Cardiovascular Diabetology

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Cardiorenal protection with dapagliflozin in patients with type 2 diabetes mellitus and chronic coronary syndrome undergoing percutaneous coronary intervention: a registry cross-sectional study

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# Abstract

**Importance** Although sodium–glucose cotransporter-2 (SGLT2) inhibitors have cardiorenal benefits, their efficacy in patients with type 2 diabetes mellitus (T2DM) and chronic coronary syndrome (CCS) undergoing percutaneous coronary intervention (PCI) remains underexplored.

**Objective** To evaluate the cardiorenal protective effects of the SGLT2 inhibitor dapagliflozin in patients with T2DM and CCS receiving PCI.

**Design, setting, and participants** This was a cross-sectional analysis of 1,430 patients from a tertiary hospital database who underwent PCI (January 1, 2018, to March 31, 2022).

Main outcomes and measures Cardiac outcomes (PMI/4aMI) and renal outcomes (eGFR and CI-AKI).

**Results** After 1:1 propensity score matching (PSM) (176 dapagliflozin vs. 176 control), the dapagliflozin group showed significantly lower PMI/4aMI rates pre-PSM (39.78% vs. 66.99%; OR 0.862, 95% CI 0.823–0.904; p < 0.001) and post-PSM (39.77% vs. 60.23%; OR 0.660, 95% CI 0.531–0.821; p < 0.001), with sustained significance after adjustment (adjusted OR 0.436, 95% CI 0.285–0.668; p < 0.001). Subgroup analyses highlighted increased protection in patients aged  $\geq 65$  years, those with multivessel disease, and those with higher contrast volumes. Renal outcomes (CI-AKI<sub>ESUR</sub> and CI-AKI<sub>KDIGOs</sub>) were not significantly different before or after PSM or after adjustment (all p > 0.05).

**Conclusions and relevance** Dapagliflozin exerted robust cardioprotective effects against PMI/4aMI in patients with T2DM and CCS undergoing PCI, particularly among patients in high-risk subgroups, but it did not significantly reduce the risk of CI-AKI. These findings support the peri-PCI use of dapagliflozin to mitigate cardiac risk while highlighting the need for further research to elucidate its renal effects in this population.

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**Keywords** Dapagliflozin, SGLT2 inhibitors, Cardiorenal protection, Type 2 diabetes mellitus, Chronic coronary syndrome, Percutaneous coronary intervention

# **Graphical abstract**

Cardio-renal protection with dapagliflozin in patients with type 2 diabetes mellitus and chronic coronary syndrome undergoing percutaneous coronary intervention: a registry cross-sectional study



# **Research insights** What is currently known about this topic?

- 1. SGLT2 inhibitors reduce cardiorenal risks in T2DM and CVD patients.
- 2. Controversy exists on SGLT2 inhibitors' renal benefits post-PCI.

# What is the key research question?

Does dapagliflozin provide cardiorenal protection in T2DM and CCS patients undergoing PCI?

# What is new?

- 1. First study linking dapagliflozin to reduced PMI/4aMI in T2DM-CCS-PCI patients.
- 2. Dapagliflozin showed cardiac protection but no significant CI-AKI reduction.
- 3. Enhanced benefits in elderly, multivessel disease, and high-contrast subgroups.

# How might this study influence clinical practice?

Supports peri-PCI dapagliflozin use for cardiac risk reduction in high-risk T2DM-CCS patients.

# Introduction

Sodium-glucose cotransporter 2 (SGLT2) inhibitors lower blood glucose levels by inhibiting glucose reabsorption in the renal proximal tubule, and they were first indicated for the treatment of type 2 diabetes mellitus (T2DM) [1]. SGLT2 inhibitors have shown cardiorenal protective properties and are particularly beneficial in patients with cardiovascular disease (CVD) and chronic kidney disease (CKD) complicated by T2DM [2].

Several theories propose that the cardiovascular effects of SGLT2 inhibitors are mediated by the inhibition of sodium-hydrogen exchanger 1 (NHE1) in heart muscles and sodium-hydrogen exchanger 3 (NHE3) in the proximal tubules of the kidneys. NHE3 is responsible for most electrolyte and water reabsorption in the kidneys, thus reducing the preload via diuresis and natriuresis [3]. In the proximal convoluted tubules (PCTs) of the kidney, SGLT2s are observed where maximal glucose reabsorption occurs in the blood. SGLT2 inhibitors block these transporters in the PCTs of the kidneys, causing glucosuria, which helps lower blood glucose levels in patients with T2DM [4].

In patients with T2DM and heart failure (HF), SGLT2 inhibitors, including dapagliflozin, have shown protective cardiac and renal effects [5–11]. Previous trials on whether SGLT2 inhibitors exert protective effects against renal events have been controversial [12, 13]. However, whether SGLT2 inhibitors exert myocardial and renal protective effects in patients with T2DM and chronic coronary syndrome (CCS) undergoing percutaneous transluminal coronary intervention (PCI) has not been determined. Therefore, our study aimed to explore the specific protective effects of dapagliflozin on the incidence of cardiorenal events.

## Methods

### Study design and data sources

This was a cross-sectional analysis of patients with T2DM and CCS undergoing PCI. Data were extracted from the hospital information system (HIS) of Beijing Hospital (a tertiary general hospital) from January 1, 2018, to December 31, 2021. The database included comprehensive details on admission and discharge, age, sex, alcohol consumption, medications, interventional procedures, and laboratory test results of the patients.

## Patient recruitment criteria

The eligibility criteria included the following: inpatients with complete datasets,  $age \ge 18$  years, diagnosis of T2DM with CCS, documentation of dapagliflozin use >7 days before PCI (study group) or no SGLT2 inhibitor use during PCI (control group), normal or mildly impaired liver function, and normal or mildly impaired renal function. For multiple related admissions, each admission data point was recorded to avoid any omission.

The exclusion criteria were as follows: drug allergies and ketoacidosis that occurred after taking dapagliflozin; noncoronary artery diseases that seriously affect heart function, such as moderate to severe valvular heart disease, artificial heart valve replacement, congenital heart disease and other heart diseases; coronary artery bypass grafting; New York Heart Association cardiac function scale III-IV; serious diseases that affect lifespan, such as malignant tumours, organ failure due to various causes, severe immune system diseases, haemodynamic instability, severe anaemia, and severe infections; use of drugs with clear cardiotoxic effects, such as anthracyclines; and incomplete information (illogical data and missing or insufficient data). Any patient with such a history was excluded.

## **Definition of outcome**

The primary outcomes included cardiac and renal outcomes. The cardiac outcome was periprocedural

myocardial infarction (PMI) or type 4aMI. The definition of PMI was  $a > 5 \times 99$ th percentile upper reference limit (URL) increase in cardiac troponin I (cTnI) within 48 h of the procedure. The definitions of type 4aMI were  $> 5 \times 99$ th percentile URL cTnI increase within 48 h of the procedure and at least one of the following: (1) evidence of prolonged ischaemia ( $\geq 20$  min) as demonstrated by prolonged chest pain; (2) ischaemic ST changes or new pathological Q waves; (3) angiographic evidence of a flow-limiting complication; or (4) imaging evidence of new loss of viable myocardium or new regional wall motion abnormality [14].

We identified contrast-induced acute kidney injury (CI-AKI) events via a laboratory-based algorithm, which identifies events on the basis of the European Society of Urogenital Radiology (ESUR) serum creatinine criteria (increase in serum creatinine levels by  $\geq$  44.2 µmol/L or 0.5 mg/dL within 72 h or increase in serum creatinine levels by  $\geq$  1.25 times the baseline value; hereafter referred to as CI-AKI<sub>ESUR</sub>) [15]. As part of a sensitivity analysis, we additionally identified inpatient episodes of acute kidney injury (AKI) via the Kidney Disease: Improving Global Outcomes (KDIGO) serum creatinine criteria (increase in serum creatinine levels by  $\geq 26.52 \ \mu mol/L \ (0.3 \ mg/dL)$ within 48 h or increase in serum creatinine levels by  $\geq 1.5$ times the baseline value before coronary arteriography (CAG); hereafter referred to as AKI<sub>KDIGO</sub>) and recorded the corresponding dates [16]. The final laboratory values before patients underwent CAG were used as the baseline data for analysis. This approach aimed to accurately represent each patient's baseline condition before the procedure. The renal functions (serum creatinine and urea nitrogen levels) of patients with CCS were assessed upon admission and at 24, 48, and 72 h after PCI.

#### Statistical analysis

Categorical data are presented as frequencies, and they were compared via the chi-square test or Fisher's exact test, as appropriate. Continuous data are reported as medians and interquartile ranges (IQRs), and they were analysed via either Student's t-test or the Mann–Whitney U test. Univariate and multivariate logistic regression analyses were performed to determine the correlation between candidate variables and nonrecommended lowdose drugs. Statistical analyses were performed via the statistical software SPSS 26.0, and p < 0.05 was considered to indicate a statistically significant difference.

# **Ethics and trial registration**

The study protocol complied with the good clinical practice standards for drugs and the ethical guidelines specified in the revised Declaration of Helsinki (2013). The Beijing Hospital Ethics Committee approved this study (Approval Letter Number: 2023BJYYEC-228-01), and the study was registered at the Chinese Clinical Trial Registry (Registration number: ChiCTR2300075232). Data extracted from medical records were retrospectively reviewed, deidentified, and anonymized before analysis; therefore, the requirement for informed consent was waived for this study.

### Results

### Participant characteristics

Among the admitted patients, 1,430 met the inclusion criteria. A total of 176 cases and 176 controls were paired after propensity score matching (PSM) based on 5 covariates. A diagram of the study process and exclusion of participants is shown in Fig. 1. All the included patients had stable vital signs before PCI. Most patients were asymptomatic after the operation. However, some patients experienced symptoms such as chest pain or oliguria, which corresponded to PMI/4aMI and AKI in the outcome indicators.

The characteristics of the randomly selected participants before PSM are shown in Table 1. The age of the participants was 65 years (range, 59-71), and 75.66% of the participants were male. Both groups had similar baseline demographics, comorbidities, and laboratory characteristics. No difference was observed in the proportions of patients with previous myocardial infarction (MI) (p=0.944), previous PCI (p=0.684), hypertension (p=0.618), or other comorbidities (p>0.05) that might affect cardiac function. No differences were noted in the hypersensitive cardiac troponin I (hs-TNI) (p = 0.090), brain natriuretic peptide (BNP) (p = 0.331), creatine kinase-MB (CK-MB) (p = 0.947), or serum creatinine (Scr) (p=0.270) levels or in the estimated glomerular filtration rate (eGFR) (p = 0.187), which are markers that reflect cardiac and renal function. In terms of the baseline transthoracic echocardiogram parameters, the mean ejection fraction was 58.00% in the dapagliflozin group and 58.69% in the non-SGLT2 inhibitor group.

In this cohort study, propensity score matching (PSM) was performed to match the study group with the control group. Five covariates were selected for PSM: two variables with statistical differences at baseline, specifically whether ARNI and GLP-1RA were used in combination therapy, and three variables that showed statistical differences after the first-round PSM, namely, age, history of hypertension, and Hgb level. These covariates were chosen from those presenting statistical significance (P < 0.05) in the univariate analysis and those displaying differences after the initial PSM. The characteristics of the randomly selected participants after PSM are shown in Table 2.

#### Cardiac and renal outcomes

Compared with the control group, the dapagliflozin group exhibited significantly lower rates of PMI/4aMI both pre-PSM (39.78% vs. 66.99%; OR 0.862, 95% CI 0.823–0.904; p < 0.001) and post-PSM (39.77% vs. 60.23%; OR 0.660, 95% CI 0.531–0.821; p < 0.001). Multivariate analysis confirmed this association post-PSM (adjusted OR 0.436, 95% CI 0.285–0.668; p < 0.001).

For renal outcomes, CI-AKIESUR showed a nonsignificant trend pre-PSM (OR 0.941, 95% CI 0.887–0.998; p=0.114), which was attenuated post-PSM (OR 0.779, 95% CI 0.492–1.233; p=0.358). Similarly, CI-AKI<sub>KDIGO</sub> demonstrated no significant differences pre-PSM (OR 0.963, 95% CI 0.890–1.042; p=0.415) or post-PSM (OR 0.828, 95% CI 0.494–1.390; p=0.521). After covariate adjustment, neither CI-AKI<sub>ESUR</sub> (adjusted OR 0.561, 95% CI 0.161–1.953; p=0.364) nor CI-AKI<sub>KDIGO</sub> (adjusted OR 0.659, 95% CI 0.183–2.376; p=0.524) achieved statistical significance.

For the subgroup analysis of cardiac events, among the populations aged  $\ge 65$  years, those with multivessel



# Table 1 Basic characteristics of patients in two groups before propensity matching

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SBR mmlg (QB)125.00 (114.00-136.00)0.807DBR mmlg (QB)125.00 (14.00-730.00)0.801DBR mmlg (QB)680.00 (44.00-72.00)60.00 (44.00-72.00)0.571DVEF, 80 (QR)680.00 (64.00-72.00)60.00 (64.00-72.00)0.570Comabilities580.00 (580.0-64.00)60.00 (64.00-72.00)0.570Previous (ARL, n(%)40 (27.73)263 (20.97)0.684Previous (ARL, n(%)31.70201.1590.764Previous (ARL, n(%)31.7021.01.590.714Hypertension, n(%)11.62.5127.72.140.632Hypertension, n(%)21.01.930.7141.55Hypertension, n(%)21.01.931.550.59Laborator, n(%)21.01.931.550.59Laborator, n(%)21.01.931.550.59Laborator, n(%)21.01.931.0010.50Laborator, n(%)20.01.911.50(12.02.01.510.59Laborator, n(%)20.01.911.50(12.02.01.510.59Laborator, n(%)20.01.01.571.500.97Laborator, n(QR)50.40 (22.15.116.49)53.41(24.75.118.84)0.331Laborator, n(QR)0.50 (0.72.90.01)7.50 (0.72.90.01)7.50 (0.72.90.01)7.50 (0.72.90.01)Scr. marg/n1 (QR)0.50 (0.72.90.01)0.50 (0.72.90.01)0.50 (0.72.90.01)0.50 (0.72.90.01)0.50 (0.72.90.01)0.72Cott, marg/n1 (QR)0.50 (0.72.90.01)0.58 (0.57.1-93.00)0.720.720.720.720.720.720.720	Drinking status, n (%)	89 (50.57)	649 (51.75)	0.830
DBP_moting (IRQN71.50 (6500 74.00)71.60 (64.00 72.00)6.831HR, bpm (IOR)6800 (64.00-72.00)6.00 (67.0-72.00)6.371UEFF, % (IOR)6800 (64.00-72.00)6.000 (67.0-66.00)3.00Comobidities7800 (58.00-64.00)6.000 (57.0-66.00)0.00Previous (N, N%)40 (22.73)278 (22.17)6.04Previous (N, N%)31 (7.30)276 (20.97)0.644Previous CAGS, n (%)31 (7.30)70 (1.59)6.033A f, n (%)11 (6.25)93 1 (72.4)0.618A f, n (%)14 (62.94)1002 (79.90)0.395Ischemic stroke n (%)11 (1.93)150 (1.23)0.968Previous chroha hemorthage, n (%)010.0041.00.040.00COPD, n (%)10.01 (20.217.80)0.9040.906CoPD, n (%)10.01 (20.217.80)0.9040.904COPD, n (%)10.01 (20.217.80)0.9040.904COPD, n (%)10.01 (20.217.80)0.9040.904COPD, n (%)10.01 (20.217.80)0.9040.904COPD, n (%)10.01 (20.215.911.648)1.80 (1.10.3.70)0.904CC, Un (OR)0.504 (21.51-116.48)1.80 (1.01.3.70)0.904CC, Un (OR)0.504 (21.51-116.48)1.80 (1.01.3.70)0.904CC, Un (OR)0.504 (21.51-116.48)1.80 (1.01.3.70)0.904CC, Un (OR)0.504 (21.51-116.48)1.80 (1.01.3.70)0.904CC, Un (OR)0.504 (21.51-116.48)1.80 (1.01.21.70)0.904 <trr>CC, Un (OR)</trr>	SBP, mmHg (IQR)	125.00 (114.00–139.00)	125.00 (114.00–136.00)	0.987
Hi, Dgm (OR)6800 (6400-72.00)6201 (67-72.00)527.LVEF, % (OR)58.00 (58.00 - 64.00)60.00 (57.00 - 65.00)00.00Comobidides78.02 (217)99.49Pervious CL, (Ng)40 (22.73)28.02 (217)0.644Pervious CL, (Ng)11.020201.029.010.651A, nobo11.070201.029.010.651Hypertension, n(%)11.023201.029.010.651Hypertension, n(%)11.623.01100.027.9000.858Hypertension, n(%)21.01.93100.027.9000.858Previous CL, Ng)21.01.93100.01.0000.968Previous Cerebral hemorrhage, n(%)010.01.020.010COPD, n (%)0.104.51.8-21.08)10.004.20-71.8010.969Previous Cerebral hemorrhage, n(%)0.454 (5.18-21.08)10.004.20-71.8010.969COPD, n (%)0.104.51.8-21.08)10.004.20-71.8010.970CoPD, n (%)0.454 (5.18-21.08)10.004.20-71.8010.970CoPD, n (%)0.454 (5.13-21.08)10.0104.20-71.8010.970CoPD, n (%)0.454 (5.13-21.08)10.004.20-71.8010.970CoPD, n (%)0.454 (5.13-10.97)0.9310.971CoPD, n (%)0.454 (5.13-21.08)10.004.20-71.8010.921CoPD, n (%)0.556 (1.79-92.00)7.001 (3.00-71.000.921CoPD, n (%)0.556 (1.79-92.00)10.61 (1.91.116)0.921CoPD, n (%)0.550 (1.79-92.00)10.62 (3.85.04-71)0.921CoPD, n (%) </td <td>DBP, mmHg (IQR)</td> <td>71.50 (65.00–78.00)</td> <td>71.00 (64.00–79.00)</td> <td>0.831</td>	DBP, mmHg (IQR)	71.50 (65.00–78.00)	71.00 (64.00–79.00)	0.831
IVF5 %OR)S800 (S800-64.00)60.00 (57.00-65.00)0.03ComorbiditiesDevious (M, 1%)40 (22.73)27.8 (2.1.7)0.944Previous (R) (%)34 (19.3)26.3 (0.07)0.654Hypertonsion, n (%)31 (7.3)20.1 (59)0.55Hypertonsion, n (%)13 (7.3)77.61.40.637Hypertonsion, n (%)11 (6.25)0.27.340.714Hypertonsion, n (%)14 (82.94)1002 (79.93)0.35Ischemic stroke, n (%)010.02.80.908Ischemic stroke, n (%)010.008,00.000COPD, n (%)010.004 (20-17.80)0.001COPD, n (%)0.441.91.511.91 (1.0.3.70)0.947Ischemic stroke, n (%)0.45 (1.821.08)1.000 (420-17.80)0.301IsRP pg/m1 (QR)0.44 (2.3.51)1.80 (1.10.3.70)0.947CK, UL (QR)67.50 (1.752.00)7.600 (3.30-118.75)0.311Str, m (GR)0.85 (0.70-10.1)8.56 (0.72-10.0)0.361Str, m (GR)0.85 (0.70-10.1)8.56 (0.50-59.5)0.372GK, m/min/L (DR)0.55 (1.752.00)7.600 (3.30-118.75)0.131GK, m/min/L (DR)0.56 (0.7-10.0)0.860 (7-21.00)0.872GK, m/min/L (DR)0.55 (1.752.00)7.600 (3.60-118.75)0.311GK, m/min/L (DR)0.55 (1.752.00)7.590 (3.50-119.152)0.372GK, m/min/L (DR)0.56 (7.7.20-10.1)8.56 (4.60-59.5)0.372GK, min/L (DR)0.56 (3.5-10.1)8.56 (4.6	HR, bpm (IQR)	68.00 (64.00-72.00)	68.00 (64.00-72.00)	0.571
Comorbidities         Vervious VI, n (%)         40 (22.73)         263 (25.97)         0.694           Previous CABG, n (%)         31 (70)         20 (1.59)         0.76           Hypertension, n (%)         13 (7.3)         27 (7.4)         0.618           Af, n (%)         13 (7.3)         27 (7.4)         0.618           Af, n (%)         13 (7.3)         27 (7.4)         0.618           Hypertension, n (%)         11 (6.2)         27 (7.4)         0.395           Ischemic stroke, n (%)         0         10.008         0.900           OPC n (%)         0         19 (1.52)         0.016           BitP parting (QR)         0.45 (5.18-21.88)         0.000 (420-17.80)         0.901           Laboratory variables	LVEF, % (IQR)	58.00 (58.00-64.00)	60.00 (57.00-65.00)	0.300
Pervious ML n (%)40227)78 (22.17)0441Pervious CABC n %)34 (19.32)63 (20.97)0.684Pervious CABC n %)127(7.16)20 (15.9)0.75Hypertnesion n (%)13 (7.39)77 (6.14)0.637Hypertnesion n (%)11 (6.25)92 (7.34)0.714Hypertnesion n (%)14 (62.84)1002 (79.90)0.958Ischemic stroke, n (%)01002 (79.90)0.958Ischemic stroke, n (%)01003 (20.91)0.900COPEn (%)01000 (4.20-17.80)0.900COPEn (%)0.942 (15.116.49)5.341(24.75-118.44)0.31Isobardov variables1.901 (20-3.51)1.801 (10-3.70)0.970CK-MAB ng/m (IQR)0.924 (72.116.49)5.341(24.75-118.44)0.31Ser, mg/d (IQR)0.800 (20-1.01)0.806 (27-1.00)0.970CK-MAB ng/m (IQR)0.800 (20-1.01)0.806 (27-1.00)0.970CK-MAB ng/m (IQR)0.224 (73.94-10.70)1.863 (5.37-1.03)0.271CK-MAB ng/m (IQR)0.826 (20-1.01)0.836 (02-1.01)0.270CK-MAB ng/m (IQR)0.824 (20-4.102.00)1.863 (4.0-6.93.00)0.272CK-MAB ng/m (IQR)0.824 (57.94-107.00)1.863 (4.0-6.91.00)0.270CK-MAB ng/m (IQR)0.826 (20-2.20)6.10 (5.20-7.10)0.861LD, Cramol/L (IQR)6.00 (5.26-6.906.10 (5.20-7.10)0.872LD, Cramol/L (IQR)1.87 (1.30-2.48)1.800 (1.40-2.30.00)0.270TC, mmol/L (IQR)1.87 (1.30-2.42.17)1.86 (1.60-1.4	Comorbidities			
Pervious PCI, n (%)94 (1932)95 (2007)068Previous CABG, n (%)31 (70)00 (159)0.756Pervious CABG, n (%)127 (7.16)931 (7.424)0.631Af, n (%)11 (6.25)92 (7.34)0.631Af, n (%)11 (6.25)0.2760.756HF, n (%)11 (6.25)1002 (7.90)0.395Ischemic stroke, n (%)14 (6.22.44)1002 (7.90)0.395Ischemic stroke, n (%)010.0080.000COPD, n (%)010.002 (7.90)0.055Laboratory variables	Previous MI, n (%)	40 (22.73)	278 (22.17)	0.944
Previous CABG, n (%)         3(1.70)         20 (1.59)         0.75 (2)           Hypertension, n (%)         12 (72.16)         391 (74.24)         0.618           Hypertension, n (%)         13 (7.39)         75 (6)         0.637           Hypertension, n (%)         11 (6.25)         92 (7.34)         0.74           Hypertension, n (%)         16 (62.94)         1002 (79.90)         0.958           Evension screension         21 (11.93)         15 (2.36)         0.958           Evension screension         14 (6.82.94)         10.008         0.000           COPD, n (%)         0         1.00.81         0.000           Laboratory variables	Previous PCI, n (%)	34 (19.32)	263 (20.97)	0.684
Hypertension, n (%)         127 (72.16)         931 (74.24)         0.618           Af, n (%)         13 (33)         77 (614)         0.637           Hyperlipemia, n (%)         11 (6.25)         027 (34)         0.714           Hyperlipemia, n (%)         11 (6.25)         1002 (79:90)         0.3955           Ischemic stroke, n (%)         0         1008         1000           COPD, n (%)         0         1000 (420-17.80)         0.055           Laboratory variables         -         151 (2.36)         0.331           FNTN pg/m (IQR)         1045 (5.18-21.08)         1800 (420-17.80)         0.331           CK-MA, ng/m (IQR)         1045 (5.18-21.08)         1800 (120-37.80)         0.331           CK-MA, ng/m (IQR)         1045 (5.18-21.08)         1800 (120-37.80)         0.331           CK-MA, ng/m (IQR)         0.049 (22.15-116.49)         5341 (24.75-118.84)         0.331           Str.Mag/m (IQR)         0.049 (22.15-116.49)         1800 (130-0.100)         0.370           Str.Mag/m (IQR)         0.049 (22.15-116.49)         1800 (130-0.100)         0.311           Str.Mag/m (IQR)         0.369 (29.1-9.30)         0.370         1.331           Cr.Mag/m (IQR)         0.350 (70-10.10)         0.350         0.270	Previous CABG, n (%)	3 (1.70)	20 (1.59)	0.756
AFn (%)         13 (7.39)         77 (6.14)         0.637           HF, n (%)         11 (6.25)         92 (7.34)         0.714           HF, n (%)         146 (8.294)         002 (79:90)         0.395           Ischemic stroke, n (%)         21 (11.93)         155 (12.36)         0.968           Previous cerebral hemornhage, n (%)         0         10.08         1.003           COPD, n (%)         0         10.01 (2.2)         1.55           Laboratory variables	Hypertension, n (%)	127 (72.16)	931 (74.24)	0.618
HF,n (%)11 (6.25)92 (7.34)0.74Hyperipernia, n (%)14 (68.294)1002 (79.01)0.35Ischemic stroke, n (%)21 (11.93)155 (12.36)0.968Previous cerebral hemorrhage, n (%)010.00810.00COPD, n (%)010.00 (4.20-17.80)0.901Isboratory variables1.901 (20.21,5-116.49)53.41(24.75-118.44)0.331CK-MB,ng/ml (QR)1.90 (12.0-3.51)1.80 (1.10-3.70)0.947CK-MB,ng/ml (QR)1.90 (12.0-3.51)1.80 (1.0-3.70)0.917CK-MB,ng/ml (QR)0.50 (5.175-92.00)76.00 (5.30-118.75)0.131Scr, mg/dl (QR)0.53 (0.70-10.1)0.85 (0.72-10.0)0.270eGR,m/min/1.73m <sup>2</sup> (QR)92.42 (7.94-107.90)94.68 (3.35-104.97)0.293BUN, mon/L (QR)75.35 (4.85-6.47)58.2 (4.80-6.95)0.293BUN, mon/L (QR)600 (5.28-6.90)610 (5.20-7.10)0.861HAJL, % (QR)67.6 (20-7.20)6.78 (6.10-7.30)0.720GL, mon/L (QR)1.87 (12.8-2.48)1.94 (1.51-2.42)0.704LD-C, mon/L (QR)1.80 (1.50-2.20)1.80 (1.40-2.300)0.312TC, mno/L (QR)1.80 (0.150-2.200)1.80 (1.40-2.300)0.312LD-C, mon/L (QR)1.80 (0.150-2.200)1.80 (1.40-2.300)0.312CG, TU, QR)1.80 (0.150-2.200)1.80 (1.40-2.300)0.312CG, TU, QR)1.80 (0.150-2.200)1.80 (1.40-2.300)0.312CG, TU, QR)1.80 (1.50-2.200)1.80 (1.40-2.300)0.312CG, TU, QR) <td>AF, n (%)</td> <td>13 (7.39)</td> <td>77 (6.14)</td> <td>0.637</td>	AF, n (%)	13 (7.39)	77 (6.14)	0.637
Hyperlipemia, n (%)146 (82.94)1002 (79.90)0.395Ischemic stroke, n (%)21 (11.93)155 (12.36)0.968Previous cerebral hemorrhage, n (%)010.00810.008COPD, n (%)010.1520.155Laboratory variables10.00 (4.20~17.80, M)0.900Laboratory variables1.901 (20.35)1.000 (4.20~17.84, M)0.331CK-MR, ng/ml (QR)50.49 (22.15~116.49)53.41 (24.75~118.84)0.331CK-MR, ng/ml (QR)1.90 (1.20~35)1.80 (1.10~3.70)0.974CK, U/L (QR)0.85 (0.70~10)0.85 (0.72~1.00)0.270cFR, m/min/1.73m <sup>2</sup> (QR)0.83 (0.70~1.01)85 (0.72~1.00)0.270cFR, m/min/L (QR)0.83 (0.70~1.01)0.85 (0.72~1.00)0.270GU, mmol/L (QR)0.85 (0.74~0.01)0.85 (0.72~1.00)0.270GU, mmol/L (QR)0.85 (2.96~6.47)5.85 (4.86~6.95)0.072GU, mmol/L (QR)6.00 (5.28~6.90)6.10 (5.20~7.10)0.668HDA L, % (QR)6.76 (6.26~6.47)5.85 (3.66~4.14)0.400LD C, mmol/L (QR)1.83 (0.80~1.20)1.86 (1.30~1.20)0.770TC, mmol/L (QR)1.80 (1.30~2.20)1.80 (1.40~2.300)0.770LT, L/L (QR)1.80 (1.30~2.20)1.80 (1.40~2.300)0.312CT, mmol/L (QR)1.80 (1.30~2.20)1.80 (1.40~2.300)0.312CT, mmol/L (QR)1.80 (1.30~2.20)1.80 (1.40~2.300)0.312CT, mmol/L (QR)1.80 (1.20~2.50)1.80 (1.20~2.50)0.876ATT, L/L (QR)<	HF, n (%)	11 (6.25)	92 (7.34)	0.714
Instrume         It (1.9.2)         155 (12.3.6)         0.968           Previous cerebral hemorrhage, n (%)         0         1 (0.08)         1.000           COPD, n (%)         0         19 (1.52)         0.055           Laboratory variables	Hyperlipemia, n (%)	146 (82.94)	1002 (79.90)	0.395
Previous cerebral hemorrhage, n (%)         0         1 (0.08)         1 (0.08)         1.000           COPD, n (%)         0         19 (1.52)         0.155           Laboratory variables         hs-TNI, pg/m1 (QR)         10.45 (5.18–21.08)         10.00 (4.20–17.80)         0.0900           BNR, pg/m1 (QR)         150 (4.275–116.49)         53.41 (24.75–118.84)         0.331           CK-MB, ng/m1 (QR)         150 (1.20–3.51)         1.80 (1.10–3.70)         0.947           CK, U/L (QR)         65.50 (5.15–5.92.00)         7.600 (53.00–118.75)         0.131           Scr, mg/dL (QR)         0.85 (0.70–1.01)         0.85 (0.72–1.00)         0.270           eGFR, mL/min/L, 7.3m <sup>2</sup> (QR)         9.24 (7.94–107.90)         9.16 (8.33–104.97)         0.187           Ccr, mg/min (QR)         8.34 (6.089–96.49)         7.689 (59.71–93.09)         0.272           Glu, mmol/L (QR)         5.75 (4.85–64.7)         5.82 (4.80–655)         0.072           Glu, mmol/L (QR)         5.77 (6.20–7.20)         6.78 (6.10–7.30)         0.270           TC, mmol/L (QR)         1.83 (1.93–1.70)         1.46 (1.03–1.47)         0.100           LDL-C, mmol/L (QR)         1.80 (1.50–2.20)         1.80 (1.40–2.300)         0.312           GGT, U/L (QR)         1.80 (1.50–2.200)         1.800 (1.40–2.3	Ischemic stroke, n (%)	21 (11.93)	155 (12.36)	0.968
CPDp. n (%)         0         19 (1.52)         0.155           Laboratory variables             0.000 (4.20–17.80)         0.090 (4.20–17.80)         0.090 (4.20–17.80)         0.090 (4.20–17.80)         0.091 (4.27–5–118.84)         0.331           DKP pg/ml (UQR)         50.409 (2.215–116.49)         53.41 (24.75–118.84)         0.331         0.947           CK, UL (UQR)         67.50 (51.75–92.00)         76.00 (50.0–118.75)         0.131           Scr, mg/dL (UQR)         0.85 (0.70–1.01)         0.85 (0.72–1.00)         0.270           CFR, ml/ml/1.73m <sup>2</sup> (UQR)         9.224 (7.94–1.07.90)         91.46 (83.35–104.97)         0.137           Ccr, mg/min (UQR)         52.46 (0.89–96.49)         76.89 (59.71–93.09)         0.293           BUN, movl/L (UQR)         60.25.8–640)         51.0 (5.20–7.10)         0.068           HbA1c, % (UQR)         60.07 (5.20–7.20)         67.8 (6.10–7.30)         0.720           TC, mmovl/L (QR)         1.33 (0.88–1.20)         1.36 (0.36–4.14)         0.940           TG, mmovl/L (QR)         1.87 (1.38–2.48)         1.94 (1.51–2.42)         0.744           HDL-C, mmovl/L (QR)         1.87 (1.38–2.48)         1.94 (1.51–2.42)         0.744           HDL-C, mmovl/L (QR)         1.87 (1.38–2.48)         1.90	Previous cerebral hemorrhage, n (%)	0	1 (0.08)	1.000
Laboratory variables         N=TNI, pg/ml (QR)         10.45 (5.18–21.08)         10.04 (2.0–17.80)         0.090           BNP, pg/ml (QR)         50.49 (22.15–116.49)         53.41 (24.75–118.84)         0.331           CK-KMB, ng/ml (QR)         67.50 (51.75–92.00)         76.00 (53.00–118.75)         0.131           Scr, mg/dL (QR)         67.50 (51.75–92.00)         76.00 (53.00–118.75)         0.131           Scr, mg/ml (QR)         92.24 (7.294–107.90)         91.46 (83.35–104.97)         0.187           Cx, mg/ml (QR)         78.34 (60.89–96.49)         76.89 (59.71–93.09)         0.293           BUN, mmol/L (QR)         75.75 (4.85–6.47)         5.82 (4.80–6.95)         0.072           Glu, mmol/L (QR)         6.77 (6.20–7.20)         6.78 (6.10–7.30)         0.780           TC, mmol/L (QR)         1.43 (0.99–1.70)         1.46 (10.3–1.47)         0.100           TC, mmol/L (QR)         1.600 (13.00–25.25)         17.00 (12.00–25.00)         0.876           AST, U/L (QR)         1.600 (13.00–22.20)         1.800 (14.00–23.00)         0.312           CGT, U/L (QR)         1.300 (12.20–14.25)         1.700 (12.00–3.800)         0.270           PLT,×10°/L (QR)         1.800 (15.0–2.220)         1.800 (14.0–2.30.0)         0.312           CGT, U/L (QR)         1.300 (12.20–14.25)	COPD. n (%)	0	19 (1.52)	0.155
hartNI, pg/m1 (QR)         10.45 (5.18-21.08)         10.00 (4.20-17.80)         0.090           BNR, pg/m1 (QR)         50.49 (22.15-116.49)         53.41 (24.75-118.84)         0.331           CK-MB, ng/m1 (QR)         67.50 (51.75-92.00)         76.00 (53.00-118.75)         0.131           Scr, mg/dL (QR)         0.85 (0.70-1.01)         0.85 (0.72-1.00)         0.270           eGFR, ml/min/1.73m² (QR)         92.24 (7.794-107.90)         91.46 (83.35-104.97)         0.187           Ccr, mg/min (QR)         575 (4.85-6.47)         5.82 (4.80-6.95)         0.072           Glu, mmol/L (QR)         6.00 (52.8-6.90)         6.10 (520-7.10)         0.068           HbA1c, % (QR)         6.77 (62.0-7.20)         5.78 (4.05-6.47)         0.920           GL, mmol/L (QR)         1.35 (0.99-1.70)         1.46 (1.03-1.47)         0.100           LDL-C, mmol/L (QR)         1.33 (0.99-1.20)         3.58 (3.06-4.14)         0.940           LDL-C, mmol/L (QR)         1.30 (0.88-1.20)         1.30 (0.96-1.11)         0.720           ST, U/L (QR)         1.80 (1.500-22.00)         1.800 (14.00-23.00)         0.312           GT, U/L (QR)         1.800 (1.500-22.00)         1.800 (14.00-23.00)         0.312           GT, U/L (QR)         2.000 (19.75-38.00)         37.00 (22.00-38.00)         0.270	Laboratory variables			
BN, pg/m1 (QR)         50.49 (22.15–116.49)         53.41 (24.75–118.84)         0.331           CK-MB, ng/m1 (QR)         1.90 (1.20–3.51)         1.80 (1.10–3.70)         0.947           CK, U/L (QR)         67.50 (51.75–92.00)         76.00 (53.00–118.75)         0.131           Scr, mg/dL (QR)         0.85 (0.70–1.01)         0.85 (0.72–1.00)         0.270           GEFR, mU/min1.73m <sup>2</sup> (QR)         92.24 (7.94–107.90)         91.46 (83.35–104.97)         0.187           Ccr, mg/min (QR)         5.75 (4.85–6.47)         5.82 (4.80–6.95)         0.722           Glu, mmol/L (QR)         6.70 (52.0–7.20)         6.78 (61.0–7.30)         0.720           Glu, mmol/L (QR)         6.70 (52.0–7.20)         6.78 (61.0–7.30)         0.720           TC, mmol/L (QR)         1.43 (0.99–1.70)         1.46 (1.03–1.47)         0.100           LDL-C, mmol/L (QR)         1.87 (13.8–4.88)         1.94 (151–2.42)         0.704           HDL-C, mmol/L (QR)         1.80 (15.00–22.00)         1.80 (14.00–23.00)         0.312           GGT, U/L (QR)         1.80 (15.00–22.00)         1.80 (14.00–23.00)         0.312           GGT, U/L (QR)         2.000 (19.70–38.00)         3.70 (22.00–38.00)         0.270           VIL/L (QR)         1.800 (15.00–22.00)         1.800 (15.00–24.400)         0.851	hs-TNI, pg/ml (IOR)	10.45 (5.18-21.08)	10.00 (4.20-17.80)	0.090
CK-MB, gryml (IQR)         190 (1.20–3.51)         1.80 (1.10–3.70)         0.947           CK-MB, gryml (IQR)         67.50 (51.75–92.00)         76.00 (53.00–118.75)         0.131           Scr, mg/dL (IQR)         0.85 (0.70–101)         0.85 (0.72–1.00)         0.270           eGFR, ml/min/1.73m <sup>2</sup> (IQR)         92.24 (7.794–107.90)         91.46 (83.35–104.97)         0.187           Cxr, mg/min (IQR)         78.34 (60.89–96.49)         76.89 (57.7–30.09)         0.293           BUN, mmol/L (IQR)         5.75 (4.85–6.47)         5.82 (4.80–6.95)         0.072           Glu, mmol/L (IQR)         6.00 (5.28–6.90)         6.10 (5.20–7.10)         0.668           HbA1c, % (IQR)         6.07 (6.20–7.20)         6.78 (6.10–7.30)         0.720           TC, mmol/L (IQR)         1.43 (0.99–1.70)         1.46 (1.03–1.47)         0.100           LDL-C, mmol/L (IQR)         1.87 (1.38–2.48)         1.94 (1.51–2.42)         0.704           HDL-C, mmol/L (IQR)         1.600 (13.00–22.55)         1.700 (12.00–25.00)         0.876           AST, U/L (IQR)         16.000 (13.00–22.00)         18.00 (14.00–23.00)         0.312           GGT, U/L (IQR)         20.750 (17.52–242.75)         20.500 (17.40–244.00)         0.876           MST, U/L (IQR)         13.00 (12.00–144.25)         31.00 (121.00–141.00)<	BNP. pg/ml (IOR)	50.49 (22.15–116.49)	53.41(24.75–118.84)	0.331
Ck U/L (QR)         G7 50 (51.75–92.00)         76.00 (53.00–118.75)         0.131           Scr, mg/dL (QR)         0.85 (0.70–1.01)         0.85 (0.72–1.00)         0.270           eGFR, ml/min/1.73m² (QR)         92.24 (77.94–107.90)         91.46 (83.35–104.97)         0.187           Ccr, mg/min (QR)         75 (485–647)         58.9 (480–655)         0.072           Glu, mmol/L (QR)         6.77 (620–7.20)         6.78 (6.10–7.30)         0.720           TC, mmol/L (QR)         1.73 (0.99–1.70)         1.46 (1.03–1.47)         0.068           HbA1c, % (QR)         6.77 (620–7.20)         6.78 (6.10–7.30)         0.720           TC, mmol/L (QR)         1.43 (0.99–1.70)         1.46 (1.03–1.47)         0.100           LDL-C, mmol/L (QR)         1.43 (0.99–1.70)         1.46 (1.03–1.47)         0.100           LDL-C, mmol/L (QR)         1.43 (0.99–1.70)         1.46 (1.03–1.47)         0.704           HDL-C, mmol/L (QR)         1.03 (0.88–1.20)         1.03 (0.96–1.11)         0.737           AT, U/L (QR)         1.800 (15.00–22.00)         1.800 (14.00–23.00)         0.270           GT, U/L (QR)         1.800 (15.00–22.00)         1.800 (14.00–23.00)         0.270           GT, W/L (QR)         2.745 (19.48–45.45)         2.970 (21.10–49.38)         0.151	CK-MB. ng/ml (IOR)	1.90 (1.20–3.51)	1.80 (1.10–3.70)	0.947
Base Details         Base Details<	CK U/L (IOR)	67 50 (51 75–92 00)	76.00 (53.00–118.75)	0.131
Base (Base)	Scr. mg/dL (IOB)	0.85 (0.70–1.01)	0.85 (0.72–1.00)	0.270
Cr, mg/mi (QR)         78.34 (60.89–96.49)         76.89 (59.71–93.09)         0.293           BUN, mmol/L (QR)         5.75 (4.85–6.47)         5.82 (4.80–6.95)         0.072           Glu, mmol/L (QR)         6.00 (5.28–6.90)         6.10 (5.20–7.10)         0.668           HbA1c, % (QR)         6.77 (6.20–7.20)         6.78 (6.10–7.30)         0.720           TC, mmol/L (QR)         3.50 (2.90–4.20)         3.58 (3.06–4.14)         0.940           TG, mmol/L (QR)         1.43 (0.99–1.70)         1.46 (1.03–1.47)         0.100           LD-C, mmol/L (QR)         1.03 (0.88–1.20)         1.03 (0.96–1.11)         0.737           ALT, U/L (QR)         1.03 (0.88–1.20)         1.03 (0.96–1.11)         0.737           ALT, U/L (QR)         1.800 (15.00–22.00)         18.00 (12.00–25.00)         0.876           ATJ, U/L (QR)         18.00 (19.75–38.00)         37.00 (22.00–38.00)         0.270           PLT_× 10 <sup>9</sup> /L (QR)         20.750 (17.52–542.75)         20.500 (174.00–244.00)         0.848           MYO, ng/L (QR)         20.750 (17.52–542.75)         20.500 (174.00–244.00)         0.851           Byb, g/L (QR)         27.45 (19.44-45.45)         29.70 (21.10–49.38)         0.153           Myo, ng/L (QR)         26.5111         669 (53.35)         0.720	$eGER. ml/min/1.73m^2$ (IOR)	92.24 (77.94–107.90)	91.46 (83.35–104.97)	0.187
BUN, mon/L (IQR)         5.75 (48.5 - 6.47)         5.82 (48.0 - 6.59)         0.072           Glu, mmol/L (IQR)         6.00 (5.28 - 6.90)         6.10 (5.20 - 7.10)         0.668           HbA1c, % (IQR)         6.77 (6.20 - 7.20)         6.78 (6.10 - 7.30)         0.720           Tc, mmol/L (IQR)         3.50 (2.90 - 4.20)         3.58 (3.06 - 4.14)         0.940           TG, mmol/L (IQR)         1.43 (0.99 - 1.70)         1.46 (1.03 - 1.47)         0.100           LDL-C, mmol/L (IQR)         1.87 (1.38 - 2.48)         1.94 (1.51 - 2.42)         0.704           HDL-C, mmol/L (IQR)         1.03 (0.88 - 1.20)         1.03 (0.96 - 1.11)         0.737           ALT, U/L (IQR)         1.800 (15.00 - 22.00)         18.00 (14.00 - 23.00)         0.312           GGT, U/L (IQR)         20.705 (175 25 - 242.75)         20.500 (174.00 - 244.00)         0.848           MYO, ng/L (IQR)         133.00 (122.00 - 144.25)         131.00 (121.00 - 141.00)         0.51           Description of the lesions         51.11         69 (53.35)         0.720           Mult-vessel disease, n (%)         79 (44.89)         58 5 (46.65)         0.720           Mult-vessel disease, n (%)         99 (55.25)         709 (56.54)         1.000           LCM lesion, n (%)         5 (2.84)         34 (2.71)         0.	Ccr. mg/min (IOR)	78.34 (60.89–96.49)	76.89 (59.71–93.09)	0.293
Bit Name Constraints         Bit Name Constraint         Bit Name Constraints         Bit Name C	BUN. mmol/L (IOR)	5.75 (4.85–6.47)	5.82 (4.80–6.95)	0.072
HbA1c, % (QR)for (2.2 - 7.20)6.78 (6.10 - 7.30)0.720TC, mmol/L (IQR)3.50 (2.90 - 4.20)3.58 (3.06 - 4.14)0.940TG, mmol/L (IQR)1.43 (0.99 - 1.70)1.46 (1.03 - 1.47)0.100LDL-c, mmol/L (IQR)1.87 (1.38 - 2.48)1.94 (1.51 - 2.42)0.704HDL-C, mmol/L (IQR)1.03 (0.88 - 1.20)1.03 (0.96 - 1.11)0.737ALT, U/L (IQR)1.600 (13.00 - 25.25)17.00 (12.00 - 25.00)0.876AST, U/L (IQR)18.00 (15.00 - 22.00)18.00 (14.00 - 23.00)0.312GGT, U/L (IQR)32.00 (19.75 - 38.00)37.00 (22.00 - 38.00)0.270PLT, × 10 <sup>9</sup> /L (IQR)207.50 (17.525 - 242.75)205.00 (174.00 - 244.00)0.848MYO, ng/L (IQR)27.45 (19.48 - 45.45)29.70 (21.10 - 49.38)0.153Hgb, g/L (IQR)133.00 (12.00 - 144.25)131.00 (12.100 - 141.00)0.051Description of the lesions5566.550.720Multi-vessel disease, n (%)9 (56.51)66 (53.35)0.720Multi-vessel disease (> 2), n (%)9 (56.25)709 (56.54)1.000LAD lesion, n (%)5 (2.84)34 (2.71)0.808LCX lesion, n (%)9 (56.25)709 (56.54)0.599RCA lesion, n (%)9 (56.25)709 (56.54)0.599RCA lesion, n (%)5 (3.18.2)384 (30.62)0.814PCI with balloon only, n(%)9 (50.0170)640 (51.04)0.932PCI with balloon only, n(%)9 (56.25)709 (56.54)0.932PCI with balloon and stent, n(%	Glu, mmol/L (IOR)	6.00 (5.28–6.90)	6.10 (5.20–7.10)	0.068
Tark (Link)         Tark (Link) <thtark (link)<="" th=""> <thtark (link)<="" th=""></thtark></thtark>	HbA1c. % (IOR)	6.77 (6.20-7.20)	6.78 (6.10–7.30)	0.720
TG, mmol/L (QR)         1.43 (0.99–1.70)         1.46 (1.03–1.47)         0.100           LDL-C, mmol/L (QR)         1.87 (1.38–2.48)         1.94 (1.51–2.42)         0.704           HDL-C, mmol/L (QR)         1.03 (0.88–1.20)         1.03 (0.96–1.11)         0.737           ALT, U/L (QR)         16.00 (13.00–25.25)         17.00 (12.00–25.00)         0.876           AST, U/L (QR)         18.00 (15.00–22.00)         18.00 (14.00–23.00)         0.312           GGT, U/L (QR)         20.00 (19.75–38.00)         37.00 (22.00–38.00)         0.270           PLT, x10 <sup>9</sup> /L (QR)         20.00 (19.75–38.00)         37.00 (22.00–38.00)         0.270           PLT, x10 <sup>9</sup> /L (QR)         20.750 (175.25–242.75)         205.00 (174.00–244.00)         0.848           MYO, ng/L (QR)         27.45 (19.48–45.45)         29.70 (21.10–49.38)         0.153           Hgb, g/L (QR)         13.00 (12.00–144.25)         13.100 (12.10–141.00)         0.051           Description of the lesions         5         5         5         0.720           Multi-vessel disease (>2), n (%)         97 (55.11)         669 (53.35)         0.720           Multi-vessel disease (>2), n (%)         5 (2.84)         34 (2.71)         0.808           LCX lesion, n (%)         5 (2.57)         294 (23.44)         0.599	TC. mmol/L (IOR)	3.50 (2.90-4.20)	3.58 (3.06–4.14)	0.940
LDL-C, mmol/L (QR)1.87 (1.38–2.48)1.94 (1.51–2.42)0.704HDL-C, mmol/L (QR)1.03 (0.88–1.20)1.03 (0.96–1.11)0.737ALT, U/L (QR)16.00 (13.00–25.25)17.00 (12.00–25.00)0.876AST, U/L (QR)18.00 (15.00–22.00)18.00 (14.00–23.00)0.312GGT, U/L (QR)207.50 (175.25–242.75)205.00 (174.00–244.00)0.848MYO, ng/L (QR)27.50 (175.25–242.75)205.00 (174.00–244.00)0.848MYO, ng/L (QR)27.45 (19.48–45.45)29.70 (21.10–49.38)0.153Hgb, g/L (QR)133.00 (122.00–144.25)131.00 (121.00–141.00)0.051Description of the lesions79 (44.89)585 (46.65)0.720Multi-vessel disease, n (%)79 (55.11)669 (53.35)0.720Multi-vessel disease, e (2.2), n (%)99 (56.25)709 (56.54)1.000LA lesion, n (%)5 (2.84)34 (2.71)0.808LCX lesion, n (%)5 (2.57)294 (23.44)0.599RCA lesion, n (%)56 (31.82)384 (30.62)0.814PCI with balloon only, n(%)91 (51.70)640 (51.04)0.932PCI with balloon and stent, n(%)17 (966)121 (965)1000	TG, mmol/L (IOR)	1.43 (0.99–1.70)	1.46 (1.03–1.47)	0.100
Init (100 - 100)       10.3 (0.88 - 1.20)       1.0.3 (0.96 - 1.11)       0.737         ALT, U/L (IQR)       16.00 (13.00 - 25.25)       17.00 (12.00 - 25.00)       0.876         AST, U/L (IQR)       18.00 (15.00 - 22.00)       18.00 (14.00 - 23.00)       0.312         GGT, U/L (IQR)       32.00 (19.75 - 38.00)       37.00 (22.00 - 38.00)       0.270         PLT, x 10 <sup>9</sup> /L (IQR)       207.50 (175.25 - 242.75)       205.00 (174.00 - 244.00)       0.848         MYO, ng/L (IQR)       27.45 (19.48 - 45.45)       29.70 (21.10 - 49.38)       0.153         Hgb, g/L (IQR)       13.00 (122.00 - 144.25)       131.00 (121.00 - 141.00)       0.051         Description of the lesions       5       585 (46.65)       0.720         Multi-vessel disease, n (%)       79 (44.89)       585 (46.65)       0.720         Multi-vessel disease, n (%)       97 (55.11)       669 (53.35)       0.720         Multi-vessel disease, n (%)       97 (55.11)       669 (53.35)       0.720         LX lesion, n (%)       5 (2.84)       34 (2.71)       0.808         LX lesion, n (%)       99 (56.25)       709 (56.54)       1.000         LX lesion, n (%)       5 (3.182)       384 (30.62)       0.814         PCI with balloon only, n(%)       91 (51.70)       640 (51.04)	I DI -C. mmol/L (IOB)	1.87 (1.38–2.48)	1.94 (1.51–2.42)	0.704
ALT, U/L (IQR)16.00 (13.00–25.25)17.00 (12.00–25.00)0.876AST, U/L (IQR)18.00 (15.00–22.00)18.00 (14.00–23.00)0.312GGT, U/L (IQR)32.00 (19.75–38.00)37.00 (22.00–38.00)0.270PLT, × 10°/L (IQR)207.50 (175.25–242.75)205.00 (174.00–244.00)0.848MYO, ng/L (IQR)27.45 (19.48–45.45)29.70 (21.10–49.38)0.153Hgb, g/L (IQR)131.00 (12.200–144.25)131.00 (12.100–141.00)0.51Description of the lesions5585 (46.65)0.720Multi-vessel disease, n (%)79 (44.89)585 (46.65)0.720Multi-vessel disease (≥ 2), n (%)97 (55.11)669 (53.35)0.720LM lesion, n (%)5 (2.84)34 (2.71)0.808LCX lesion, n (%)95 (52.57)294 (23.44)0.599RCA lesion, n (%)45 (25.57)294 (23.44)0.599PCI with balloon only, n(%)91 (51.70)640 (51.04)0.932PCI with balloon and stent, n(%)19 (51.70)640 (51.04)0.932PCI with balloon and stent, n(%)17 (9.66)121 (9.65)1.000	HDI-C. mmol/L (IOR)	1.03 (0.88–1.20)	1.03 (0.96–1.11)	0.737
AST, U/L (IQR)       18.00 (15.00-22.00)       18.00 (14.00-23.00)       0.312         GGT, U/L (IQR)       32.00 (19.75-38.00)       37.00 (22.00-38.00)       0.270         PLT, × 10 <sup>9</sup> /L (IQR)       207.50 (175.25-242.75)       205.00 (174.00-244.00)       0.848         MYO, ng/L (IQR)       27.45 (19.48-45.45)       29.70 (21.10-49.38)       0.153         Hgb, g/L (IQR)       133.00 (122.00-144.25)       131.00 (121.00-141.00)       0.051         Description of the lesions         0.720         Multi-vessel disease, n (%)       79 (44.89)       585 (46.65)       0.720         Multi-vessel disease (≥ 2), n (%)       97 (55.11)       669 (53.35)       0.720         LM lesion, n (%)       5 (2.84)       34 (2.71)       0.808         LCX lesion, n (%)       99 (56.25)       709 (56.54)       1.000         LAD lesion, n (%)       45 (25.57)       294 (23.44)       0.599         RCA lesion, n (%)       56 (31.82)       384 (30.62)       0.814         PCI with balloon only, n(%)       91 (51.70)       640 (51.04)       0.932         PCI with balloon and stent, n(%)       17 (9.66)       121 (9.65)       1000	ALT, U/L (IOR)	16.00 (13.00–25.25)	17.00 (12.00–25.00)	0.876
GGT, U/L (IQR)         32.00 (19.75–38.00)         37.00 (22.00–38.00)         0.270           PLT,×10 <sup>9</sup> /L (IQR)         207.50 (175.25–242.75)         205.00 (174.00–244.00)         0.848           MYO, ng/L (IQR)         27.45 (19.48–45.45)         29.70 (21.10–49.38)         0.153           Hgb, g/L (IQR)         133.00 (122.00–144.25)         131.00 (121.00–141.00)         0.051           Description of the lesions         585 (46.65)         0.720           Multi-vessel disease, n (%)         79 (44.89)         585 (46.65)         0.720           Multi-vessel disease, n (%)         79 (44.89)         585 (46.65)         0.720           Multi-vessel disease, n (%)         97 (55.11)         669 (53.35)         0.720           LL lesion, n (%)         5 (2.84)         34 (2.71)         0.808           LCX lesion, n (%)         99 (56.25)         709 (56.54)         1.000           LAD lesion, n (%)         56 (31.82)         384 (30.62)         0.814           PCI with balloon only, n(%)         91 (51.70)         640 (51.04)         0.932           PCI with balloon and stent, n(%)         17 (9.66)         121 (965)         1000	AST, U/L (IOR)	18.00 (15.00–22.00)	18.00 (14.00–23.00)	0.312
PLT,×10 <sup>9</sup> /L (IQR)       207.50 (175.25–242.75)       205.00 (174.00–244.00)       0.848         MYO, ng/L (IQR)       27.45 (19.48–45.45)       29.70 (21.10–49.38)       0.153         Hgb, g/L (IQR)       133.00 (122.00–144.25)       131.00 (121.00–141.00)       0.051         Description of the lesions       585 (46.65)       0.720         Multi-vessel disease, n (%)       79 (44.89)       585 (46.65)       0.720         Multi-vessel disease, n (%)       97 (55.11)       669 (53.35)       0.720         LM lesion, n (%)       5 (2.84)       34 (2.71)       0.808         LCX lesion, n (%)       99 (56.25)       709 (56.54)       1.000         LAD lesion, n (%)       45 (25.57)       294 (23.44)       0.599         RCA lesion, n (%)       91 (51.70)       640 (51.04)       0.932         PCI with balloon only, n(%)       91 (51.70)       640 (51.04)       0.932         PCI with stent only, n(%)       68 (38.64)       493 (39.31)       0.928         PCI with balloon and stent, n(%)       17 (9.66)       121 (9.65)       1000	GGT, U/L (IOR)	32.00 (19.75–38.00)	37.00 (22.00–38.00)	0.270
MYO, ng/L (lQR)       27.45 (19.48–45.45)       29.70 (21.10–49.38)       0.153         Hgb, g/L (lQR)       133.00 (122.00–144.25)       131.00 (121.00–141.00)       0.051         Description of the lesions       585 (46.65)       0.720         Multi-vessel disease, n (%)       79 (44.89)       585 (46.65)       0.720         Multi-vessel disease, n (%)       97 (55.11)       669 (53.35)       0.720         LM lesion, n (%)       5 (2.84)       34 (2.71)       0.808         LCX lesion, n (%)       99 (56.25)       709 (56.54)       1.000         LAD lesion, n (%)       45 (25.57)       294 (23.44)       0.599         RCA lesion, n (%)       56 (31.82)       384 (30.62)       0.814         PCI with balloon only, n(%)       91 (51.70)       640 (51.04)       0.932         PCI with stent only, n(%)       68 (38.64)       493 (39.31)       0.928         PCI with balloon and stent, n(%)       17 (9.66)       121 (9.65)       1000	PLT.×10 <sup>9</sup> /L (IOR)	207.50 (175.25–242.75)	205.00 (174.00–244.00)	0.848
Hgb, g/L (IQR)       133.00 (122.00-144.25)       131.00 (121.00-141.00)       0.051         Description of the lesions       585 (46.65)       0.720         Single-vessel disease, n (%)       79 (44.89)       585 (46.65)       0.720         Multi-vessel disease (≥ 2), n (%)       97 (55.11)       669 (53.35)       0.720         LM lesion, n (%)       5 (2.84)       34 (2.71)       0.808         LCX lesion, n (%)       99 (56.25)       709 (56.54)       1.000         LAD lesion, n (%)       45 (25.57)       294 (23.44)       0.599         RCA lesion, n (%)       56 (31.82)       384 (30.62)       0.814         PCI with balloon only, n(%)       91 (51.70)       640 (51.04)       0.932         PCI with stent only, n(%)       68 (38.64)       493 (39.31)       0.928         PCI with balloon and stent, n(%)       17 (9.66)       121 (9.65)       1000	MYO, ng/L (IQR)	27.45 (19.48–45.45)	29.70 (21.10–49.38)	0.153
Description of the lesions       79 (44.89)       585 (46.65)       0.720         Multi-vessel disease, n (%)       97 (55.11)       669 (53.35)       0.720         LM lesion, n (%)       5 (2.84)       34 (2.71)       0.808         LCX lesion, n (%)       99 (56.25)       709 (56.54)       1.000         LAD lesion, n (%)       45 (25.57)       294 (23.44)       0.599         RCA lesion, n (%)       56 (31.82)       384 (30.62)       0.814         PCI with balloon only, n(%)       91 (51.70)       640 (51.04)       0.932         PCI with stent only, n(%)       68 (38.64)       493 (39.31)       0.928         PCI with balloon and stent, n(%)       17 (9.66)       121 (9.65)       1000	Hab. a/L (IOR)	133.00 (122.00–144.25)	131.00 (121.00–141.00)	0.051
Single-vessel disease, n (%)       79 (44.89)       585 (46.65)       0.720         Multi-vessel disease (≥ 2), n (%)       97 (55.11)       669 (53.35)       0.720         LM lesion, n (%)       5 (2.84)       34 (2.71)       0.808         LCX lesion, n (%)       99 (56.25)       709 (56.54)       1.000         LAD lesion, n (%)       45 (25.57)       294 (23.44)       0.599         RCA lesion, n (%)       56 (31.82)       384 (30.62)       0.814         PCI information          91 (51.70)       640 (51.04)       0.932         PCI with balloon only, n(%)       91 (51.70)       640 (51.04)       0.932       925         PCI with stent only, n(%)       68 (38.64)       493 (39.31)       0.928         PCI with balloon and stent, n(%)       17 (9.66)       121 (9.65)       1000	Description of the lesions			
Multi-vessel disease (≥ 2), n (%)       97 (55.11)       669 (53.35)       0.720         LM lesion, n (%)       5 (2.84)       34 (2.71)       0.808         LCX lesion, n (%)       99 (56.25)       709 (56.54)       1.000         LAD lesion, n (%)       45 (25.57)       294 (23.44)       0.599         RCA lesion, n (%)       56 (31.82)       384 (30.62)       0.814         PCI information       701       640 (51.04)       0.932         PCI with balloon only, n(%)       91 (51.70)       640 (51.04)       0.932         PCI with stent only, n(%)       68 (38.64)       493 (39.31)       0.928         PCI with balloon and stent, n(%)       17 (9.66)       121 (9.65)       1000	Single-vessel disease. n (%)	79 (44.89)	585 (46.65)	0.720
LM lesion, n (%)       5 (2.84)       34 (2.71)       0.808         LCX lesion, n (%)       99 (56.25)       709 (56.54)       1.000         LAD lesion, n (%)       45 (25.57)       294 (23.44)       0.599         RCA lesion, n (%)       56 (31.82)       384 (30.62)       0.814         PCI information       701 (51.04)       0.932         PCI with balloon only, n(%)       91 (51.70)       640 (51.04)       0.932         PCI with stent only, n(%)       68 (38.64)       493 (39.31)       0.928         PCI with balloon and stent, n(%)       17 (9.66)       121 (9.65)       1000	Multi-vessel disease (> 2), n (%)	97 (55.11)	669 (53.35)	0.720
LCX lesion, n (%)       99 (56.25)       709 (56.54)       1.000         LAD lesion, n (%)       45 (25.57)       294 (23.44)       0.599         RCA lesion, n (%)       56 (31.82)       384 (30.62)       0.814         PCI information       91 (51.70)       640 (51.04)       0.932         PCI with balloon only, n(%)       91 (51.70)       640 (51.04)       0.928         PCI with stent only, n(%)       68 (38.64)       493 (39.31)       0.928         PCI with balloon and stent, n(%)       17 (9.66)       121 (9.65)       1000	I M lesion. n (%)	5 (2.84)	34 (2.71)	0.808
LAD lesion, n (%)       45 (25.57)       294 (23.44)       0.599         RCA lesion, n (%)       56 (31.82)       384 (30.62)       0.814         PCI information       91 (51.70)       640 (51.04)       0.932         PCI with balloon only, n(%)       91 (51.70)       640 (51.04)       0.932         PCI with stent only, n(%)       68 (38.64)       493 (39.31)       0.928         PCI with balloon and stent, n(%)       17 (9.66)       121 (9.65)       1000	I CX lesion n (%)	99 (56 25)	709 (56 54)	1 000
RCA lesion, n (%)       56 (31.82)       384 (30.62)       0.814         PCI information       91 (51.70)       640 (51.04)       0.932         PCI with balloon only, n(%)       91 (51.70)       640 (51.04)       0.932         PCI with stent only, n(%)       68 (38.64)       493 (39.31)       0.928         PCI with balloon and stent, n(%)       17 (9.66)       121 (9.65)       1000	LAD lesion. n (%)	45 (25.57)	294 (23.44)	0.599
PCI with balloon only, n(%)         91 (51.70)         640 (51.04)         0.932           PCI with stent only, n(%)         68 (38.64)         493 (39.31)         0.928           PCI with balloon and stent, n(%)         17 (9.66)         121 (9.65)         1000	RCA lesion, n (%)	56 (31.82)	384 (30.62)	0.814
PCI with balloon only, n(%)       91 (51.70)       640 (51.04)       0.932         PCI with stent only, n(%)       68 (38.64)       493 (39.31)       0.928         PCI with balloon and stent, n(%)       17 (9.66)       121 (9.65)       1000	PCI information	(- · · )	,	0.011
PCI with stent only, n(%)         68 (38.64)         493 (39.31)         0.928           PCI with balloon and stent, n(%)         17 (9.66)         121 (9.65)         1 000	PCI with balloon only, n(%)	91 (51.70)	640 (51.04)	0.932
PCI with balloon and stent, n(%) 17 (9.66) 121 (9.65) 1000	PCI with stent only. n(%)	68 (38.64)	493 (39.31)	0.928
	PCI with balloon and stent. n(%)	17 (9.66)	121 (9.65)	1.000

# Table 1 (continued)

	DAPA user (n = 176)	non-SGLT2i user (n = 1254)	<i>p</i> value
Contrast volume, mL (IQR)	156.50 (120.00–190.00)	150.00 (130.00–185.75)	0.761
Medications			
Antiplatelets, n (%)	175 (99.43)	1220 (97.29)	0.114
Anticoagulation, n (%)	2 (1.14)	21 (1.67)	1.000
β-blockers, n (%)	134 (76.14)	931 (74.24)	0.655
RAASi, n (%)	103 (58.52)	712 (56.78)	0.722
CCB, n (%)	76 (43.18)	479 (38.20)	0.235
ARNI, n (%)	39 (22.16)	147 (11.72)	< 0.001
Statin, n (%)	157 (89.20)	1137 (90.67)	0.629
Ezetimibe, n (%)	67 (38.07)	492 (39.23)	0.830
Diuretic, n (%)	50 (28.41)	322 (25.68)	0.495
Metformin, n (%)	57 (32.39)	426 (33.97)	0.740
DPP-4i, n (%)	31 (17.61)	193 (15.39)	0.516
GLP-1RA, n (%)	12 (6.82)	41 (3.27)	0.034
SU, n (%)	14 (7.95)	86 (6.86)	0.707
Insulin, n (%)	51 (28.98)	286 (22.81)	0.087
construction of the start of th	and the standard sector and the sector of th		

Standardized hydration is not performed for patients during the peri-operative period of PCI. The type of contrast agent used in PCI is iodine contrast agent

disease, and those with high contrast agent dosages ( $\geq$  150 mL), the use of dapagliflozin could better reduce the incidence of cardiac events (Fig. 2). In terms of renal outcomes, subgroup analyses revealed pronounced benefits in patients aged  $\geq$  65 years, those with multivessel disease, and those receiving greater contrast volume (Fig. 3). Compared with the control group, the dapagliflozin (DAPA) group demonstrated significantly greater baseline eGFRs (91.24 vs. 87.48, *p*=0.036) and post-PCI eGFRs (91.27 vs. 87.75, *p*<0.001), indicating preserved renal function in the DAPA-treated patients (Fig. 4).

# Discussion

## Key results

In this retrospective study, we compared the cardiac and renal outcomes of patients with T2DM and CCSs undergoing PCI, stratified by their concomitant use of the SGLT2 inhibitor dapagliflozin. Our analysis revealed three novel clinical findings. (1) Dapagliflozin significantly improved cardiac outcomes. Both before and after PSM, patients in the dapagliflozin group had lower PMI/4aMI rates than those in the control group. Multivariate analysis post-PSM further confirmed this association. (2) In terms of renal outcomes, dapagliflozin did not exert a significant effect on contrast-induced acute kidney injury according to the CI-AKI<sub>ESUR</sub> and CI-AKI<sub>KDIGO</sub> criteria, either before or after PSM, even after covariate adjustment. However, subgroup analyses indicated that dapagliflozin provided notable benefits in terms of renal outcomes among patients aged  $\geq 65$  years, those with multivessel disease, and those receiving a high contrast volume. (3) Compared with the control group, the dapagliflozin group had significantly greater baseline and post-PCI eGFRs, suggesting that dapagliflozin may contribute to the preservation of renal function. (4) An analysis of cardiac events showed that dapagliflozin was more effective in reducing the incidence of cardiac events in populations aged  $\geq$  65 years, those with multivessel disease, and those with high contrast agent dosages ( $\geq$  150 mL). To our knowledge, this is the first study to describe data associating dapagliflozin with improved cardiac and renal outcomes among patients with T2DM and CCSs undergoing PCI.

### Myocardial injury protection

Previous studies have shown that SGLT2 inhibitors can significantly increase both survival and left ventricular (LV) function in patients [17]. Research on the pathophysiological mechanisms has shown that SGLT2 inhibitors attenuate fibrosis and autophagy in border cardiac tissue in mice with MI. In Beclin1+/- and NHE1 cKO mice, Beclin1 deficiency improved survival. Mechanistically, SGLT2 inhibitors exert a significant cardioprotective effect by inhibiting autophagy by targeting Beclin1 rather than NHE1. In addition, an SGLT2 inhibitor rescued cardiomyocyte autosis induced by Tat-beclin1 or GD, exerting cardioprotective effects by decreasing autophagic cell death. These findings provide new evidence that SGLT2 inhibitors effectively ameliorate myocardial injury in myocardial infarction by suppressing beclin1-dependent autosis rather than effectively targeting NHE1 in cardiomyocytes [18–20].

An in-hospital investigation in T2DM patients presenting with acute MI (AMI) who underwent PCI and were treated with SGLT2 inhibitors revealed that the use of SGLT2 inhibitors was associated with a lower risk of major adverse cardiovascular events [21]. A prospective, multicentre, randomized, double-blind,

# Table 2 Basic characteristics of patients in two groups in propensity-matched dataset

DAPA group (n = 176)	Control group (n = 176)	<i>p</i> value
Demographics		
Female, n (%) 45 (25.57)	37 (21.02)	0.254
Age, year (IQR) 65.00 (59.75–71.00)	66.00 (58.00-71.25)	0.827
BMI, kg/m <sup>2</sup> (IQR) 25.46 (24.04–27.73)	26.17 (24.60–28.16)	0.179
Smoking status, n (%) 92 (52.27)	95 (53.98)	0.749
Drinking status, n (%) 89 (50.57)	98 (55.11)	0.336
SBP, mmHg (IQR) 125.00 (114.00–139.00)	124.50 (115.75–140.00)	0.619
DBP, mmHg (IQR) 71.50 (65.00–78.00)	71.00 (64.00-80.00)	0.556
HR, bpm (IQR) 68.00 (64.00–72.00)	68.00 (64.00-72.00)	0.394
LVEF, % (IQR) 58.00 (58.00–64.00)	60.00 (56.00–65.00)	0.867
Comorbidities		
Previous MI, n (%) 40 (22.73)	49 (27.84)	0.270
Previous PCI, n (%) 34 (19.32)	36 (20.46)	0.789
Previous CABG, n (%) 3 (1.71)	4 (2.27)	1.000
Hypertension, n (%) 127 (72.16)	137 (77.84)	0.051
AF, n (%) 13 (7.39)	13 (7.39)	1.000
HE n (%) 11 (6.25)	15 (8.52)	0.415
Hyperlipemia. n (%) 146 (82.96)	145 (82.39)	0.888
Ischemic stroke, n (%) 21 (11.93)	19 (10.80)	0.737
Previous cerebral hemorrhage n (%) 0	1 (0 57)	1 000
(OPD n (%) 0	2 (1 14)	0.499
Laboratory variables	2 ()	0.122
hs-TNI ng/ml (IOR) 10.45 (5.18–21.08)	10 10 (5 30–17 83)	0.451
BNP pg/ml (IQR) 50.49 (22.15–116.49)	57.06 (25.58–149.40)	0.127
CK-MB ng/ml (IQR) 1 90 (1 20–3 51)	1 90 (1 20–3 53)	0.963
CK L/L (IOR) 67.50 (51.75–92.00)	70.00 (55.00–101.00)	0.051
Scr mg/dL (IOR) 085 (070–101)	0.86 (0.74–1.00)	0.135
eGER ml/min/1 73m <sup>2</sup> (IOR) 91 24 (77 94–107 90)	91 27 (86 17–105 26)	0.082
Cr mg/min (IOR) 78 34(60.89–96.49)	76 56 (62 08–90 06)	0 346
BUN mmol/L (IOR) 5 75 (4 85–6 47)	5 91 (4 77–6 85)	0.150
Glu mmol/L (IOR) 600 (5 28–6 90)	610 (520-733)	0.053
HbA1c, % (IQR) 6.77 (6.20–7.20)	6.78 (6.10-7.40)	0.742
TC, mmol/L (IOR) 3.50 (2.90–4.20)	3.47 (2.99–4.22)	0.547
TG. mmol/L (IOR) 1.43 (0.99–1.70)	1.47 (1.03–1.47)	0.462
I DI - C mmol/L (IOR) 1 87 (1 38–2 48)	1 84 (1 44–2 46)	0.425
HDI-C mmol/l (IOR) $1.03(0.88-1.20)$	1 03 (0 98–1 12)	0.682
AIT. U/L (IOR) 16.00 (13.00–25.25)	17.50 (13.00–24.00)	0.171
AST. U/L (IQR) 18.00 (15.00–22.00)	18.00 (14.00–24.00)	0.126
GGT U/L (IOR) 32.00 (19.75–38.00)	36.00 (24.00–38.00)	0.155
PLT.×10 <sup>9</sup> /L (IOR) 207.50 (175.25–242.75)	205.50 (174.75–244.25)	0.667
MYO, ng/L (IOR) 27.45 (19.48–45.45)	30.30 (21.38–49.48)	0.123
Hab. a/L (IOR) 133.00 (122.00–144.25)	133.00 (121.75–143.00)	0.637
Description of the lesions		
Single-vessel disease. n (%) 79 (44.89)	93 (52.84)	0.135
Multi-vessel disease (> 2). $n(\%)$ 97 (55.11)	83 (47.16)	0.135
LM lesion, n (%) 5 (2.84)	4 (2.27)	1.000
LCX lesion. n (%) 99 (56.25)	103 (58.52)	0.666
AD lesion, n (%) 45 (25.57)	38 (21.59)	0.379
RCA lesion, n (%) 56 (31.82)	52 (29.55)	0.644
PCI information		
PCI with balloon only, n (%) 91 (51 71)	84 (47.73)	0.456
PCI with stent only. n (%) 68 (38.64)	75 (42.62)	0.447
PCI with balloon and stent, n (%) 17 (9.66)	17 (9.66)	1.000

## Table 2 (continued)

	DAPA group (n = 176)	Control group (n = 176)	<i>p</i> value
Contrast volume, mL (IQR)	156.50 (120.00–190.00)	152.50 (135.00–190.00)	0.778
Medications			
Antiplatelets, n (%)	175 (99.43)	172 (97.73)	0.371
Anticoagulation, n (%)	2 (1.14)	4 (2.27)	0.685
β-blockers, n (%)	134 (76.14)	136 (77.27)	0.801
RAASi, n (%)	103 (58.52)	113 (64.21)	0.274
CCB, n (%)	76 (43.18)	80 (45.46)	0.668
ARNI, n (%)	39 (22.16)	39 (22.16)	1.000
Statin, n (%)	157 (89.21)	162 (92.05)	0.361
Ezetimibe, n (%)	67 (38.07)	70 (39.77)	0.743
Diuretic, n (%)	50 (28.41)	53 (30.11)	0.725
Metformin, n (%)	57 (32.39)	47 (26.71)	0.243
DPP-4i, n (%)	31 (17.61)	34 (19.32)	0.680
GLP-1RA, n (%)	12 (6.82)	12 (6.82)	1.000
SU, n (%)	14 (7.96)	13 (7.39)	0.841
Insulin, n (%)	51 (28.98)	43 (24.43)	0.335

placebo-controlled trial analysed whether SGLT2 inhibitor treatment initiated within 72 h following PCI in patients with or without diabetes mellitus would result in a decrease in N-terminal prohormone of brain natriuretic peptide (NT-proBNP) levels. The results revealed that in patients with a recent MI, SGLT2 inhibitors were associated with substantially increased NT-proBNP levels [22].

According to the 4th Universal Definition of Myocardial Infarction, MI associated with PCI is categorized as type 4aMI, which is primarily determined by the elevation level of cTnI [23]. Numerous studies have demonstrated that the PMI is related to the subsequent increased risk of mortality and other adverse cardiovascular events [24]. Therefore, we chose the PMI/4aMI as our cardiac outcome indicator, which could better reflect myocardial damage during PCI. To our knowledge, our study is the first trial in which PMI/4aMI was used to assess cardiac and myocardial impairment outcomes. Consistent with previous results, our study revealed that dapagliflozin obviously improved cardiac outcomes. Initiating dapagliflozin more than 1 week before PCI in patients with T2DM and CCS could significantly reduce PMI/4aMI events compared with no use of SGLT2 inhibitors. Our results indicate that early dapagliflozin intake before PCI (more than 1 week) may be associated with improved cardiovascular benefits.

The results of the forest plots in the subgroup analysis of this study revealed that, for people aged 65 and above, the use of dapagliflozin before PCI had a more significant myocardial protective effect. In addition, in patients with multivessel lesions, the use of dapagliflozin provides better myocardial protection. The subgroup analysis also revealed that in the subgroup with a high dose of contrast agent, the protective effect of dapagliflozin was more obvious, and this result was consistent with that of the multivessel lesion subgroup. A larger dosage of contrast agent may suggest a longer PCI time, more diseased blood vessels, and more complex PCI procedures.

In the subgroup analysis, we also included whether DPP4 inhibitors or GLP-1 receptor agonists were used in combination because these two types of drugs are currently known to have cardioprotective effects. We did this to rule out the confounding factors of combined medications that might affect the results. However, based on the results of this study, the combined use of medications did not have an effect on the outcomes.

#### **Renal injury protection**

PCI is a widely used treatment for patients with coronary heart disease. Intra-arterial administration of iodinated contrast media during PCI may induce renal impairment [25–27]. CI-AKI is a substantial concern following exposure to iodinated contrast media that are used in diagnostic or interventional procedures and may represent a significant cause of iatrogenic renal dysfunction, contributing to adverse clinical outcomes [25, 26].

Several clinical trials have consistently indicated that the use of an SGLT2 inhibitor can provide renal protection through a decreased rate of decline in the eGFR and reduced onset or progression of albuminuria [28]. According to previous experiments, the pathophysiological mechanisms underlying the renoprotective effects of SGLT2 inhibitors include the following: (1) osmotic diuresis, natriuretic and hypovolaemia [29–31]; (2) tubuloglomerular feedback [32–34]; (3) tubular oxygenation [35–37]; (4) tubular energetics and sodium-hydrogen exchange [36–38]; and (5) inflammation and fibrosis [39]. Several other mechanisms are considered to contribute to the renoprotective effect of SGLT2 inhibition [40].

	PIM/4aMI	
Subgroups	OR (95%CI)	P interation
Total	0.44 [0.29, 0.67]	
Age		0.706
< 65 years	0.77 [0.42, 1.41]	-
≥ 65 years	0.26 [0.14, 0.47]	
Gender		0.442
Male	0.48 [0.30, 0.78]	
Female	0.30 [0.12, 0.76]	
Smoking history		0.844
No	0.36 [0.19, 0.68]	
Yes	0.51 [0.29, 0.92]	
eGFR		0.055
60 ~< 90 ml/min/1.73m <sup>2</sup>	0.42 [0.22, 0.79]	
≥ 90 ml/min/1.73m²	0.44 [0.25, 0.80]	
Previous MI		0.989
No	0.44 [0.27, 0.72]	
Yes	0.38 [0.16, 0.91]	
Description of the lesion	s	0.516
Single-vessel disease	0.57 [0.31, 1.04]	
Multi-vessel disease (≥ 2)	0.33 [0.18, 0.61]	
PCI		0.176
DCB only	0.49 [0.27, 0.90]	
DES only	0.44 [0.23, 0.87]	
DES+DCB	0.22 [0.05, 0.95]	
Contrast volume		0.539
< 150 mL	0.58 [0.29, 1.16]	
150 ~< 200 mL	0.37 [0.19, 0.73]	
≥ 200 mL	0.32 [0.12, 0.83]	
Medication		0.378
without DPP4i or GLP-1RA	0.45 [0.27, 0.74]	
with DPP4i or GLP-1RA	0.39 [0.16, 0.95]	
	· · · · ·	
	0 0.5 1	1.5 2
	Low risk of DAPA group l	ow risk of Control group

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Fig. 2 Subgroup analyses for cardiac events (PIM/4aMI). DCB: drug-coated balloon; DES: drug-eluting stent

Previous studies that examined the real-world risk of CI-AKI in patients who received SGLT2 inhibitors during PCI did not identify an association between CI-AKI reduction and the use of SGLT2 inhibitors [25]. In contrast, other trials confirmed the benefit of SGLT2 inhibitors in protecting against CI-AKI [21, 41]. A multicentre international registry trial revealed that the use of SGLT2 inhibitors was associated with a significantly lower occurrence of CI-AKI in patients with T2DM and AMI [21].

In this study, for the two renal event outcomes of CI- $AKI_{EUSR}$  and CI- $AKI_{KDIGO}$ , neither the univariate analysis nor the multivariate regression analysis revealed a

significant difference between the dapagliflozin group and the control group. The results of the subgroup forest plot analysis revealed pronounced benefits in patients aged  $\geq$  65 years, those with multivessel disease, and those receiving greater contrast volume.

Considering that CI-AKI is a relatively strict indicator that is used to evaluated renal injury and that eGFR can more sensitively reflect the trend of change in patients' renal function, we conducted a paired analysis of the changes in eGFR before and after PCI in the two groups. The results showed that the dapagliflozin group had

Total       0.69 [0.26, 1.86]       P interaction       0.706         Age       0.776       0.706         65 years       0.66 [0.11, 4.18]       0.257       0.77 [0.42, 1.41]         Gender       0.85 [0.22, 3.24]       0.857       0.44 [0.29, 0.67]       0.442         Male       0.85 [0.22, 3.24]       0.44 [0.30, 0.78]       0.442         Female       0.44 [0.10, 1.99]       0.544       0.30 [0.12, 0.76]       0.844         No       0.81 [0.26, 2.53]       0.544       0.36 [0.19, 0.68]       0.551         Yes       0.34 [0.03, 3.0]       0.715       0.42 [0.22, 0.79]       0.555         GO << 90 m/min/1.73m <sup>2</sup> 0.84 [0.25, 2.86]       0.51 [0.29, 0.92]       0.555         Yes       0.36 [0.19, 0.68]       0.51       0.555       0.555         Frevious Mi       0.44 [0.27, 0.72]       0.555       0.555       0.516         Single-vessel disease       0.80 [0.13, 4.91]       0.33 [0.18, 0.61]       0.516       0.516         Single-vessel disease       0.80 [0.17, 241]       0.57 [0.31, 1.04]       0.516       0.559         DCB only       0.80 [0.27, 241]       0.589       0.558 [0.9, 0.53]       0.559       0.539         OCHC only       0.49 [0.21, 3.70]	Subgroups	CI-AKI <sub>ESUR</sub> OR (95%CI)	-	1	CI-AKI <sub>KDK</sub> OR (95%C	iO ) <b>–</b> i – i – i – i – i – i – i – i – i – i	
Age       0.576       0.706         < 65 years       0.67 [0.20, 2.0]       0.77 [0.42, 1.41]         26 years       0.68 [0.11, 4.18]       0.26 [0.14, 0.47]         Gender       0.357       0.442         Male       0.85 [0.22, 3.24]       0.48 [0.30, 0.78]         Female       0.44 [0.10, 1.99]       0.544       0.30 [0.12, 0.76]         Smoking history       0.544       0.36 [0.19, 0.68]       1.1         Yes       0.34 [0.03, 3.0]       0.51 [0.29, 0.92]       0.651         GerR       0.715       0.44 [0.25, 0.80]       0.51 [0.29, 0.92]         90 ml/min/1.73m <sup>2</sup> 0.47 [0.08, 2.67]       0.44 [0.22, 0.79]       0.651         Yes       0.36 [0.19, 0.68]       0.44 [0.25, 0.80]       0.511         Previous MI       0.511       0.42 [0.22, 0.79]       0.45 [0.27, 0.72]         Yes       0.60 [0.05, 6.90]       0.262       0.516         Description of the lesions       0.262       0.516       0.516         Single-vessel disease (>2)       0.59 [0.18, 1.93]       0.44 [0.27, 0.72]       0.44 [0.27, 0.72]         DES only       0.30 [0.17, 79]       0.44 [0.27, 0.72]       0.516         Contrast volume       0.59 [0.18, 1.93]       0.56 [0.01, 0.59]       0.58 [	Total	0.69 [0.26, 1.85]	Pinteraction	H	0.44 [0.29, 0.	67 Pinteraction	
	Age		0.976			0.706	
$ \begin{tabular}{ c c c c c } \hline $ 0.68 [0.11, 4.18] & $ 0.367 & $ 0.442 & $ 0.440 & $ 0.30 & $ 0.78 \\ \hline $ $ $ $ $ 0.44 [0.30, 0.78] & $ 0.442 & $ $ $ 0.440 & $ 0.30 & $ 0.716 & $ 0.844 & $ $ $ $ $ 0.30 & $ 0.12, 0.76] & $ $ $ $ $ $ $ $ $ $ $ $ $ $ $ $ $ $ $	< 65 years	0.67 [0.20, 2.20]		H <b>E</b>	0.77 [0.42, 1.	41]	I
Gender       0.367       0.442         Male       0.85 [0.22, 3.24]       0.44 [0.10, 1.99]       0.30 [0.12, 0.76]         Female       0.44 [0.10, 1.99]       0.544       0.30 [0.12, 0.76]       0.844         No       0.81 [0.26, 2.53]       0.544       0.36 [0.19, 0.68]       0.844         Ves       0.34 [0.03, 3.30]       0.715       0.45 [0.22, 0.79]       0.655         60 ~< 90 ml/min/1.73m²	≥ 65 years	0.68 [0.11, 4.18]		H <b>B</b>	0.26 [0.14, 0.	47]	H
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	Gender		0.357			0.442	
Female $0.44$ [ $0.10, 1.99$ ] $0.544$ $0.30$ [ $0.12, 0.76$ ] $0.844$ No $0.81$ [ $0.26, 2.53$ ] $0.36$ [ $0.19, 0.68$ ] $0.844$ Yes $0.34$ [ $0.03, 3.30$ ] $0.35$ [ $0.19, 0.68$ ] $0.51$ eGFR $0.34$ [ $0.25, 2.68$ ] $0.42$ [ $0.22, 0.79$ ] $0.42$ Yes $0.69$ [ $0.23, 2.04$ ] $0.44$ [ $0.27, 0.72$ ] $0.899$ Previous MI $0.60$ [ $0.56, 2.98$ ] $0.44$ [ $0.27, 0.72$ ] $0.516$ Description of the lesions $0.262$ $0.57$ [ $0.31, 1.04$ ] $0.516$ Single-vessel disease $0.80$ [ $0.7, 2.41$ ] $0.44$ [ $0.27, 0.90$ ] $0.516$ DCB only $0.80$ [ $0.27, 2.41$ ] $0.44$ [ $0.27, 0.90$ ] $0.516$ Single-vessel disease ( $\ge 2$ ) $0.59$ [ $0.13, 4.91$ ] $0.33$ [ $0.18, 0.61$ ] $0.516$ DCB only $0.80$ [ $0.27, 2.41$ ] $0.44$ [ $0.23, 0.87$ ] $0.516$ DCB only $0.80$ [ $0.21, 3.70$ ] $0.445$ [ $0.27, 0.70$ ] $0.539$ DCS only $0.49$ [ $0.27, 0.71$ ] $0.42$ [ $0.22, 0.83$ ] $0.539$ Contrast volume $0.485$ $0.37$ [ $0.19, 0.73$ ] $0.32$ [ $0.16, 0.95$ ] $0.378$	Male	0.85 [0.22, 3.24]			0.48 [0.30, 0.	78]	
Smoking history       0.544       0.644       0.844         No       0.81 [0.26, 2.53]       0.33 [0.19, 0.68]       0.51 [0.29, 0.92]         Yes       0.34 [0.03, 3.0]       0.51 [0.29, 0.92]       0.655         60 ~< 90 ml/min/1.73m <sup>2</sup> 0.47 [0.08, 2.67]       0.42 [0.22, 0.79]       0.655 $60 \sim 90$ ml/min/1.73m <sup>2</sup> 0.47 [0.08, 2.67]       0.44 [0.25, 0.80]       0.989         Previous MI       0.511       0.44 [0.27, 0.72]       0.989         No       0.69 [0.23, 2.04]       0.33 [0.16, 0.91]       0.516         Single-vessel disease       0.60 [0.05, 6.90]       0.38 [0.16, 0.91]       0.516         Previous MI       0.59 [0.18, 1.93]       0.33 [0.18, 0.61]       0.516         PCI       0.899       0.33 [0.18, 0.61]       0.176         DCB only       0.80 [0.27, 2.41]       0.44 [0.23, 0.87]       0.44 [0.23, 0.87]         DES+DCB       0.30 [0.11, 7.9]       0.445 [0.27, 0.90]       0.559         Cottrast volume       0.485       0.32 [0.12, 0.83]       0.516          0.32 [0.12, 0.83]       0.378       0.378         vithout DPP4i or GLP-1RA       0.62 [0.21, 1.79]       0.45 [0.27, 0.74]       0.39 [0.16, 0.95]         vithout DPP4i or GLP-1RA       0.62 [0.21	Female	0.44 [0.10, 1.99]		-	0.30 [0.12, 0.	76]	
No $0.81 [0.26, 2.53]$ $0.36 [0.19, 0.68]$ $1.9 - 10.68$ Yes $0.34 [0.3, 3.30]$ $0.51 [0.29, 0.92]$ $0.55 [0.29, 0.92]$ eGFR $0.715$ $0.42 [0.22, 0.79]$ $0.44 [0.25, 0.80]$ Previous MI $0.44 [0.27, 0.72]$ $0.38 [0.16, 0.91]$ No $0.69 [0.23, 2.04]$ $0.44 [0.27, 0.72]$ $0.38 [0.16, 0.91]$ Description of the lesions $0.262$ $0.57 [0.31, 1.04]$ $0.516$ Single-vessel disease $0.80 [0.27, 2.41]$ $0.49 [0.27, 0.90]$ $0.516$ DCB only $0.80 [0.27, 2.41]$ $0.49 [0.27, 0.90]$ $0.516$ DCS only $0.30 [0.11, 3.49]$ $0.44 [0.23, 0.87]$ $0.539$ Contrast volume $0.44 [0.22, 0.73]$ $0.58 [0.29, 1.16]$ $0.539$ < 150 mL $0.89 [0.21, 3.70]$ $0.652$ $0.58 [0.29, 1.16]$ $0.57 [0.31, 1.04]$ Medication $0.62 [0.21, 1.79]$ $0.652$ $0.58 [0.29, 0.71]$ $0.39 [0.16, 0.95]$ $0.37 [0.19, 0.73]$ without DPP4i or GLP-1RA $0.62 [0.21, 1.79]$ $0.45 [0.7, 8]$ $0.45 [0.27, 0.74]$ $0.39 [0.16, 0.95]$ $0.12 2 3 4 5 6 7 8$ $0.055 [0.95 1 1.5 2]$	Smoking history		0.544			0.844	
Yes $0.34 [0.03, 3.30]$ $0.51 [0.29, 0.92]$ $1.41 [0.25, 0.80]$ eGFR $0.715$ $0.60 [50, 2.67]$ $0.42 [0.22, 0.79]$ $0.655$ $60 \sim 490$ ml/min/1.73m² $0.47 [0.08, 2.67]$ $0.42 [0.22, 0.79]$ $0.42 [0.22, 0.79]$ $0.45 [0.27, 0.72]$ $90$ ml/min/1.73m² $0.60 [0.05, 6.90]$ $0.511$ $0.44 [0.27, 0.72]$ $0.8989$ No $0.60 [0.05, 6.90]$ $0.262$ $0.38 [0.16, 0.91]$ $0.516$ Single-vessel disease $0.80 [0.13, 4.91]$ $0.33 [0.18, 0.61]$ $0.57 [0.31, 1.04]$ Multi-vessel disease (2.2) $0.59 [0.18, 1.93]$ $0.44 [0.27, 0.90]$ $0.57 [0.31, 1.04]$ DCB only $0.80 [0.27, 2.41]$ $0.49 [0.27, 0.90]$ $0.416 [0.27, 0.90]$ DES only $0.89 [0.21, 3.70]$ $0.485$ $0.58 [0.29, 1.16]$ $0.57 [0.31, 1.04]$ DES +DCB $0.30 [0.01, 7.79]$ $0.485$ $0.58 [0.29, 1.16]$ $0.37 [0.19, 0.73]$ $0.32 [0.12, 0.83]$ Contrast volume $0.485$ $0.552$ $0.32 [0.12, 0.83]$ $0.37 [0.16, 0.95]$ $0.37 [0.16, 0.95]$ $0.57 [0.31, 0.4]$ Without DPP4i or GLP-1RA $0.62 [0.21, 1.79]$ $0.45 [0.27, 0.74]$ <t< td=""><td>No</td><td>0.81 [0.26, 2.53]</td><td></td><td>H<b>H</b></td><td>0.36 [0.19, 0.</td><td>68]</td><td></td></t<>	No	0.81 [0.26, 2.53]		H <b>H</b>	0.36 [0.19, 0.	68]	
eGFR       0.715       0.715       0.055         60 ~ 90 ml/min/1.73m²       0.47 [0.08, 2.67]       0.42 [0.22, 0.79]       0.44 [0.27, 0.72]         2 90 ml/min/1.73m²       0.84 [0.25, 2.86]       0.44 [0.27, 0.72]       0.989         No       0.69 [0.23, 2.04]       0.44 [0.27, 0.72]       0.989         Yes       0.60 [0.05, 6.90]       0.262       0.38 [0.16, 0.91]       0.516         Single-vessel disease       0.80 [0.13, 4.91]       0.33 [0.18, 0.61]       0.516         Wulti-vessel disease (≥ 2)       0.59 [0.18, 1.93]       0.44 [0.27, 0.90]       0.516         DCB only       0.80 [0.27, 2.41]       0.49 [0.27, 0.90]       0.516         DES +DCB       0.30 [0.01, 7.79]       0.485       0.58 [0.29, 1.16]       0.539         Contrast volume       0.485       0.58 [0.29, 1.16]       0.57 [0.31, 1.04]       0.552         Vithout DPP4i or GLP-1RA       0.62 [0.21, 1.79]       0.45 [0.27, 0.74]       0.378       0.378         without DPP4i or GLP-1RA       0.65 [0.05, 6.44]       0.45 [0.27, 0.74]       0.39 [0.16, 0.95]       0.378         without DPP4i or GLP-1RA       0.65 [0.05, 6.44]       0.45 [0.27, 0.74]       0.39 [0.16, 0.95]       0.378	Yes	0.34 [0.03, 3.30]		<b></b> i	0.51 [0.29, 0.	92]	
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	eGFR		0.715	_		0.055	
$ \begin{tabular}{ c c c c c c } $$ $$ $$ $$ $$ $$ $$ $$ $$ $$ $$ $$ $$$	60 ~< 90 ml/min/1.73m <sup>2</sup>	0.47 [0.08, 2.67]		1	0.42 [0.22, 0.	79]	F
Previous MI       0.511       0.511       0.989         No       0.69 [0.23, 2.04]       0.60 [0.05, 6.90]       0.38 [0.16, 0.91]         Description of the lesions       0.262       0.38 [0.16, 0.91]       0.516         Single-vessel disease       0.80 [0.13, 4.91]       0.57 [0.31, 1.04]       0.516         Wulti-vessel disease (2 2)       0.59 [0.18, 1.93]       0.3899       0.176         PCI       0.899       0.44 [0.27, 0.72]       0.516         DCB only       0.80 [0.27, 2.41]       0.57 [0.31, 1.04]       0.516         DES only       0.44 [0.24, 4.97]       0.44 [0.23, 0.87]       0.22 [0.05, 0.95]         DES only       0.44 [0.21, 3.70]       0.485       0.539         < 150 ~< 200 mL	≥ 90 ml/min/1.73m²	0.84 [0.25, 2.86]			0.44 [0.25, 0.	80]	<b></b>
$\begin{array}{c c c c c c c c c c c c c c c c c c c $	Previous MI		0.511			0.989	
Yes $0.60 \ [0.05, 6.90]$ $0.38 \ [0.16, 0.91]$ $0.38 \ [0.16, 0.91]$ Description of the lesions $0.262$ $0.57 \ [0.31, 1.04]$ $0.516$ Single-vessel disease $0.80 \ [0.13, 4.91]$ $0.33 \ [0.18, 0.61]$ $0.57 \ [0.31, 1.04]$ Multi-vessel disease ( $\geq 2$ ) $0.59 \ [0.18, 1.93]$ $0.899$ $0.33 \ [0.18, 0.61]$ $0.176$ PCI $0.33 \ [0.18, 0.61]$ $0.176$ $0.176$ DCB sonly $0.44 \ [0.04, 4.97]$ $0.44 \ [0.23, 0.87]$ $0.22 \ [0.05, 0.95]$ $0.539$ DES +DCB $0.30 \ [0.17, 7.9]$ $0.485$ $0.539$ $0.539$ $0.539$ Contrast volume $0.485$ $0.37 \ [0.19, 0.73]$ $0.58 \ [0.29, 1.16]$ $0.37 \ [0.19, 0.73]$ $0.37 \ [0.19, 0.73]$ $\geq 200 \text{ mL}$ $0.24 \ [0.02, 2.42]$ $0.452 \ [0.27, 0.74]$ $0.37 \ [0.19, 0.73]$ $0.378 \ [0.378]$ $0.378 \ [0.16, 0.95]$ $0.378 \ [0.16, 0.95]$ $0.56 \ [0.27, 0.74]$ $0.45 \ [0.27, 0.74]$ $0.39 \ [0.16, 0.95]$ $0.57 \ [0.27, 0.74]$ $0.56 \ [0.05, 6.44]$ $0.32 \ [0.16, 0.95]$ $0.57 \ [0.55 \$	No	0.69 [0.23, 2.04]			0.44 [0.27, 0.	72]	
Description of the lesions       0.262       0.516         Single-vessel disease       0.80 [0.13, 4.91]       0.57 [0.31, 1.04]       0.33 [0.18, 0.61]         Multi-vessel disease (≥ 2)       0.59 [0.18, 1.93]       0.899       0.176         PCI       0.899       0.44 [0.27, 0.90]       0.44 [0.23, 0.87]         DES only       0.30 [0.17, 7.9]       0.44 [0.23, 0.87]       0.22 [0.05, 0.95]         DES+DCB       0.30 [0.17, 7.9]       0.485       0.539         < 150 mL       0.89 [0.21, 3.70]       0.485       0.37 [0.19, 0.73]       0.539         < 150 mL       0.89 [0.21, 3.70]       0.652       0.332 [0.12, 0.83]       0.337 [0.19, 0.73]         < 200 mL       0.24 [0.02, 2.42]       0.652       0.332 [0.12, 0.83]       0.378         Medication       0.652 [0.21, 1.79]       0.455 [0.27, 0.74]       0.39 [0.16, 0.95]         without DPP4i or GLP-1RA       0.62 [0.21, 1.79]       0.45 [0.27, 0.74]       0.39 [0.16, 0.95]         0       1 2 3 4 5 6 7 8       0       0.516       0	Yes	0.60 [0.05, 6.90]		H	0.38 [0.16, 0.	91]	
Single-vessel disease       0.80 [0.13, 4.91]       0.57 [0.31, 1.04]         Multi-vessel disease (≥ 2)       0.59 [0.18, 1.93]       0.33 [0.18, 0.61]         PCI       0.899       0.176         DCB only       0.80 [0.27, 2.41]       0.49 [0.27, 0.90]         DES sonly       0.30 [0.01, 7.79]       0.44 [0.23, 0.87]         DES+DCB       0.30 [0.01, 7.79]       0.485         < 150 mL	Description of the lesions		0.262			0.516	
$\begin{array}{c c c c c c c c c c c c c c c c c c c $	Single-vessel disease	0.80 [0.13, 4.91]		-	• 0.57 [0.31, 1.	04]	2
PCI       0.899       0.176         DCB only       0.80 [0.27, 2.41]       0.49 [0.27, 0.90]       0.44 [0.23, 0.87]         DES only       0.44 [0.04, 4.97]       0.44 [0.23, 0.87]       0.42 [0.22, 0.05, 0.95]         DES+DCB       0.30 [0.01, 7.79]       0.485       0.539         Contrast volume       0.485       0.58 [0.29, 1.16]       0.539         ≤ 150 mL       0.61 [0.11, 3.46]       0.37 [0.19, 0.73]       0.37 [0.19, 0.73]         ≥ 200 mL       0.24 [0.02, 2.42]       0.652       0.32 [0.12, 0.83]       0.378         Medication       0.652       0.45 [0.27, 0.74]       0.39 [0.16, 0.95]       0.378         without DPP4i or GLP-1RA       0.56 [0.05, 6.44]       0.45 [0.27, 0.74]       0.39 [0.16, 0.95]       0.57         0       1.2 3 4 5 6 7 8       0       0.55 1 1.5 2       0       0.55 1 1.5 2	Multi-vessel disease (≥ 2)	0.59 [0.18, 1.93]		HE	0.33 [0.18, 0.	61]	1- <b></b>
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DES+DCB       0.30 [0.01, 7.79]         Contrast volume       0.485         < 150 mL	DES only	0.44 [0.04, 4.97]		H	→ 0.44 [0.23, 0.	87]	I
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150 ~< 200 mL	< 150 mL	0.89 [0.21, 3.70]			0.58 [0.29, 1.	16]	E
≥ 200 mL 0.24 [0.02, 2.42] Medication 0.652 0.652 0.652 0.378 0.378 0.39 [0.16, 0.95] with DPP4i or GLP-1RA 0.62 [0.21, 1.79] 0.56 [0.05, 6.44] 0.12 3 4 5 6 7 8 0.39 [0.16, 0.95] 0.12 3 4 5 6 7 8 0 0.55 1 1.5 2	150 ~< 200 mL	0.61 [0.11, 3.46]			0.37 [0.19, 0.	73]	I
Medication         0.652         0.378           without DPP4i or GLP-1RA         0.62 [0.21, 1.79]         0.45 [0.27, 0.74]         Image: constraint of the second s	≥ 200 mL	0.24 [0.02, 2.42]			0.32 [0.12, 0.	83]	2
with out DPP4i or GLP-1RA       0.62 [0.21, 1.79]         with DPP4i or GLP-1RA       0.56 [0.05, 6.44]         0       1       2       3       4       5       6       7       8       0       0.5       1       1.5       2	Medication		0.652			0.378	
with DPP4i or GLP-1RA     0.56 [0.05, 6.44]     0.39 [0.16, 0.95]       0 1 2 3 4 5 6 7 8     0 0.5 1 1.5 2	without DPP4i or GLP-1RA	0.62 [0.21, 1.79]			0.45 [0.27, 0.	74]	I-B
0 1 2 3 4 5 6 7 8 0 0.5 1 1.5 2	with DPP4i or GLP-1RA	0.56 [0.05, 6.44]		P	0.39 [0.16, 0.	95]	
Low risk of DADA group Low risk of Control group Low risk of DADA group Low risk of DADA			Low risk of DAI	0 1 2 3 4	5 6 7 8	Low rick - (DA	0 0.5 1 1.5 2

Fig. 3 Subgroup analyses for cardiac events (CI-AKI $_{\rm ESUR}$  and CI-AKI $_{\rm KDIGO}$ )



Fig. 4 Box plot and line plot comparing the distribution of the eGFR before and after PCI in the DAPA group vs. the control group

better performance in terms of eGFR reduction before and after PCI than did the control group.

Currently available measures, such as the eGFR, are sensitive indicators that help in the early identification of renal impairment [42]. Hence, we chose the eGFR and CI-AKI to evaluate renal injury. To our knowledge, this is the first trial employing both the eGFR and two distinct criteria for CI-AKI as renal outcomes. Our results showed that dapagliflozin initiation more than 1 week before PCI was associated with a decrease in the eGFR. No significant reduction in CI-AKI events was detected in patients treated with dapagliflozin compared with controls. These results suggest that dapagliflozin could protect against early renal injury in patients with T2DM and CCS undergoing PCI.

#### **Study limitations**

Our results should be interpreted in light of several limitations. This was a retrospective study based on a moderately sized cohort from a single centre; thus, sampling bias is possible because of the retrospective nature of the data. Moreover, because of the limited number of patients enrolled, an assessment of specific outcome measures and subgroup analysis could not be conducted. Third, long-term outcomes were not evaluated. Larger cohorts and multicentre studies are necessary to further assess the potential protective effects of dapagliflozin on the risk of myocardial and kidney damage in patients with T2DM and CCS undergoing PCI.

## Conclusions

This cohort study demonstrated that dapagliflozin significantly reduces the rates of PMI/4aMI before and after PSM, and this association was confirmed by post-PSM multivariate analysis. However, no significant effects were found on renal outcomes (CI-AKI $_{\rm ESUR}$  and CI-AKI<sub>KDIGO</sub>) before or after PSM, even after covariate adjustment. Subgroup analyses revealed that dapagliflozin was more effective in reducing the incidence of cardiac events in patients aged  $\geq$  65 years, those with multivessel disease, and those receiving high contrast agent dosages (≥150 mL). Similar benefits are observed for renal outcomes in these subgroups. The dapagliflozin group had higher baseline and post-PCI eGFRs, indicating potential preservation of renal function. In summary, dapagliflozin holds promise for improving cardiac outcomes and may also benefit renal function, particularly in specific high-risk subgroups. These findings provide valuable insights for clinical decision-making about the use of dapagliflozin in relevant patient populations.

#### Author contributions

Deping LIU, Naixin ZHENG and Zinan ZHAO designed the research. Tianqi ZHANG, Yuwei LI, Ming LAN, Ni ZHANG, Hui LI, and Hu AI performed the experiments and collected the data. Chi ZHANG and Zinan ZHAO analysed

the data. Zinan ZHAO wrote the manuscript. Deping LIU, Tianqi ZHANG, and Zinan ZHAO participated in the discussion of the results. All the authors have read and approved the final manuscript.

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#### Availability of data and materials

All data relevant to the study are included in the art icle or uploaded assupplementary information.

#### Declarations

#### **Consent for publication**

All the authors provided consent for publication.

#### **Comepting interests**

The authors declare that the research was conducted in the absence of any commercialor financial relationships.

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