Cardiovascular Diabetology

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Exploring the effect of dapagliflozin on coronary inflammation in type 2 diabetes patients based on the coronary artery perivascular fat attenuation index

Xuehua Liu[1,2], Tian Zhang[1,2], Rong Fu[4], Dan Liu[2,5], Jingyi Zhang[2,5], Qing Hu[2,5], Guangyao Song[2,3*] and Luping Ren[2,3*]

Abstract

Background The pericoronary fat attenuation index (FAI) is a novel biomarker that serves as an indicator of coronary artery inflammation. Dapagliflozin has become an important component of standard treatment for type 2 diabetes because of its cardioprotective and renoprotective effects. The objective of this research was to explore how dapagliflozin impacts coronary artery inflammation in T2DM patients and to establish a novel theoretical framework for the protective role of dapagliflozin in the cardiovascular system.

Methods This research retrospectively included 271 T2DM patients treated with coronary computed tomography angiography (CCTA) at Hebei Provincial People's Hospital from January 2021 to November 2024, with 103 patients receiving dapagliflozin therapy (dapagliflozin+) and 168 patients not receiving dapagliflozin (dapagliflozin-) (oral dapagliflozin 10 mg/day for no less than 6 months). Baseline clinical information, laboratory markers, and CCTA-related metrics were collected and analysed across both groups. The relationship between dapagliflozin treatment and the pericoronary FAI was analysed using multiple linear regression to control for confounding variables, and the correlation between the two variables was further examined across various subgroups.

Results Compared with those in the dapagliflozin- group, the patients in the dapagliflozin+ group were younger ($P<0.001$), and the proportion of men was higher ($P<0.05$). There were no between-group differences in the baseline data, such as diabetes course, BMI, and blood lipid status ($P>0.05$). The FAI of the LAD and RCA in the dapagliflozin+ group was lower than that in the other groups, and the average FAI of the three coronary arteries was also significantly lower, while there was no significant difference in the LCX (LAD: dapagliflozin- group: -85.50 (-90.43, -78.27)，dapagliflozin+ group：-86.94 (-92.81, -81.57)，P= 0.044；RCA：dapagliflozin- group：-86.31 (-92.12, -80.09), dapagliflozin+ group：-88.79 (-94.59, -83.31), $P= 0.019$; Mean: dapagliflozin- group: -84.05 (-87.73, -77.45), dapagliflozin+ group: -84.88 (-89.82, -79.67), $P= 0.022$; LCX: dapagliflozin- group：-77.81 (-82.57, -71.75), dapagliflozin+ group: -78.25 (-84.56, -72.15), $P = 0.260$). Multiple linear regression analyses revealed an independent association

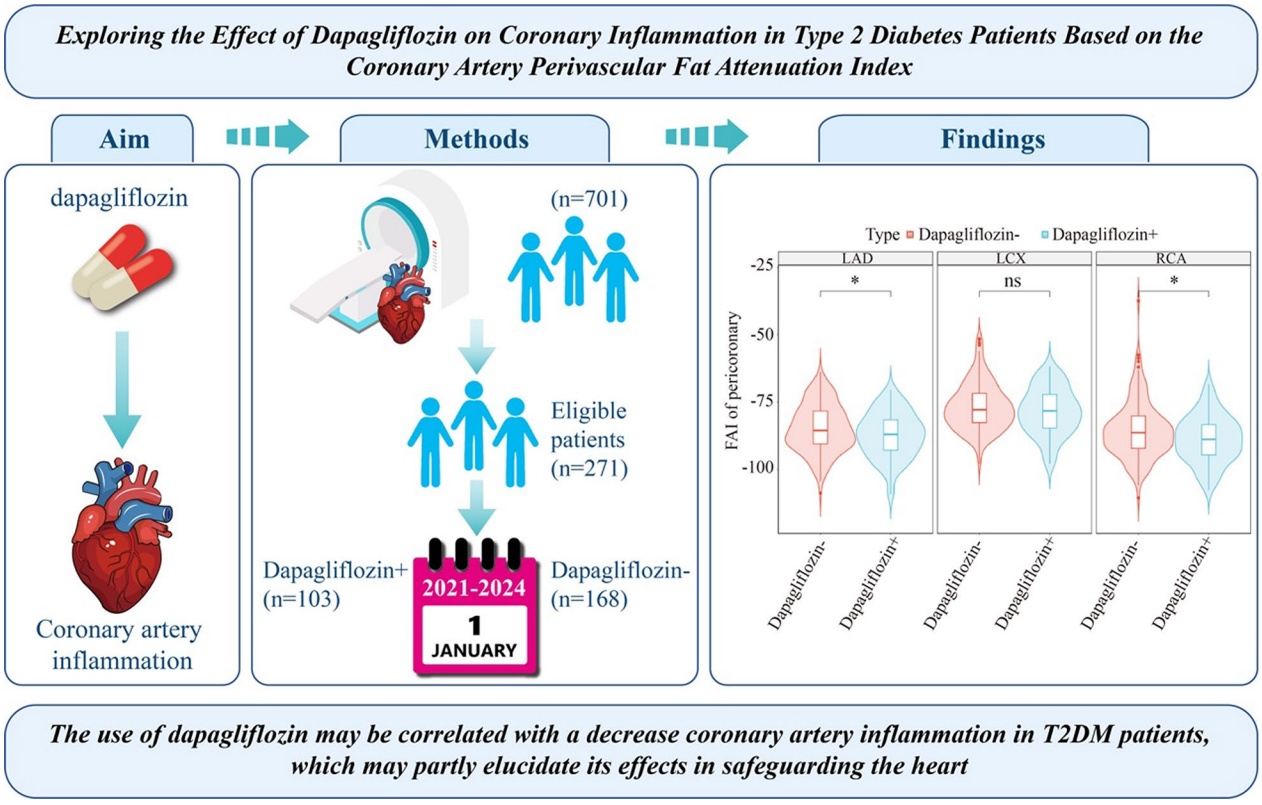
*Correspondence:
Guangyao Song
sguangyao2@163.com
Luping Ren
renluping1122@163.com

Full list of author information is available at the end of the article

between dapagliflozin treatment and a decreased in FAI in the LAD and RCA (LAD: β=-2.449; RCA: β=-3.897; *P* values are all less than 0.05). This association was different across various subsets of T2DM patients.

Conclusion Dapagliflozin treatment is associated with a significant reduction in coronary artery inflammation in T2DM patients, which may partly explain its beneficial effects on reducing cardiovascular risk.

Graphical abstract



Keywords Dapagliflozin, Type 2 diabetes mellitus, Pericoronary fat attenuation index, Coronary artery inflammation, Cardiovascular protection effect

Introduction

Diabetes is a major challenge in the global public health field. As of 2021, the global number of adults with diabetes was 536.6 million, and this figure is expected to increase to 783.2 million by 2045 [1–4]. Compared with the per capita cost of $242 in low-income countries, the cost of type 2 diabetes in high-income countries is $10,801, with complications of type 2 diabetes being the primary cost driver of diabetes [5]. Type 2 diabetes, which accounts for 90-95% of diabetes cases, is mainly characterized by insulin resistance, hyperglycaemia caused by pancreatic β-cell dysfunction, and a series of complications [6]. In type 2 diabetes patients, atherosclerotic cardiovascular disease (ASCVD) is the primary cause of mortality. The prevalence of ASCVD in patients with T2DM is 32.2% [7]. More than 70% of patients with type 2 diabetes die from cardiovascular complications [8]. The endothelial dysfunction, vascular inflammation and oxidative stress caused by long-term hyperglycaemia are strongly associated with the emergence and progression of ASCVD in T2DM patients. Chronic low-grade inflammation in T2DM, driven by pathways involving NF-κB activation, oxidative stress, and proinflammatory cytokines (e.g., IL-6 and TNF-α), contributes to coronary inflammation and the progression of atherosclerosis [9, 10]. Coronary artery inflammation promotes the formation and progression of arterial plaques, thereby increasing the risk of cardiovascular events [11]. Therefore, reducing cardiovascular mortality by improving coronary artery inflammation in T2DM patients is crucial.

Dapagliflozin functions as a selective inhibitor of sodium–glucose cotransporter 2 (SGLT-2), lowers blood glucose by inhibiting SGLT2 in the renal proximal tubules, reducing glucose reabsorption and increasing

urinary glucose excretion, and it has become an important component of standard treatment for type 2 diabetes due to its cardiovascular and renal protective effects [12, 13]. Previous clinical studies have demonstrated that dapagliflozin is effective at lowering blood pressure, promoting weight loss, and significantly decreasing cardiovascular mortality rates among individuals with type 2 diabetes [14–16]. The cardioprotective effects of dapagliflozin include multiple mechanisms independent of its glucose-lowering effects, such as anti-inflammatory effects, antioxidant activity, and improvements in the cardiac load [17]. Nonetheless, the particular anti-inflammatory properties of dapagliflozin in relation to coronary arteries have yet to be investigated more.

Pericoronary adipose tissue (PCAT) is a special type of adipose tissue surrounding the adventitia of the coronary arteries. It is part of the epicardial adipose tissue (EAT). Its metabolic and inflammatory activities are crucial in the emergence and progression of atherosclerotic cardiovascular diseases [18, 19]. As an active secretory tissue, PCAT secretes proinflammatory cytokines (e.g., IL-6 and TNF-α) in an autocrine or paracrine manner to act on the coronary arteries when it is dysfunctional, thus accelerating endothelial dysfunction and leading to coronary artery disease. Dysfunction of PCAT is strongly associated with obesity, insulin resistance, and metabolic syndrome [20–22]. Additionally, coronary inflammation affects the lipolysis and lipogenesis of the surrounding adipose tissue through the paracrine signaling of proinflammatory cytokines, thereby causing changes in the size and volume of adipocytes. This alteration can be observed through the fat attenuation index (FAI) of PCAT as measured by coronary computed tomography angiography (CCTA) [19, 23, 24]. Serum biomarkers (such as hs-CRP and IL-6) can reflect only systemic inflammation, whereas the FAI can reflect local coronary inflammation more sensitively through direct imaging evaluation of the density of adipose tissue around the coronary artery. As an imaging indicator, the FAI can detect local inflammation in the subclinical stage of coronary artery disease (no significant stenosis has occurred), with increased specificity. The FAI provides anatomical localization information for inflammation, thus helping to identify vulnerable plaques and high-risk vascular segments. As a novel biomarker reflecting coronary artery inflammation, the FAI of PCAT has been used to monitor the effects of therapeutic interventions, especially the metabolic changes in adipose tissue during treatment with anti-inflammatory and lipid-lowering drugs [19, 25].

Recent studies have demonstrated that dapagliflozin has anti-inflammatory effects on coronary arteries through the modulation of epicardial adipose tissue and metabolic activity. A randomized controlled trial revealed that dapagliflozin significantly reduced EAT thickness by up to 20% over 24 weeks, independent of weight loss [26]. Another study involving patients with acute coronary syndrome reported no significant reduction in epicardial fat volume after 12 months of dapagliflozin treatment, although a lower incidence of major adverse cardiovascular events was observed in the dapagliflozin group than in the placebo group [27]. Additionally, a prospective trial in T2DM patients with stable coronary artery disease demonstrated that dapagliflozin significantly reduced EAT thickness by 19% [28]. These studies highlight the potential role of dapagliflozin in reducing epicardial fat thickness, although its effect on the total epicardial fat volume is uncertain. However, epicardial fat is not only metabolically active in volume and thickness but also has an attenuation index that may better reflect the inflammatory state and metabolic characteristics of adipose tissue. Therefore, further attention should be given to the effect of dapagliflozin on the pericoronary fat attenuation index to explore its mechanisms in improving the local inflammatory environment and potential cardiovascular protection effects.

Considering this association, the current study sought to examine the impact of dapagliflozin on coronary artery inflammation in individuals with T2DM based on the coronary artery perivascular fat attenuation index, aiming to offer a novel theoretical foundation for the cardioprotective effects of this drug.

Materials and methods

Study population

The study retrospectively included 701 T2DM patients who underwent CCTA at Hebei Provincial People's Hospital from January 2021 to November 2024. The Ethics Committee of Hebei Provincial People's Hospital approved the study's protocol and waived the requirement for informed consent (No. 2025-LW-0019). The inclusion criteria were as follows: at least 18 years old; and had received a diagnosis of T2DM in accordance with established clinical guidelines [29].

The exclusion criteria were as follows: (1) a medical history that included prior cardiovascular conditions, such as myocardial infarction, stroke, and heart failure; (2) treated with dapagliflozin for less than 6 months (10 mg/day); (3) concomitant use of other SGLT-2 inhibitors such as empagliflozin or GLP-1RA drugs; (4) insufficient image quality to calculate relevant data; or (5) relevant clinical or laboratory data were missing. Overall, 271 patients fulfilled the criteria for inclusion and exclusion (Fig. 1), 103 of whom received dapagliflozin treatment (dapagliflozin+) and 168 of whom did not receive dapagliflozin treatment (dapagliflozin-).

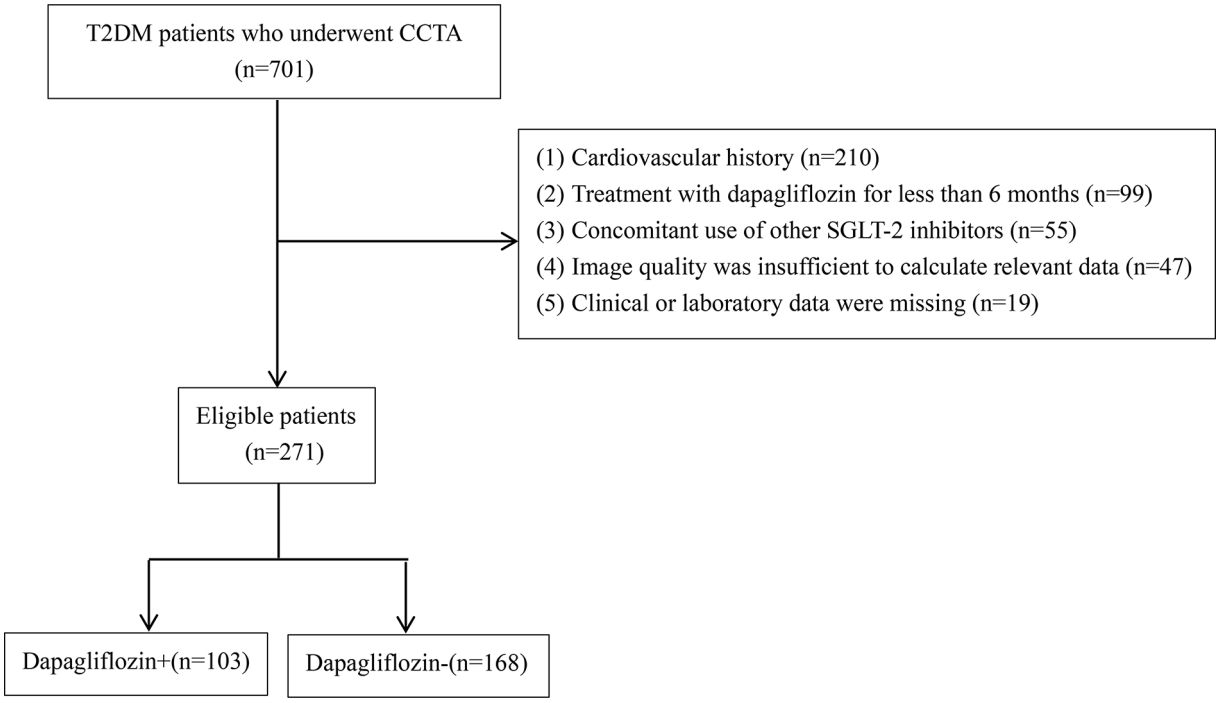


Fig. 1 Flow chart of patient screening for this study

Data collection

The clinical data included several factors, including the age of the participants, sex, body mass index (BMI), duration of type 2 diabetes, smoking status (ongoing smoking for more than 6 months), drinking history, blood pressure, blood lipids and glucose-lowering and lipid-lowering drug use, etc. Blood pressure was measured while the participants were in a seated position after a 5-minute rest, using a calibrated digital sphygmomanometer. The average of three consecutive measurements taken at 1-minute intervals was used for analysis. The laboratory data included baseline data such as white blood cell count, the lymphocyte–neutrophil ratio; and total cholesterol, triglyceride, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), lipoprotein a, fasting plasma glucose (FPG), and glycosylated haemoglobin (HbA1c) levels. The diagnostic criteria for dyslipidaemia were as follows: ① TC ≥ 5.20 mmol/L; ② LDL-C ≥ 3.4 mmol/L; and ③ TG ≥ 1.70 mmol/L. The diagnosis is confirmed when the test results meet either ① + ③ or ② + ③.

CCTA acquisition

CCTA acquisition was performed in our hospital using a two-source CT scanner (Somatom ForceCT, Siemens Healthcare GmbH, Germany). Oral metoprolol was administered to maintain the patient's heart rate at approximately 70 beats per minute. Scanning was conducted starting from the tracheal carina and extending up to 2 cm beneath the apex of the heart, with a control tube voltage set at 100 kVp and a tube current-time product ranging from 380 to 410 mAs. The control scan was completed in one breath hold to ensure image quality.

Analysis of coronary inflammation

To minimize interobserver variability, all image analysts were trained following a standardized protocol. FAI measurements were conducted using a single software platform with consistent parameters. Two independent analysts, blinded to the patient data, performed the measurements. Discrepancies were resolved through consensus. The best coronary artery image sequence for each patient was selected by a professional radiographer at our hospital and imported into professional FAI analysis software developed by Shukun Technology (version 1.0.4, China). The software automatically tracked the three main blood vessels, LAD, LCX, and RCA. To reduce the interference from the aorta, the right coronary artery (RCA) was measured from 10 mm below its origin to 40 mm, and the coronary artery origin was measured from 40 mm below the left anterior descending artery (LAD) (Fig. 2) and the left circumflex artery (LCX). The FAI was calculated by automatically evaluating and documenting the weighted average CT attenuation of adipose tissue located within the radial distance from the outer wall of the vessel equidistant from the average diameter of the vessel (attenuation coefficient between − 190 and − 30 HU).

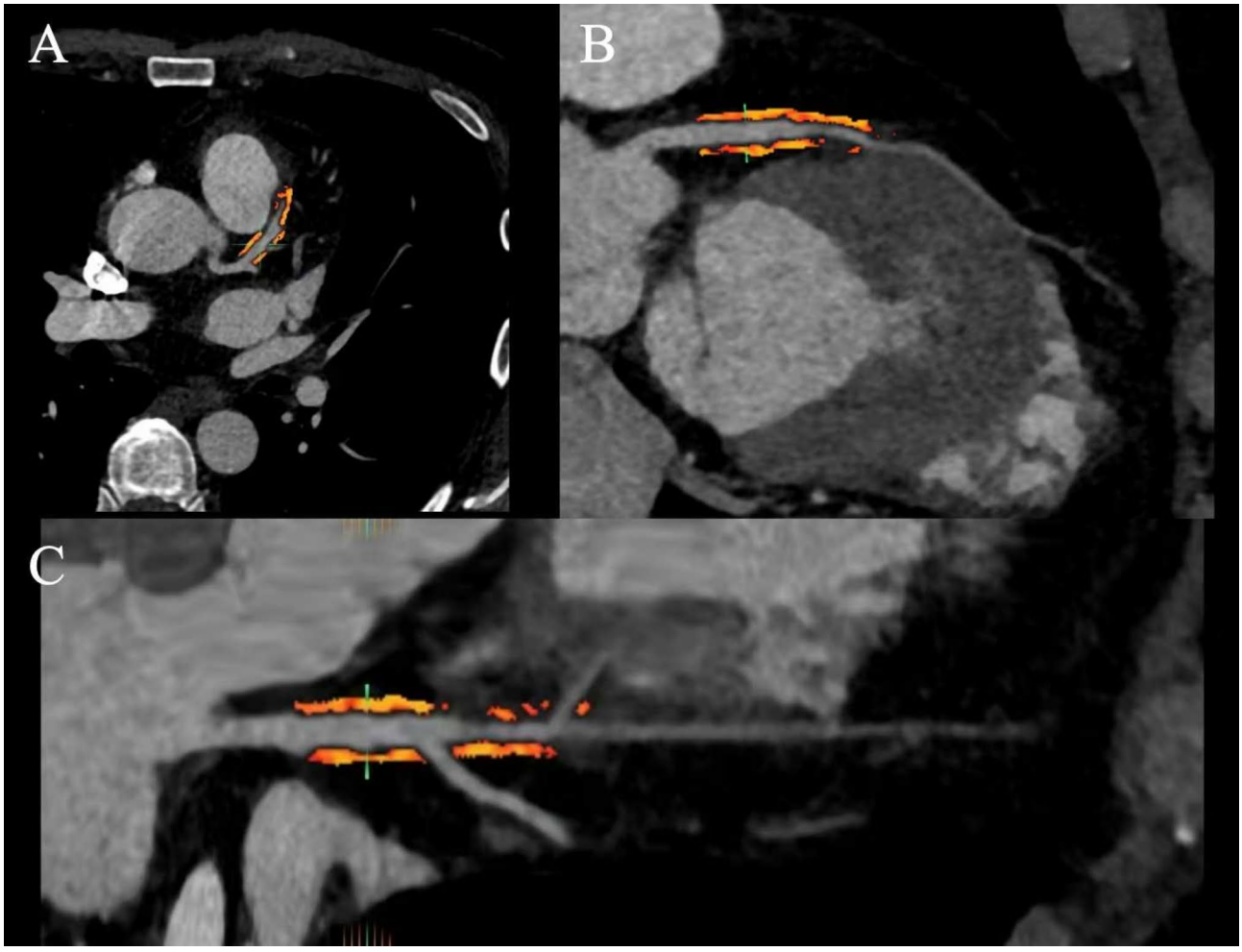


Fig. 2 Representative case of PCAT attenuation in the LAD measured by CCTA. **A** Cross-sectional view showing PCAT (CT values between − 190 and − 30 HU). **B** Image after surface recombination displaying PCAT (40 mm). **C** Straightened view around the proximal 40 mm of the LAD. PCAT: pericoronary adipose tissue; LAD: left anterior descending artery; CCTA: coronary computed tomography angiography

Statistical analysis

First, tests were performed on the measurement data to assess both the normal distribution and the homogeneity of variance. Variables that followed a normal distribution are expressed as the mean and standard deviation (SD), and independent samples t tests were used for comparisons. Variables following a nonnormal distribution are expressed as the median along with the 25th and 75th percentiles (P25, P75) and were compared using the Mann–Whitney U test. Categorical variables are represented as frequencies (%) and were compared using the chi-square test.

The relationship between dapagliflozin therapy and the pericoronary FAI in patients with T2DM was investigated through multivariate stepwise linear regression analysis. The covariates included age, sex, BMI, dyslipidaemia status, smoking status, duration of diabetes, LVEF, HbA1c, and use of statins. Subgroup analysis was performed by stratifying patients according to sex, age, BMI, blood lipid profile, duration of diabetes, and smoking status. A P value of less than 0.05 was considered statistically significant. The statistical analyses were conducted utilizing SPSS version 27.0.

Results

Initial characteristics of patients

The detailed initial data are shown in Table 1. The study encompassed 271 patients, with 160 (59.0%) males and a median age of 64.00 years. Compared with the dapagliflozin- group, the dapagliflozin + cohort was younger, with a median age of 61.00 years ($P < 0.001$); had a higher proportion of males ($P < 0.05$); and had a nonsignificantly longer duration of type 2 diabetes ($P > 0.05$). No notable differences were observed in cardiovascular risk factors (such as smoking, blood lipid profile, hypertension), use of glucose-lowering, antihypertensive, or lipid-lowering drugs, or HbA1c between the two groups ($P > 0.05$). No significant differences in the levels of inflammatory

Table 1 Baseline characteristics of the participants

	Total (*n* = 271)	Dapagliflozin- (*n* = 168)	Dapagliflozin+ (*n* = 103)	*P*
Age (years)	64.00 (57.50, 70.00)	66.00(60.00,71.25)	61.00 (53.00, 67.50)	**< 0.001**
Male, n (%)	160 (59.0%)	91 (54.2%)	69(67.0%)	**0.037**
BMI (kg/m^2)	26.30 (24.56, 28.89)	26.01 (23.93, 28.69)	26.78 (25.17, 29.07)	0.116
T2DM duration (years)	7.00 (2.00, 11.00)	6.00 (1.75, 10.00)	7.00 (3.00, 11.00)	0.073
Smoking	67 (24.7%)	38 (22.6%)	29 (28.2%)	0.305
Drinking	59 (21.8%)	32 (19.1%)	27 (26.2%)	0.165
Hypertension	206 (76.0%)	128 (76.2%)	78 (75.7%)	0.931
Dyslipidaemia	101 (37.3%)	56 (33.3%)	45 (43.7%)	0.087
Medication				
Insulin	101 (37.3%)	60 (35.7%)	41 (39.8%)	0.499
Metformin	120 (44.3%)	72 (42.9%)	48 (46.6%)	0.547
α-glycosidase inhibitor	132 (48.7%)	86 (51.2%)	46 (44.7%)	0.296
Statins	219 (80.8%)	135 (80.4%)	84 (81.6%)	0.808
Anti-hypertensive	207 (76.4%)	128 (76.2%)	79 (76.7%)	0.924
Laboratory indicators				
Fast glucose (mmol/L)	7.73 (6.40, 9.71)	7.73 (6.36, 9.74)	7.67 (6.83, 9.68)	0.422
HbA1c (mmol/L)	7.70 (6.90, 8.90)	7.70 (6.90, 8.90)	7.60 (6.90, 9.10)	0.901
Triglycerides (mmol/L)	1.41 (0.99, 2.20)	1.38 (0.99, 2.05)	1.49 (1.04, 2.53)	0.441
Total cholesterol (mmol/L)	4.38 (3.63, 5.42)	4.37 (3.65, 5.57)	4.40 (3.62, 5.29)	0.635
LDL-C (mmol/L)	2.75 (2.12, 3.43)	2.75 (2.11, 3.54)	2.73 (2.17, 3.42)	0.630
HDL-C (mmol/L)	1.10 (0.94, 1.28)	1.11 (0.96, 1.28)	1.09 (0.91, 1.27)	0.553
Lipoprotein a (mg/L)	132.30 (63.35, 288.55)	137.40 (62.20, 287.78)	113.90 (63.90, 297.65)	0.846
White blood cells (×109 /L)	6.31 (5.30, 7.57)	6.21 (5.23, 7.55)	6.38 (5.59, 7.57)	0.260
Neutrophils (%)	63.30 (56.65, 70.00)	62.35 (56.58, 67.03)	65.10 (56.70, 71.10)	0.231
Leukocytes (%)	28.30 (23.13, 33.27)	29.35 (23.87, 33.50)	25.70 (21.77, 33.10)	0.106
LVEF (%)	64.00 (61.00, 68.00)	65.00 (61.00, 69.00)	64.00 (61.50, 67.00)	0.226
CCTA parameters				
CACS	127.01 (17.15, 385.78)	129.45 (17.20, 372.61)	111.60 (17.15, 423.54)	0.789
FAI				
LAD-PCAT (HU)	-85.92 (-91.70, -79.04)	-85.50 (-90.43, -78.27)	-86.94 (-92.81, -81.57)	**0.044**
LCX-PCAT (HU)	-77.88 (-83.53, -71.95)	-77.81 (-82.57, -71.75)	-78.25 (-84.56, -72.15)	0.260
RCA-PCAT (HU)	-87.11 (-92.94, -81.78)	-86.31 (-92.12, -80.09)	-88.79 (-94.59, -83.31)	**0.019**
Mean	-84.33 (-88.74, -78.36)	-84.05 (-87.73, -77.45)	-84.88 (-89.82, -79.67)	**0.022**

markers (the ratio of white blood cells, lymphocytes and neutrophils) or the coronary artery calcium score (CACS) were detected between the two groups ($P > 0.05$). Compared with the dapagliflozin- group, those in the dapagliflozin + group presented a reduced pericoronary FAI in the LAD and RCA, and the average values of the pericoronary FAI in the three coronary arteries were also significantly lower, whereas the LCX showed no notable statistical variance (LAD: $P = 0.044$; RCA: $P = 0.019$; mean: $P = 0.022$; LCX: $P = 0.260$). The pericoronary FAI values in three main coronary arteries are shown in Fig. 3.

Association between dapagliflozin treatment and pericoronary FAI reduction in patients with T2DM

Univariate linear regression analysis revealed a link between dapagliflozin therapy and a reduced pericoronary FAI in the LAD (β = -2.550, $P < 0.05$) and RCA (β = -3.394, $P < 0.05$) among T2DM patients but no correlation with the LCX (β = -1.754, $P > 0.05$). After adjustment for pertinent covariates, the impact of dapagliflozin therapy on the pericoronary FAI in patients with T2DM still existed (LAD β = -2.449, RCA β = -3.897, *P* values were all less than 0.05) (Table 2).

Correlation between dapagliflozin therapy and a decrease in the pericoronary FAI in subgroups of T2DM patients

Analysis of various subgroups revealed a notable link between dapagliflozin therapy and a decrease in the pericoronary FAI (Table 3). In patients who are younger than 70 years old and have experienced diabetes for a duration of less than 10 years, treatment with dapagliflozin was notably linked to a decrease in pericoronary FAI (age < 70 years: LAD β = -4.132, $P = 0.001$; LCX β = -3.122, $P = 0.013$; RCA β = -4.158, $P = 0.003$; T2DM

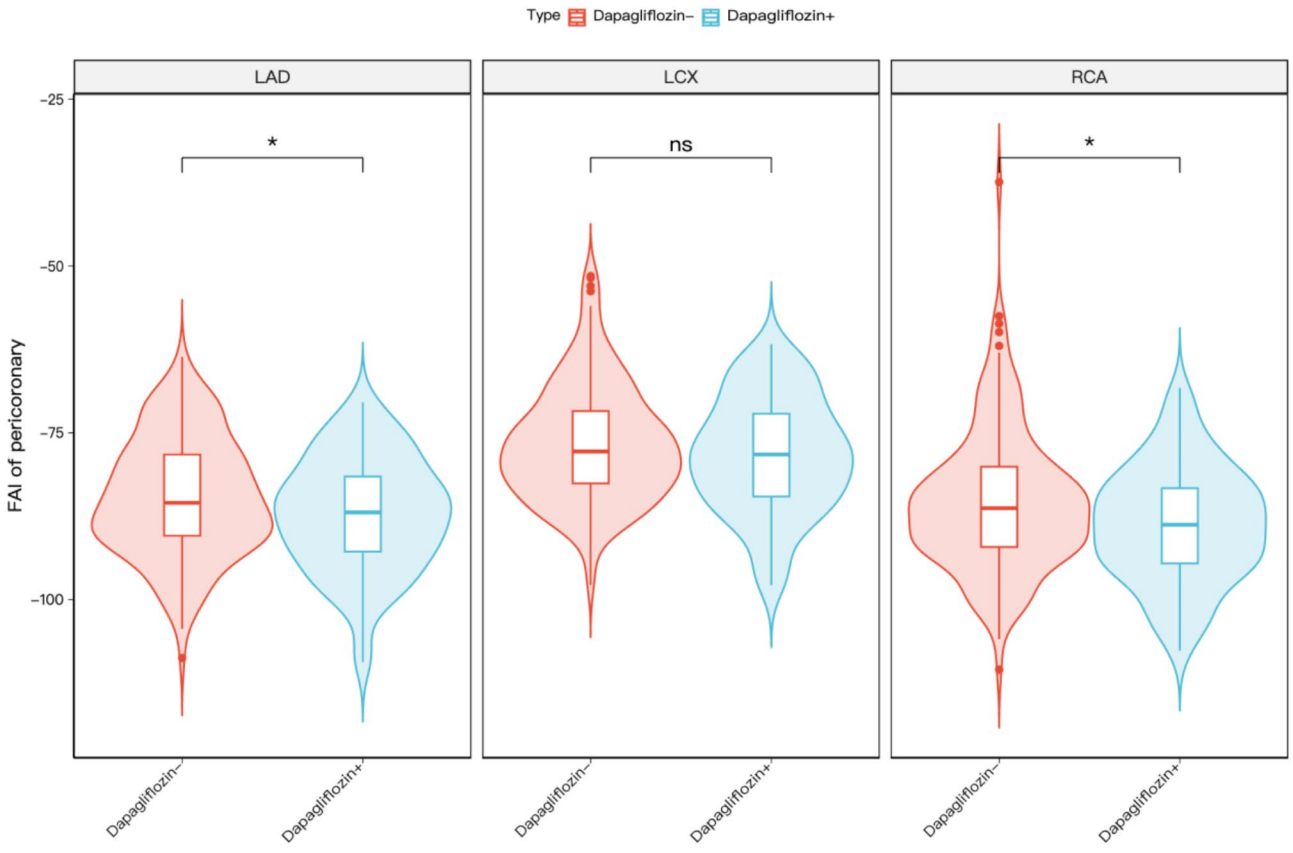


Fig. 3 Pericoronary FAI values in three main coronary arteries (168 in the dapagliflozin- group and 103 in the dapagliflozin + group). FAI: fat attenuation index; LAD: left anterior descending artery; LCX: left circumflex artery; RCA, right coronary artery; $^{*}P < 0.05$, $^{ns}P > 0.05$)

duration < 10 years: LAD β = -3.656, $P = 0.013$; LCX β = -3.317, $P = 0.016$; RCA β = -6.435, $P < 0.001$). This association was not observed among patients older than 70 years, those with diabetes for more than a decade, or those who smoked.

Dapagliflozin treatment was significantly associated with a decrease in the pericoronary FAI observed in men with T2DM (LAD β= -3.901, $P = 0.005$; LCX β= -3.637, $P = 0.010$; RCA β= -3.756, $P = 0.017$). In women, dapagliflozin treatment was significantly associated with a decrease in FAI only for the RCA (RCA β = -4.410, $P = 0.042$).

In the subgroup analysis of individuals with a BMI less than 24 kg/m^2, treatment with dapagliflozin significantly reduced the FAI of the LCX and continued to be associated with a decrease in the FAI of the LAD (LAD β = -5.630; $P = 0.048$; LCX β = -6.251, $P = 0.035$). In contrast, in patients with a BMI ≥ 24 kg/m^2 and nonsmokers, treatment with dapagliflozin was linked exclusively to a decrease in the FAI of the RCA only (BMI ≥ 24 kg/m^2: RCA β = -4.266, $P = 0.003$; nonsmoking: RCA β = -4.893, $P < 0.001$). Treatment with dapagliflozin correlated solely with a decrease in the FAI of the RCA, regardless of the presence or absence of dyslipidaemia (with dyslipidaemia: RCA β = -4.697, $P = 0.014$; without dyslipidaemia: RCA β = -3.708, $P = 0.031$).

Discussion

This study is the first to explore whether the cardiovascular benefits of dapagliflozin in patients with T2DM are partly attributed to its effects on coronary artery inflammation. Our study revealed that after treatment with dapagliflozin, the pericoronary FAI of the LAD and RCA in T2DM patients was significantly reduced, and this independent and related effect still existed after adjusting for confounding factors. That is, dapagliflozin treatment is associated with the downregulation of coronary artery inflammation, and this association is significantly different between T2DM patients in various situations. These findings may provide a new theoretical reference for the clinical treatment of T2DM patients.

The results of this study show that dapagliflozin significantly reduced the pericoronary FAI of the LAD and RCA in T2DM patients. Although previous studies have shown that dapagliflozin can reduce EAT thickness and volume, these traditional EAT indicators do not fully reflect the cellular and metabolic activities of adipose tissue [26, 27]. The pericoronary FAI we studied provides a

Table 2 Univariate and multivariate linear regression analyses of Dapagliflozin treatment and the pericoronary FAI

Variables	LAD-PCAT		LCX-PCAT		RCA-PCAT	
	β coefficient (95%CI)	*P*	β coefficient (95%CI)	*P*	β coefficient (95%CI)	*P*
Dapagliflozin						
Model 1	-2.550 (-4.692 ~ -0.408)	**0.020**	-1.754 (-3.900 ~ 0.391)	0.110	-3.394 (-5.806 ~ -0.981)	**0.006**
Model 2	-2.449 (-4.676 ~ -0.221)	**0.032**	-1.839 (-4.058 ~ 0.380)	0.106	-3.897 (-6.382 ~ -1.411)	**0.002**
Age						
Model 1	0.116 (0.010 ~ 0.222)	**0.032**	0.033 (-0.073 ~ 0.139)	0.539	0.008 (-0.113 ~ 0.129)	0.897
Model 2	0.119 (0.000 ~ 0.237)	0.050	0.045 (-0.073 ~ 0.162)	0.457	0.004 (-0.127 ~ 0.136)	0.949
Sex						
Model 1	0.456 (-1.679 ~ 2.591)	0.676	2.004 (-0.110 ~ 4.119)	0.064	2.040 (-0.362 ~ 4.443)	0.097
Model 2	1.489 (-0.880 ~ 3.857)	0.219	2.176 (-0.183 ~ 4.535)	0.072	1.947 (-0.696 ~ 4.589)	0.150
BMI						
Model 1	-0.026 (-0.298 ~ 0.246)	0.850	0.058 (-0.213 ~ 0.329)	0.676	0.268 (-0.038 ~ 0.574)	0.087
Model 2	0.048 (-0.226 ~ 0.323)	0.730	0.107 (-0.167 ~ 0.380)	0.445	0.311 (0.005 ~ 0.618)	**0.048**
T2DM duration						
Model 1	0.139 (-0.027 ~ 0.304)	0.101	0.198 (0.035 ~ 0.362)	**0.018**	0.210 (0.024 ~ 0.396)	**0.028**
Model 2	0.125 (-0.046 ~ 0.295)	0.153	0.187 (0.017 ~ 0.356)	**0.032**	0.238 (0.048 ~ 0.428)	**0.015**
Dyslipidaemia						
Model 1	0.843 (-1.326 ~ 3.013)	0.447	-2.161 (-4.310 ~ -0.012)	0.050	-2.223 (-4.665 ~ 0.218)	0.075
Model 2	1.374 (-0.801 ~ 3.549)	0.217	-1.689 (-3.855 ~ 0.478)	0.128	-1.554 (-3.981 ~ 0.872)	0.210
Smoking						
Model 1	0.086 (-2.349 ~ 2.520)	0.945	0.904 (-1.520 ~ 3.327)	0.465	1.053 (-1.697 ~ 3.803)	0.454
Model 2	0.117 (-2.547 ~ 2.782)	0.931	0.443 (-2.211 ~ 3.097)	0.744	0.549 (-2.424 ~ 3.522)	0.718
Stains						
Model 1	-0.512 (-3.178 ~ 2.155)	0.707	-0.022 (-2.679 ~ 2.636)	0.987	0.758 (-2.256 ~ 3.773)	0.622
Model 2	-1.173 (-3.850 ~ 1.504)	0.391	-0.594 (-3.261 ~ 2.072)	0.663	0.027 (-2.959 ~ 3.014)	0.986
LVEF						
Model 1	-0.026 (-0.240 ~ 0.187)	0.808	0.032 (-0.181 ~ 0.245)	0.768	-0.079 (-0.321 ~ 0.162)	0.521
Model 2	-0.054 (-0.267 ~ 0.159)	0.620	0.024 (-0.189 ~ 0.236)	0.828	-0.084 (-0.322 ~ 0.154)	0.491
HbA1c						
Model 1	0.435 (-0.041 ~ 0.912)	0.074	0.336 (-0.140 ~ 0.812)	0.167	0.316 (-0.224 ~ 0.856)	0.253
Model 2	0.375 (-0.108 ~ 0.858)	0.130	0.236 (-0.245 ~ 0.717)	0.338	0.149 (-0.390 ~ 0.689)	0.588

Model 1: unadjusted; Model 2: adjusted for age, sex, BMI, diabetes duration, dyslipidaemia, smoking, statins, LVEF, and HbA1c

more sensitive assessment method that can reveal deeper adipose tissue changes, especially in response to inflammation and metabolism. This finding is consistent with the findings of Cinti et al., who also noted to the potential of coronary CT imaging in evaluating pericoronary fat metabolism, especially in patients with increased levels of inflammation [28]. Future research should continue to focus on the relationship between the pericoronary FAI and cardiovascular events and explore changes in the pericoronary FAI associated with different treatment options. In particular, the effect of the combined application of the pericoronary FAI and EAT is worthy of further study.

An increasing number of studies indicate that the pericoronary FAI represents a novel biomarker indicative of coronary inflammation. A follow-up coronary CTA study revealed that high-dose statin therapy led to a significantly reduction in the risk factors for coronary artery disease (CAD), as evidenced by the reduction in PCAT attenuation [25]. PCAT attenuation has predictive value for the risk of fatal or nonfatal myocardial infarction, and increased attenuation of PCAT is significantly correlated with the occurrence of plaque rupture in individuals diagnosed with non-ST-segment elevation myocardial infarction (NSTEMI) [30, 31]. Our study revealed that there was an inverse correlation between dapagliflozin treatment and coronary artery inflammation. Additionally, there was a positive association between age, duration of diabetes, and BMI and coronary artery inflammation, which is consistent with the findings of previous studies [32]. Part of the mechanism by which dapagliflozin can benefit cardiovascular health may involve reducing coronary artery inflammation, and the specific mechanism requires further study.

An increase in the pericoronary FAI could be a contributing factor to increased cardiovascular disease risk in T2DM patients [33]. High pericoronary adipose tissue attenuation can predict cardiovascular events in T2DM patients [34]. Research by Liu et al. revealed a notably higher RCA-PCAT attenuation index in patients with

Table 3 Multivariate linear regression analyses between Dapagliflozin treatment and the pericoronary FAI in different subgroups of T2DM patients

Subgroup	LAD-PCAT		LCX-PCAT		RCA-PCAT	
	β coefficient (95%CI)	*P*	β coefficient (95%CI)	*P*	β coefficient (95%CI)	*P*
Age (years)						
< 70(*n* = 199)	-4.132 (-6.590 ~ -1.673)	**0.001**	-3.122 (-5.566 ~ -0.678)	**0.013**	-4.158 (-6.892 ~ -1.424)	**0.003**
≥ 70(*n* = 72)	1.804 (-3.449 ~ 7.058)	0.503	1.668 (-3.531 ~ 6.867)	0.532	-3.397 (-9.228 ~ 2.433)	0.258
Sex						
Male(*n* = 160)	-3.901 (-6.606 ~ -1.195)	**0.005**	-3.637 (-6.375 ~ -0.899)	**0.010**	-3.756 (-6.817 ~ -0.696)	**0.017**
Female(*n* = 111)	-0.299 (-4.167 ~ 3.570)	0.880	0.757 (-2.841 ~ 4.355)	0.681	-4.410 (-8.616 ~ -0.203)	**0.042**
Body mass index (kg/m^2)						
< 24(*n* = 60)	-5.630 (-11.086 ~ -0.174)	**0.048**	-6.251 (-11.920 ~ -0.581)	**0.035**	-1.714 (-7.612 ~ 4.185)	0.571
≥ 24(*n* = 211)	-1.708 (-4.183 ~ 0.767)	0.178	-1.228 (-3.621 ~ 1.165)	0.316	-4.266 (-7.054 ~ -1.477)	**0.003**
T2DM duration(years)						
< 10(*n* = 165)	-3.656 (-6.513 ~ -0.799)	**0.013**	-3.317 (-5.974 ~ -0.660)	**0.016**	-6.435 (-9.456 ~ -3.414)	**< 0.001**
≥ 10(*n* = 106)	0.871 (-2.629 ~ 4.372)	0.627	0.283 (-3.579 ~ 4.145)	0.886	0.133 (-0.111 ~ 0.377)	0.287
Dyslipidaemia						
With(*n* = 101)	-2.324 (-5.697 ~ 1.049)	0.180	-2.194 (-5.617 ~ 1.228)	0.212	-4.697 (-8.357 ~ -1.037)	**0.014**
Without(*n* = 170)	-2.759 (-5.741 ~ 0.223)	0.072	-2.345 (-5.176 ~ 0.486)	0.106	-3.708 (-7.042 ~ -0.375)	**0.031**
Smoking						
Yes(*n* = 67)	-3.644 (-8.335 ~ 1.048)	0.133	-1.851 (-6.383 ~ 2.681)	0.426	-1.654 (-6.606 ~ 3.297)	0.515
No(*n* = 204)	-2.156 (-4.715 ~ 0.402)	0.100	-2.162 (-4.705 ~ 0.380)	0.097	-4.893 (-7.763 ~ -2.022)	**< 0.001**

T2DM than in those without T2DM, with a notable link between inadequate glycaemic management and coronary artery inflammation [35, 36]. A retrospective study revealed that elevated lesion-specific pericoronary FAI values independently predict significant cardiovascular complications in T2DM patients [37]. These results indicate that reducing the pericoronary FAI could serve as a viable therapeutic strategy to mitigate the risk of cardiovascular disease in T2DM patients.

In patients with CAD, increased pericoronary fat is a known marker of adverse cardiovascular events, as this fat contributes to local inflammation, endothelial dysfunction, and plaque instability. Previous studies have shown that an increase in the pericoronary FAI is correlated with worse outcomes in CAD patients, including a higher incidence of major adverse cardiovascular events [38]. Therefore, the observed decrease in the pericoronary FAI with dapagliflozin treatment could translate into a reduction in these adverse events by improving coronary artery inflammation. Furthermore, the relationship between the pericoronary FAI reduction and improved outcomes has important implications for risk stratification in CAD patients. While traditional imaging modalities, such as coronary artery calcium scoring and CT angiography, provide valuable information about the degree of atherosclerosis, the pericoronary FAI may offer additional predictive power. This could lead to more precise cardiovascular risk assessment, helping to identify high-risk patients earlier and potentially guiding more targeted interventions. Specifically, the ability to monitor the pericoronary FAI over time could help clinicians assess the effectiveness of therapies aimed at reducing inflammation and improving metabolic control, particularly in patients with diabetes or other inflammatory states.

SGLT-2 inhibitors play crucial roles in treating diabetes. Dapagliflozin, a typical representative SGLT-2 inhibitor, has been mentioned many times in heart failure guidelines [39, 40]. Its cardioprotective effect has been shown in many studies. confirmed in one study. Dapagliflozin can improve multiple metabolic factors, such as blood sugar, blood pressure, uric acid, and body weight, and increase cardiovascular risk [41]. A study by Scott D et al. demonstrated that the use of dapagliflozin has been shown to lower the risk of cardiovascular mortality in heart failure patients who have either a slightly decreased or maintained ejection fraction [42]. A recent network meta-analysis revealed that dapagliflozin significantly improved endothelial function and arterial stiffness in diabetic patients [43]. Li et al. reported that dapagliflozin can reduce damage to heart microvessels and the endothelium during myocardial ischaemia/reperfusion injury by inhibiting the XO-SERCA2-CaMKII-cofilin pathway [44]. In patients with T2DM, dapagliflozin can also directly exert anti-atherosclerotic effects independent of glucose lowering by improving endothelial function [45]. The activation of the NLRP3 inflammasome and release of interleukin 1β (IL-1β) in the heart can cause atherosclerosis and induce heart failure, whereas SGLT-2 inhibitors can produce anti-inflammatory effects by attenuating NLRP3 activation [46]. In animal and cell experiments, dapagliflozin not only improved the

oxidative stress caused by increased mitochondrial ROS production due to increased glucose uptake but also reduced the production of ROS and exerted anti-inflammatory effects by activating the AKT pathway [47–49]. In this study, dapagliflozin treatment was significantly associated with a lower pericoronary FAI, and the above mechanisms may partly explain the protective effect of dapagliflozin against coronary artery inflammation.

Our study suggested that dapagliflozin treatment significantly improved coronary artery inflammation in the subgroups of patients younger than 70 years, those with a period of diabetes shorter than 10 years, and males. Treatment with dapagliflozin solely correlated with a decrease in inflammation of the RCA in patients with a BMI ≥ 24 kg/m^2, nonsmokers, and females, regardless of the presence or absence of dyslipidaemia. This association did not exist in the subgroups of patients aged over 70 years, those with diabetes for a period exceeding 10 years, and smokers. This finding may provide a more precise option for the treatment of T2DM patients with dapagliflozin.

This retrospective study has the following limitations. First, the research data came from only one hospital, the sample size was relatively limited, and the research results may lack universality. Future research needs to be multicentre and include a larger sample size. Second, although we used regression analysis to adjust for recognized confounding factors, there is still a lack of research data on physical exercise, dietary habits, complications, etc., that may affect coronary inflammation. A more complete dataset needs to be constructed in the future for further analysis. Another limitation of this study is the lack of formal reproducibility assessments, such as intraclass correlation coefficients. Future studies could further strengthen the reliability of FAI measurements by including such evaluations. Third, we cannot directly determine a causal relationship between dapagliflozin treatment and coronary artery inflammation, and additional randomized controlled studies are needed in the future.

Conclusion

Dapagliflozin treatment is associated with a significant reduction in coronary artery inflammation in T2DM patients, which may partly explain its beneficial effects on reducing cardiovascular risk.

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None.

Author contributions
XH contributed to the study design, data collection, and statistical analysis and drafted the manuscript. TZ and RF participated in the collection of the experimental and imaging data. JY and QH contributed to the data collection and statistical analysis. DL participated in the study design and improved the figures. GY and LP were responsible for the quality control of the experimental data and reviewed the final manuscript. All the authors have read and approved the final manuscript.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
This study protocol was approved by the Ethics Review Committee of Hebei Provincial People's Hospital (No. 2025-LW-0019) and was conducted in accordance with the principles outlined in the Declaration of Helsinki. However, because this was a retrospective study, patient informed consent was waived.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Author details
[1]Department of Medicine, Hebei North University, Zhangjiakou, Hebei, China
[2]Department of Endocrinology, Hebei General Hospital, Shijiazhuang, Hebei, China
[3]Hebei Key Laboratory of Metabolic Diseases, Shijiazhuang, Hebei, China
[4]Department of Medical Imaging, Hebei General Hospital, Shijiazhuang, Hebei, China
[5]Department of Medicine, Hebei Medical University, Shijiazhuang, Hebei, China

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