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*Article*

# Efficacy and Safety of Canagliflozin in STEMI Patients with Type 2 Diabetes after PCI: A Retrospective Study

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## Abstract

**Objective**: To assess the effectiveness and safety of canagliflozin in the management of ST segment elevation myocardial infarction (STEMI) patients with type 2 diabetes mellitus (T2DM) post-percutaneous coronary intervention (PCI). **Methods**: A retrospective analysis on data of patients diagnosed with STEMI and T2DM who underwent PCI treatment at our hospital was performed from June 2020 to September 2023. The patients were divided into two groups based on the exposure factor: the canagliflozin and conventional treatment groups and the canagliflozin and routine treatment groups. Various parameters, such as demographic characteristics, cardiac function indicators, and insulin-related factors, were collected and compared postprocedure. In addition, evaluation of the insulin sensitivity index (ISI), lipid profile parameters, and safety outcomes was conducted. A balanced baseline characteristics of patients was achieved via propensity score matching (PSM) at a 1:1 ratio. Statistical analyses were performed through *t*-tests, nonparametric tests, and chi-square tests. **Results**: This work included data on 156 patients, including 63 and 93 patients in the canagliflozin and routine treatment groups, respectively. Later, each group comprised 63 patients after 1:1 matching by PSM. After treatment, the canagliflozin treatment group exhibited notably reduced levels of N-terminal B-type natriuretic peptide, cardiac troponin T (cTnT), and creatine kinase-MB and a significantly higher level of left ventricular ejection fraction in comparison with the routine treatment group ($p < 0.05$). In addition, following treatment, the canagliflozin treatment group exhibited a significant decrease in homeostatic model assessment (HOMA)-insulin resistance levels and a significant increase in HOMA-$\beta$ levels ($p < 0.05$). Conversely, the groups manifested no significant variances in terms of major adverse cardiovascular events, hypoglycemia, diabetic ketoacidosis, acute kidney injury, and urinary tract infection ($p > 0.05$). **Conclusion**: The concurrent administration of canagliflozin following PCI improves cardiac function, insulin sensitivity, and lipid profile in patients with STEMI and T2DM, which ultimately lowers the likelihood of cardiovascular incidents. Canagliflozin demonstrates favorable clinical safety profiles in such individuals and displays promising prospects for clinical utility.

## Keywords

ST segment elevation myocardial infarction; percutaneous coronary intervention; type 2 diabetes mellitus; canagliflozin

## Introduction

Coronary heart disease represents a prevalent type of atherosclerotic condition with rising incidence and mortality rates annually and emerges as a formidable threat to human health. Atherosclerosis accounts for the primary pathophysiological process underlying coronary heart disease, where perturbation in blood sugar regulation induced by type 2 diabetes mellitus (T2DM) can expedite disease progression. Consequently, coronary heart disease contributes greatly to the mortality of individuals suffering from diabetes; thus, an important interconnection exists between the two conditions throughout disease progression [1,2]. Clinical practices frequently indicate the presence of acute ST segment elevation myocardial infarction (STEMI), which is considered a prevalent cardiovascular emergency, as a form of acute myocardial infarction (AMI). Percutaneous coronary intervention (PCI) is currently the standard treatment for this condition despite its limited clinical efficacy. Following PCI of individuals with type 2 diabetes, the increased risk of cardiovascular adverse events may affect short- and long-term prognoses [3]. As such, the concurrent management of blood glucose levels and the prevention and treatment of chronic cardiovascular complications have emerged as novel focal points in diabetes care research.

Sodium-glucose cotransporter 2 (SGLT2) inhibitor is a novel oral antidiabetic medication and a promising treatment option for T2DM. By hindering glucose reabsorption in renal proximal convoluted tubules, this medication facilitates glucose excretion through the urine [4,5]. In addition to its hypoglycemic properties, studies have highlighted ad-

ditional cardiovascular benefits associated with SGLT2 inhibitors. International guidelines recommend the administration of SGLT2 inhibitors to T2DM patients with coexisting atherosclerotic cardiovascular disease to reduce the risks of hospitalization and mortality resulting from heart failure [6]. Canagliflozin is another type of SGLT2 inhibitor that can target the expression of SGLT2, specifically in renal tubular epithelial cells. This targeted action leads to a decreased glucose reabsorption within the kidneys, which facilitates glucose excretion and ultimately lowers blood sugar levels. In addition, the distinctive mechanism of glucose excretion associated with this medication not only assists in energy expenditure but also contributes to the reduced glucose levels and body weight of patients [7]. Other SGLT2 inhibitors, such as empagliflozin, also present positive cardiovascular effects, including the reduced incidence of heart failure among hospitalized patients and delayed development of renal and cardiovascular disease [8,9]. Nevertheless, additional investigation should be conducted to determine the clinical effectiveness of canagliflozin in individuals with T2DM who have undergone PCI for STEMI.

Given the background provided earlier, an investigation involving propensity score matching (PSM) was performed to examine variances in cardiac function, insulin function, lipid metabolism, and safety among individuals with STEMI and T2DM following PCI compared with those under standard management. We aimed to assess the beneficial effect of incorporating canagliflozin to establish a scientific rationale for post-PCI adjunct therapy with canagliflozin for individuals dealing with STEMI and T2DM.

## Methods

### *Data Source*

This study followed the Declaration of Helsinki in its entirety. In addition, this retrospective cohort study received approval from the Ethics Committee of Affiliated Nantong Hospital of Shanghai University (the Sixth People's Hospital of Nantong). The data were de-identified, the study still obtained informed consent from all respondents. Specifically, the study focused on patients with concomitant T2DM and STEMI who underwent PCI treatment at our hospital between June 2020 and September 2023. The patients were divided into two categories based on whether they received adjunctive therapy or not.

Inclusion criteria: Participants were included if they (1) met the clinical diagnostic criteria for STEMI [10], which is based on distinct evidence from electrocardiograms and echocardiography; (2) fulfilled the clinical diagnostic criteria for T2DM [11], were on long-term hypoglycemic medication, and presented stable blood glucose levels; (3) were hospitalized for STEMI within 12 h of symptom onset; (4) had been diagnosed and treated and were regularly followed up at our medical center; (5) had no prior history of canagliflozin treatment prior to admission; (6) be aged 18 years old or older; (7) had complete observation indexes and clinical data.

Exclusion criteria: The participants were excluded if they had (1) a concomitant malignant tumor, (2) severe dysfunction of vital organs and tissues, (3) a history of antipsychotic therapy, or (4) a history of surgical intervention for valvular heart disease or any form of AMI.

To ensure the proper grouping of T2DM patients with STEMI, we consulted their primary care physicians to verify their medical history and treatment plans. Patients who were already using canagliflozin prior to the onset of STEMI were excluded from the canagliflozin group. For these patients, medication was initiated on the first day of hospitalization and applied the recommended dosage.

Both groups underwent the same surgical procedures performed by the identical surgical team, in accordance standardized PCI protocols. The radial artery approach was consistently applied for all cases, and other standard operating procedures were uniformly applied across both groups. In addition, each patient's individual medical history, comorbidities, and other factors were considered to provide personalized treatment as possible during the formulation of the standardized treatment protocol.

### *Exposure Factors*

All patients were routinely medicated with aspirin (China National Pharmaceutical H20233157, Jiangsu Diseno Pharmaceutical Co., Ltd., Jiangsu, China, 5mg/tablet), oratadine (State Drug License J20120006, AstraZeneca China Pharmaceutical Co.,Ltd., Shanghai, China, 10 mg/tablet), and rosuvastain for antiplatelet aggregation and antihistamine and lipid regulation after PCI. The routine treatment group received standard hypoglycemic medications, including insulin (State Drug License S20191007, Novo Nordisk, Beijing, China, 300 lU/3 mL/strike), metformin (State Drug License No. H20023370, Schweppes, Zhongmei Shanghai, 0.5 g/tablet), and sulfonylureas (State Drug License H10970310, Jinheng Pharmaceutical, Jilin, China), in accordance with their preoperative treatment plan. Blood glucose levels were monitored daily for any fluctuations. Meanwhile, the experimental group received canagliflozin (Janssen-Cilag International NV Company, Belgium, H20170375, Xi'an, China, 100 mg) in addition to routine treatment. The patients were given tablets once daily for 3 months. Follow-up evaluations were conducted for all patients at our hospital 3 months postsurgery.

## *Data Collection*

### Baseline Characteristic

Data on patient demographics, such as age, gender, body mass index (BMI), presence of hypertension, history of T2DM, and duration from symptom onset to treatment initiation, were obtained. Following surgical procedure, laboratory assessments encompassing parameters, including red blood cell count (RBC), white blood cell count (WBC), platelet count (PLT), and hemoglobin levels (Hb), were conducted. The postoperative blood chemistry profile was obtained through measurements of serum albumin (ALB), alanine aminotransferase (ALT), and serum creatinine (Scr). Evaluation of postoperative coagulation function primarily focused on the assessment of prothrombin time (PT).

### Study Variables

The study involved the assessment of cardiovascular risk factor markers, cardiac function index, lipid metabolism index, and clinical safety on the day following the surgery and at the 3-month mark after treatment. The cardiac function indexes analyzed comprised N-terminal B-type natriuretic peptide (NT-proBNP), cardiac troponin T (cTnT), creatine kinase-MB (CK-MB), left ventricular ejection fraction (LVEF), left ventricular end-diastolic diameter (LVEDD), and left ventricular end-systolic diameter (LVESD). In addition, lipid metabolism markers, including triglyceride (TG), total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), and apolipoprotein B (ApoB), were obtained. Moreover, safety variances between the two groups during treatment were compared.

### Detection Method

On the same day postsurgery and at the 3-month follow-up, the NT-proBNP level was assessed using an automatic chemiluminescence instrument, and echocardiography was utilized to measure cardiac function parameters, including LVEF, LVEDD, and LVESD.

Fasting blood glucose (FBG) and fasting insulin (INS) levels were determined postsurgery and at the 3-month follow-up using a blood glucose analyzer and via the chemiluminescence method. Insulin sensitivity indices, such as homeostasis model assessment of insulin resistance (HOMA-IR), HOMA-$\beta$, and insulin sensitivity index (ISI), were derived from specific formulas: HOMA-IR = INS $\times$ FBG/22.5, HOMA-$\beta$ = 20 $\times$ INS/(FBG–3.5), and ISI = ln[1/(FBG $\times$ INS)].

On the day of surgery and at 3 months posttreatment, 5 mL fasting peripheral venous blood was collected from each patient for lipid metabolism index analysis, including TG, TC, LDL-C, ApoB, and other parameters, using the HCC200 plus automatic biochemistry analyzer (Shanghai, China).

The clinical safety of the treatment regimen was assessed based on the incidence of major adverse cardiovascular events (MACE; included myocardial infarction, ischemic stroke, and death from cardiovascular causes), hypoglycemia, diabetic ketoacidosis (DKA), acute kidney injury (AKI), and urinary tract infection during the postoperative period.

## *Statistical Methods*

Statistical analysis was performed using IBM SPSS (IBM Corp., Armonk, NY, USA, Version 27.0). PSM was conducted using a caliper width set at 0.2 standard deviations of the logit to account for baseline differences. The pairing of patients at a 1:1 ratio via nearest neighbor matching ensured the matching of each individual in the canagliflozin treatment group with a corresponding patient in the conventional treatment group. PSM was assessed for effectiveness using the standardized mean deviation (SMD), with SMD $\leq$0.1 indicating an optimal balance in the baseline propensity model.

Through the $\chi^2$ test, the data on counts (gender, prevalence of hypertension, and occurrence of adverse events), that is, the number of cases (%), were analyzed for intergroup differences. Shapiro–Wilk method was used to test the normal distribution of continuous data (such as age, BMI, WBC, RBC, PLT, Hb, ALB, ALT, Scr, PT, NT-proBNP, cTnT, CK-MB, LVEF, LVEDD, LVESD, HOMA-IR, HOMA-$\beta$, ISI, TG, TC, LDL-C, and ApoB). Normally distributed continuous data were expressed as mean $\pm$ standard deviation ($\bar{x} \pm$ s) and compared between groups via an independent sample *t*-test. Within-group comparisons before and after treatment were performed using paired sample *t*-tests. Nonnormally distributed continuous data were presented as median (first and third quartile) [M (P25, P75)]. Pre- and posttreatment comparisons involved repeated-measures analysis of variance. $p < 0.05$ indicated statistical significance before and after management.

# Results

## *Patient Characteristic*

This study enrolled 156 patients, including 63 and 93 patients in the canagliflozin and routine treatment group, respectively. After 1:1 PSM, 63 patients were included in each group. Prior to PSM, notable variances were observed in the mean age, BMI, duration of T2DM, and gender ratio between the two groups ($p < 0.05$). Following the PSM process, 63 patients from the canagliflozin and routine treatment groups were successfully matched. Subsequently, no significant variations were noticed in the mean age, gen-

**Table 1A. Between-group comparison of general clinical characteristics before PSM.**

| Index | Before PSM | | $t/Z/\chi^2$ | $p$ | *SMD* |
|---|---|---|---|---|---|
| | Canagliflozin treatment group (n = 63) | Routine treatment group (n = 93) | | | |
| Age [years, M (P25, P75)] | 56 (54, 59) | 55 (51, 59) | 2.074 | 0.038 | 0.435 |
| Gender [Female, n (%)] | 23 (36.51) | 53 (56.99) | 6.306 | 0.012 | 0.601 |
| BMI (kg/m$^2$, $\bar{x} \pm s$) | 22.71 ± 1.99 | 23.56 ± 2.48 | 2.275 | 0.024 | 0.502 |
| Hypertension [n (%)] | 27 (42.86) | 34 (36.56) | 0.626 | 0.429 | 0.004 |
| Course of T2DM [years, M (P25, P75)] | 10 (9, 11) | 11 (10, 13) | 2.587 | 0.010 | 0.619 |
| RBC [$\times 10^{12}$/L, M (P25, P75)] | 5.03 (4.11, 5.75) | 4.81 (3.80, 5.53) | 1.615 | 0.106 | 0.017 |
| WBC [$\times 10^9$/L, M (P25, P75)] | 5.35 (4.61, 6.32) | 5.31 (4.21, 5.99) | 1.010 | 0.313 | 0.007 |
| PLT [$\times 10^9$/L, M (P25, P75)] | 237.13 (224.53, 268.34) | 248.20 (226.35, 265.98) | 0.876 | 0.381 | 0.006 |
| Hb [g/L, M (P25, P75)] | 134.59 (127.29, 146.84) | 135.91 (120.74, 146.85) | 0.717 | 0.473 | 0.003 |
| ALB [g/L, M (P25, P75)] | 48.52 (42.97, 52.57) | 48.87 (43.51, 53.85) | 0.681 | 0.496 | 0.002 |
| ALT [U/L, M (P25, P75)] | 13.27 (11.49, 16.59) | 14.26 (12.56, 17.50) | 1.690 | 0.091 | 0.019 |
| Scr [μmol/L, M (P25, P75)] | 71.21 (62.38, 81.06) | 69.94 (61.48, 80.61) | 0.576 | 0.565 | 0.002 |
| PT [s, M (P25, P75)] | 11.53 (10.37, 13.21) | 11.63 (10.59, 12.48) | 0.507 | 0.612 | 0.002 |

Note: PSM, propensity score matching; BMI, body mass index; T2DM, type 2 diabetes mellitus; RBC, red blood cell; WBC, white blood cell; PLT, platelet; Hb, hemoglobin; ALB, albumin; ALT, alanine aminotransferase; Scr, serum creatinine; PT, prothrombin time.

**Table 1B. Between-group comparison of general clinical characteristics after PSM.**

| Index | After PSM | | $t/Z/\chi^2$ | $p$ | *SMD* |
|---|---|---|---|---|---|
| | Canagliflozin treatment group (n = 63) | Routine treatment group (n = 63) | | | |
| Age [years, M (P25, P75)] | 56 (54, 59) | 56 (51, 59) | 1.253 | 0.210 | 0.009 |
| Gender [Female, n (%)] | 23 (36.51) | 29 (46.03) | 1.179 | 0.278 | 0.007 |
| BMI (kg/m$^2$, $\bar{x} \pm s$) | 22.71 ± 1.99 | 22.63 ± 1.69 | 0.256 | 0.798 | 0.001 |
| Hypertension [n (%)] | 27 (42.86) | 25 (39.68) | 0.131 | 0.717 | 0.001 |
| Course of T2DM [years, M (P25, P75)] | 10 (9, 11) | 11 (9, 12) | 0.914 | 0.361 | 0.005 |
| RBC [$\times 10^{12}$/L, M (P25, P75)] | 5.03 (4.11, 5.75) | 4.88 (3.77, 5.57) | 1.381 | 0.167 | 0.012 |
| WBC [$\times 10^9$/L, M (P25, P75)] | 5.35 (4.61, 6.32) | 5.31 (4.23, 6.15) | 0.973 | 0.330 | 0.005 |
| PLT [$\times 10^9$/L, M (P25, P75)] | 237.13 (224.53, 268.34) | 248.20 (224.99, 265.09) | 0.646 | 0.518 | 0.003 |
| Hb [g/L, M (P25, P75)] | 134.59 (127.29, 146.84) | 136.41 (122.49, 147.31) | 0.271 | 0.787 | 0.001 |
| ALB [g/L, M (P25, P75)] | 48.52 (42.97, 52.57) | 49.73 (43.64, 54.11) | 0.942 | 0.346 | 0.004 |
| ALT [U/L, M (P25, P75)] | 13.27 (11.49, 16.59) | 14.66 (12.73, 17.46) | 1.918 | 0.055 | 0.019 |
| Scr [μmol/L, M (P25, P75)] | 71.21 (62.38, 81.06) | 69.94 (61.31, 80.12) | 0.507 | 0.612 | 0.002 |
| PT [s, M (P25, P75)] | 11.53 (10.37, 13.21) | 11.86 (10.60, 12.48) | 0.198 | 0.843 | 0.001 |

Note: PSM, propensity score matching; BMI, body mass index; T2DM, type 2 diabetes mellitus; RBC, red blood cell; WBC, white blood cell; PLT, platelet; Hb, hemoglobin; ALB, albumin; ALT, alanine aminotransferase; Scr, serum creatinine; PT, prothrombin time.

**Table 2. Discrepancies in cardiac function parameters between the two groups ($\bar{x} \pm s$).**

| Index | Canagliflozin treatment group (n = 63) | Routine treatment group (n = 63) | $t$ | $p$ |
|---|---|---|---|---|
| NT-proBNP (ng/L) | 365.34 ± 52.54 | 390.62 ± 76.95 | 2.154 | 0.033 |
| cTnT (ng/mL) | 0.23 ± 0.08 | 0.31 ± 0.09 | 2.068 | 0.036 |
| CK-MB (ng/mL) | 4.73 ± 1.23 | 5.43 ± 1.42 | 2.957 | 0.004 |
| LVEF (%) | 49.56 ± 3.09 | 46.02 ± 2.91 | 6.626 | <0.001 |
| LVEDD (mm) | 48.69 ± 2.43 | 48.11 ± 2.48 | 1.337 | 0.184 |
| LVESD (mm) | 39.65 ± 2.52 | 39.54 ± 2.54 | 0.237 | 0.813 |

Note: NT-proBNP, N-terminal brain natriuretic peptide precursor; cTnT, cardiac troponin T; CK-MB, creatine kinase-MB; LVEF, left ventricular ejection fraction; LVEDD, left ventricular end-diastolic dimension; LVESD, left ventricular end systolic diameter.

der distribution, BMI, presence of hypertension, duration of T2DM, average levels of WBC, RBC, PLT, Hb, ALB, ALT, Scr, and PT between the matched groups ($p > 0.05$, Table 1A, Table 1B).

### *Discrepancies in Cardiac Function Parameters between the Two Groups*

Following treatment, the canagliflozin treatment group exhibited significant decreases in the NT-proBNP,

**Table 3. Discrepancies in insulin function parameters between the two groups ($\bar{x} \pm$ s).**

| Index | Canagliflozin treatment group (n = 63) | Routine treatment group (n = 63) | $t$ | $p$ |
|---|---|---|---|---|
| HOMA-IR | 1.58 ± 0.34 | 1.74 ± 0.37 | 2.587 | 0.011 |
| HOMA-$\beta$ | 42.43 ± 3.04 | 38.95 ± 3.5 | 5.966 | <0.001 |
| ISI | –3.91 ± 1.01 | –3.73 ± 1.00 | 1.006 | 0.316 |

Note: HOMA-IR, homeostasis model assessment of insulin resistance; HOMA-$\beta$, homeostasis model assessment of $\beta$ cell function index; ISI, insulin sensitivity index.

**Table 4. Discrepancies in lipid metabolism parameters between the two groups ($\bar{x} \pm$ s, mmol/L).**

| Index | Canagliflozin treatment group (n = 63) | Routine treatment group (n = 63) | $t$ | $p$ |
|---|---|---|---|---|
| TG | 2.15 ± 0.29 | 2.45 ± 0.39 | 4.819 | <0.001 |
| TC | 3.22 ± 0.50 | 3.68 ± 0.46 | 5.335 | <0.001 |
| LDL-C | 2.91 ± 0.43 | 3.00 ± 0.46 | 1.126 | 0.263 |
| ApoB | 1.37 ± 0.21 | 1.34 ± 0.19 | 0.835 | 0.405 |

Note: TG, triacylglycerol; TC, total cholesterol; LDL-C, low density lipoprotein cholesterol; ApoB, apolipoprotein B.

**Table 5. Discrepancies in adverse event rates between the two groups [n (%)].**

| Adverse Event | Canagliflozin Treatment Group (n = 63) | Routine Treatment Group (n = 63) | $\chi^2$ | $p$ |
|---|---|---|---|---|
| MACE | 2 (3.17%) | 4 (6.35%) | 0.680 | 0.340 |
| Myocardial Infarction | 1 (1.59%) | 1 (1.59%) | 1.000 | 0.752 |
| Ischemic Stroke | 1 (1.59%) | 2 (3.17%) | 1.000 | 0.500 |
| Death | 0 | 1 (1.59%) | 1.000 | 0.500 |
| Hypoglycemia | 4 (6.35%) | 2 (3.17%) | 0.680 | 0.340 |
| DKA | 3 (4.76%) | 2 (3.17%) | 1.000 | 0.500 |
| AKI | 2 (3.17%) | 2 (3.17%) | 1.000 | 0.691 |
| Urinary tract infection | 1 (1.59%) | 2 (3.17%) | 1.000 | 0.500 |

Note: MACE, major adverse cardiovascular events; DKA, diabetic ketoacidosis; AKI, acute kidney injury.

cTnT, and CK-MB levels and a significant increase in the LVEF level compared with the routine treatment group ($p < 0.05$, Table 2). No notable variances were detected in the mean LVEDD and LVESD values between the two groups ($p > 0.05$, Table 2). These findings imply a substantial improvement in the cardiac function of STEMI patients with T2DM post-PCI treatment.

### *Discrepancies in Insulin Function Parameters between the Two Groups*

Compared with the routine treatment group, the canagliflozin treatment group showed a notable decrease in the HOMA-IR level and a significant increase in the HOMA-$\beta$ level ($p < 0.05$, Table 3). The two groups revealed no substantial difference in their ISI ($p > 0.05$, Table 3). Given these findings, the concurrent administration of canagliflozin post-PCI may improve insulin functionality in STEMI patients with T2DM.

### *Discrepancies in Lipid Metabolism Parameters between the Two Groups*

The canagliflozin treatment group presented markedly reduced levels of TG and TC compared with the routine treatment group ($p < 0.05$, Table 4). Conversely, the two groups showed no significant variances in the levels of LDL-C and ApoB ($p > 0.05$, Table 4). These findings prove the effective amelioration of lipid metabolism abnormalities in STEMI patients with T2DM through concurrent administration of canagliflozin following PCI.

### *Discrepancies in Adverse Event Rates between the Two Groups*

Following management, the two cohorts exhibited no notable differences in terms of MACE, hypoglycemia, DKA, AKI, and urinary tract infection ($p > 0.05$, Table 5). These findings indicate the clinical safety if concurrent administration of canagliflozin subsequent to PCI.

## Discussion

STEMI is primarily caused by the rupture of vulnerable plaques in coronary arteries, which results in the formation of a secondary thrombus that causes complete blockage of the artery. This condition poses a considerable threat, with the potential to cause shock, heart failure, or become life threatening in severe cases. According to research, the majority of AMI patients exhibit elevated blood sugar levels due to metabolic irregularities. Various studies have

identified elevated blood sugar levels as a prognostic indicator upon admission of patients diagnosed with AMI or acute STEMI [12]. Canagliflozin is an SGLT inhibitor, with SGLT1 and SGLT2 as the two main subtypes found in the body. SGLT1 primarily occupies the brush border of the small intestinal mucosa and S3 segment of the renal proximal convoluted tubule. This subtype inhibitor is characterized as a transporter with a high affinity but low transport capacity. On the other hand, SGLT2 is located in the S1–S2 segment of the renal proximal convoluted tubule and functions as a transporter with a low affinity but a high transport capacity. During its enty to the patient's intestine, the drug promptly inhibits SGLT1, which leads to a reduction in glucose absorption. In addition, although 10% of glucose in glomerular filtrate is reabsorbed through SGLT1 and the remaining 90% through SGLT2, the inhibition of the reabsorption of 30% to 50% of glucose in the kidney promotes the increase in urinary glucose excretion for patients [13]. Moreover, SGLT2 inhibitors can lower blood pressure, decrease body weight, and reduce the levels of urinary protein and serum uric acid; such findings indicate that the improvement pf metabolic factors with these medications may offer potential advantages for patients following STEMI [14–16].

The canagliflozin treatment group revealed a notable decrease in the level of NT-proBNP and a substantial increase in the level of LVEF compared with the conventional treatment group. This finding indicates that the utilization canagliflozin post-PCI can substantially improve the cardiac function of STEMI patients with T2DM. Canagliflozin may improve ventricular remodeling and heart function through reduction of inflammation and oxidative stress response mechanisms. Cardiac microvascular endothelial cells (CMECs) contribute to coronary microcirculation given that the preservation of their structural integrity and functionality directly affects coronary flow reserve and myocardial perfusion [17]. In individuals with T2DM, chronic disturbances in blood sugar regulation may lead to structural impairment of CMEC, which contributes to coronary artery microcirculation abnormalities [18]. These impairments can result in crucial consequences for the cardiac health of patients. Therefore, this study was focused on emphasizing the pivotal role of CMECs in coronary microcirculation in patients with T2DM and the potential of canagliflozin to improve their activity and functionality. Canagliflozin can potentially enhance the viability of CMECs and vascular endothelial function and ameliorate coronary artery microcirculation in diabetic mice [19]. These findings indicate that through targeting of CMEC and improvement in microcirculation, canagliflozin may benefit the cardiac function of patients with STEMI. Although coronary angiography is considered the most effective diagnostic tool for coronary heart disease, it primarily focuses on structural visualization of larger coronary arteries, which account for a small portion (5%) of the entire coronary artery circulation. Consequently, the remaining 95% of the coronary artery microcirculation is often disregarded during diagnosis, which creates a diagnostic "blind spot" [20]. The improvement of coronary microcirculation function may be a key factor to improving the cardiac function among STEMI patients following PCI.

By increasing glucose excretion in the urine, canagliflozin directly influences pancreatic $\alpha$ cells, which leads to elevated levels of glucagon, decreased stress response of the endoplasmic reticulum, and mitigation of high glucose toxicity of the system. This condition, in turn, mitigates glycolipid toxicity-induced islet $\beta$-cell death, fosters $\beta$-cell proliferation, hastens functional recovery, and ultimately improves insulin resistance (IR) and blood glucose control [21,22]. Consistent with these findings, the canagliflozin treatment group exhibited substantially reduced levels of HOMA-IR and markedly higher levels of HOMA-$\beta$ compared with the routine treatment group. However, the two groups showed no disparity in terms of their ISI, which indicates that the concurrent administration of canagliflozin post-PCI may ameliorate insulin function in individuals with STEMI and concomitant T2DM.

TC and TG commonly serve as indicators for the assessment of the status of blood lipid metabolism, and their levels exhibit a positive association with the extent of abnormal lipid metabolism. ApoB, a lipid akin to low-density lipoprotein, is synthesized by the liver and considered an independent risk factor for STEMI. Elevated ApoB levels in the body show linkage toe increased occurrence of cardiovascular complications [23]. This research unveiled the considerably reduced TG and TC levels of the canagliflozin treatment group compared with the routine treatment group. This outcome suggests the ameliorated lipid metabolism disorders in STEMI patients complicated with T2DM after concurrent administration of canagliflozin post-PCI. Although insulin alone can stabilize blood glucose levels and minimize fluctuations, it performs poorly diminishing visceral fat deposition, which leads to limited improvement in the waist circumference (WC) among obese T2DM patients. Canagliflozin intervenes with energy metabolism by restraining sodium-glucose co-transporters, activating adenylate-activated protein kinase, and improving the phosphorylation of acetyl-CoA carboxylase. This action decreases the efficiency of fatty acid synthesis and promotes oxidative breakdown. Through modulation of excessive energy metabolism and consistent facilitation of calorie expenditure, canagliflozin ultimately aids in reducing subcutaneous and visceral fat levels [24]. Furthermore, canagliflozin can promote the secretion and release of insulin, boost insulin sensitivity, inhibit glucagon secretion after meals, regulate the apoptosis of islet $\beta$-cells, decrease appetite, improve the feeling of satiety, extend gastric emptying, curb appetite, break down fat efficiently, and regulate fat synthesis [25].

A CANVAS study investigated the effect of canagliflozin on cardiovascular risk of patients afflicted with T2DM. Its methodology and outcomes closely mirrored those of the EMPA-REG OUTCOME study. The results reveal the reduced incidence of MACE in the canagliflozin group compared with the placebo group. In addition, more than a 30% decrease was observed in the occurrence of heart failure among patients in the canagliflozin group compared with those in the placebo group. Another clinical trial, the CREDENCE study, further validated the benefits of canagliflozin in cardiovascular protection and the risk reduction for T2DM patients with concomitant coronary heart disease [9,26,27]. In this research, following management, the two cohorts showed no notable variance in terms of MACE, hypoglycemia, DKA, AKI, and urinary tract infection. Whether the administration of canagliflozin can mitigate the prevalence of unfavorable outcomes post-PCI in individuals with STEMI and comorbid T2DM remains inconclusive. Such observation will underscore the overall safety profile associated with the concurrent application of canagliflozin in post-PCI settings.

Both treatment groups received standard care for T2DM, including the use of other glucose-lowering agents, that might have influenced our observations. Although a specific subanalysis of the contribution of these medications was not performed, their potential effect must be acknowledged. Future studies should evaluate the influence of concomitant hypoglycemic medications on the therapeutic efficacy of canagliflozin to better understand its role in T2DM management. Physicians must consider a patient's overall condition, including concurrent medication use, to make informed treatment decisions. Despite the valuable insights of our study, further research is needed to validate and expand upon our findings.

However, we must also acknowledge the limitations of our study. First, being a single-center retrospective research with a relatively limited sample size, inherent bias of the findings, was still possible regardless of the utilization of PSM. Second, although we examined the effects of canagliflozin treatment on patients with T2DM and STEMI, we did not conduct a hierarchical analysis on the degree of the disease. This limitation possibly restricts the generalizability of our results given that the severity of illness can affect treatment outcomes. Moreover, our study only conducted a 3-month follow-up after PCI surgery, which limits our ability to assess the long-term efficacy of the intervention. Therefore, future research with extended follow-up periods, considering stratification based on disease severity, is necessary to evaluate the sustained effectiveness of these interventions. Moreover, further investigations utilizing animal models would be valuable in elucidating the underlying mechanisms responsible for the therapeutic effect of PCI on this patient population. Lastly, our study was unable to obtain more detailed data on the surgical procedures, which adds to the limitations.

## Conclusion

In this retrospective analysis involving PSM, the administration of canagliflozin post-PCI considerably improved cardiac function, insulin sensitivity, and lipid metabolism in patients with STEMI concomitant with T2DM. As a result, a reduced risk of cardiovascular events was observed. Significant differences were observed between the canagliflozin and conventional treatment groups in terms of several key indicators, such as NT-proBNP, cTnT, CK-MB levels, LVEF levels, HOMA-IR levels, HOMA-$\beta$ levels, TG levels, and TC levels, which highlight the effectiveness of canagliflozin in these areas. Importantly, canagliflozin showed a favorable safety profile in this patient population, supporting its potential for widespread clinical use. However, future research should focus on the confirmation of these outcomes and exploration of the long-term efficacy and safety of canagliflozin in this patient population.

## Availability of Data and Materials

Data to support the findings of this study are available on reasonable request from the corresponding author.

## Author Contributions

LC and NZ designed the research study; LC and LZ performed the research; NZ collected and analyzed the data. All authors have been involved in drafting the manuscript and all authors have been involved in revising it critically for important intellectual content. All authors give final approval of the version to be published. All authors have participated sufficiently in the work to take public responsibility for appropriate portions of the content and agreed to be accountable for all aspects of the work in ensuring that questions related to its accuracy or integrity.

## Ethics Approval and Consent to Participate

The patients all signed an informed consent form.This study has been approved by the ethics committee of Affiliated Nantong Hospital of Shanghai University (the Sixth People's Hospital of Nantong), approval No. NT-LYLL2024011.

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## Conflict of Interest

The authors declare no conflict of interest.

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