the two groups of patients and performed propensity score matching (PSM), which showed that the two groups were comparable. Despite the above limitations, the results of this study still provide substantial verification of the effectiveness of SGLT-2 inhibitors in patients with T2DM after PCI. Refined studies with long durations and large sample sizes are hoped to supplement the above limitations in the future.

Conclusions

In this retrospective cohort study, SGLT-2 inhibitors had a positive effect on patients with T2DM after PCI. SGLT-2 inhibitors demonstrated good effects in improving cardiac function, blood glucose level, and reducing adverse reactions in patients.

Availability of Data and Materials

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

Author Contributions

XN and LT designed the study; all authors conducted the study; CH and QS collected and analyzed the data. LW and SW participated in drafting the manuscript, and all authors contributed to critical revision of the manuscript for important intellectual content. All authors contributed to editorial changes in the manuscript. All authors gave final approval of the version to be published. All authors participated fully in the work, take public responsibility for appropriate portions of the content, and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or completeness of any part of the work are appropriately investigated and resolved.

Ethics Approval and Consent to Participate

Informed consent to participate in the study was obtained from all the participants. This study was approved by the Medical Ethics Committee of Xuancheng People's Hospital (Approval No.:2023-lw011-01). All methods were carried out in accordance with relevant guidelines and regulations.

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Conflict of Interest

The authors declare no conflict of interest.

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