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Coronary Artery Disease Features and Epicardial Adipose on CT are Predictive Factors for Cardiovascular Events in Type 2 Diabetic Patients at High/Very High Cardiovascular Risk: A Pilot Retrospective Study

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Abstract

Aim: The study aimed to estimate the association between characterizations on coronary computed tomography angiography (CCTA) and cardiovascular events in type 2 diabetic patients at high/very high cardiovascular risk without known coronary artery disease (CAD), to investigate the incremental value of CCTA in these individuals.

Methods: 82 type 2 diabetes patients without known CAD were enrolled according to the 2019 European Society of Cardiology (ESC) guidelines of high/very high cardiovascular risk. The coronary artery calcium score, plaque location and extent and composition, stenosis severity, and epicardial adipose tissue (EAT) volume were evaluated. The cardiovascular events included cardiac death, non-fatal myocardial infarction, coronary revascularization, non-fatal stroke, hospitalization for unstable angina, and hospitalization for congestive heart failure during a mean follow-up period of 4.7±1.5 years. Univariate analysis and multivariate regression were used to obtain independent risk factors for CVEVs in these patients. The increased discriminative value after the addition of CAD features and EATS volume to the established clinical risk factors were estimated using the area under a receiver-operating characteristic curve (AUC).

Results: CVEVs occurred in 26.8% of the patients. Independent predictors of CVEVs included hypertension (odds ratio (OR) 3.844, P=0.020), diabetes duration (OR 1.129, P=0.049), creatinine (OR 1.072, P=0.022), ABOS (OR 1.729, P=0.031), SSS (OR 1.213, P=0.021), and EAT volume (OR 1.025, P=0.012) The combination of ABOS, SSS and clinical risk factors improved the identify of CVEVs, with an area under the receiver operating characteristic curve of 0.955 (95% confidence interval 0.885 to 0.989; P=0.004) for the prediction of the endpoints.

Conclusion: The extent and severity of overall coronary atheroma burden and EAT volume based on CCTA are associated with long-term CVEVs for type 2 diabetic patients at high/very high cardiovascular risk. CCTA has incremental value in evaluating the heterogeneity of such subclinical patients and beneficial forewarning for these individuals with CVEVs.

Keywords: Coronary CT angiography; Epicardial adipose tissue; Cardiovascular risk; Cardiovascular events; Type 2 diabetes mellitus

Introduction

Cardiovascular diseases (CVD) affect approximately one-third of type 2 diabetic people and account for half of all deaths in this population, most of which are caused by coronary artery disease (CAD) [1]. According to the 2019 European Society of Cardiology (ESC) guidelines [2], patients with type 2 diabetes mellitus (T2DM) and CVD, other target-organ damage, or three or more major risk factors should be considered to be very high cardiovascular (CV) risk; those with T2DM duration ≥10 years and any additional clinical risk factor but without target-organ damage, to be at high risk. The 10-year cardiovascular mortality of T2DM patients at high and very high risk is 5-10% and greater than 10%, respectively. The more risk factors, the higher percentage of coronary segments with the stenosed plaques and more multivessel obstructive disease [3]. Although the extent and severity of coronary atherosclerosis were associated with significantly elevated risk for adverse events in asymptomatic type 2 diabetics in previous studies using coronary computed tomography angiography (CCTA) [4]. However, whether CCTA may have a role in screening individuals with diabetes at high or very high cardiovascular risk is still much less studied and remains controversial. FACTOR-64 [5] study showed the use of routine CCTA screening for CAD did not reduce death and nonfatal coronary outcomes in asymptomatic diabetic patients with high risk. Nevertheless, results from other studies [4,6] supported the potential CCTA benefit to evaluate the

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heterogeneity of this population and guide their aspirin therapy in diabetic patients with high risk. Therefore, further forewarning indicators of cardiovascular events in type 2 diabetic patients should be established in the CCTA parameters, especially in these individuals with high/very high cardiovascular risk.

Several previous reports had established some CCTA parameters for quantifying the anatomical patterns of CAD, including atheroma burden obstructive score (ABOS), segment involvement score (SIS), and segment stenosis score (SSS). These scores have been confirmed to be associated with clinical outcomes in asymptomatic individuals with type 2 diabetes [7-9]. Meanwhile, CCTA can quantify epicardial adipose tissue (EAT) volume, which was indicated as visceral obesity and a systemic inflammatory biomarker in T2DM [10-13]. Studies showed that increased EAT volume is associated with CAD and major adverse cardiovascular events (MACEs) in these individuals [14-16]. So, it is worthwhile to study whether the atherosclerosis scores and EAT volume according to CCTA are associated with the poor future prognosis in type 2 diabetic patients at high/very risk.

We retrospectively analyzed the clinical and CCTA characteristics of type 2 diabetic patients at high/very high risk, who had a cardiovascular event (CVEV) within 3-6 years, to investigate whether some CCTA parameters can be the forewarning indicators of CVEVs in these patients. To further explore the necessity of CCTA examination in this patient population.

Materials and Methods

Study population

This was a retrospective study and was approved by the local institutional review board. In this study, 173 hospitalized patients with T2DM, without known CAD or typical ischemia, who underwent CCTA in the First Affiliated Hospital of Xi'an Jiaotong University between 2012 and 2014 were screened. A diagnosis of T2DM was based on the criteria by the American Cardiology College and the American Diabetes Association [17]. The inclusion criteria included the following: (1) CCTA performed within 1 month before or after hospitalization; (2) Patients under the very high risk or high-risk categories according to the 2019 ESC guidelines [2]; (3) Medical records with adequate baseline clinical status. The exclusion criteria were (1) Previous myocardial infarction, cerebral infarction, heart failure, typical angina, coronary stent, or bypass therapy; (2) Active cancer or blood disease, immune disease, thyroid dysfunction; and [4] subjects with poor cardiac CT image quality, with insufficient clinical data, or failing to complete follow-up. Finally, 82 patients were included in the study (Figure 1). The CCTA images, clinical and laboratory results, and follow-up records of these patients were reviewed.

Data collection

We obtained data on demographic characteristics, traditional CVD risk factors, diabetes characteristics, laboratory tests, and treatment after CCTA on admission from electronic medical records. Peripheral blood was sampled from patients within 24h of admission. All of these laboratory tests were implemented using standard methods. Echocardiographs were performed on admission by experienced echo cardiologists, and systolic function was expressed as the left ventricle ejection fraction.

Outcome data

CVEVs including non-fatal myocardial infarction (MI), non-fatal stroke, cardiac deaths, hospitalization for unstable angina, or hospitalization for congestive heart failure were defined as endpoints. Participants were followed up by telephone interviews and hospital records. In patients who experienced two CVEVs, the first event was chosen. When two CVEVs occurred simultaneously, the worse event was chosen (i.e., death over MI, MI over revascularization, and revascularization over hospital readmission). All those CVEVs and outcomes were performed by individuals blinded to the patients' CT data.

CCTA data acquisition

CCTA was performed using a 128-section multidetector CT (Brilliance iCT; Philips, Medical Systems, Best, The Netherlands). First, the patients underwent non-enhanced prospective electrocardiography (ECG)-gated sequential scan to measure the coronary artery calcium score. Thereafter, CCTA was performed using retrospective ECG-gated tube current modulation. The imaging parameters were as follows: slice collimation 256×0.625 mm; gantry rotation time, 270ms; tube voltage, 80-120 kVp; and automated choice of mAs value based on patient weight. A double-head power injector (Ulrich Medical AG, Ulm-Jungingen, Germany) was used to inject contrast media through a 20G trocar in an antecubital vein. A weight-dependent bolus of 70-90 ml iodine contrast agent (iohexol (350mg iodine/ml); GE Healthcare, Shanghai, China) was administered at a speed of 4 to 5.5 ml/s, which was followed by a 30ml saline flush. Cardiac CT images were reconstructed at 75% and 45% of the RR interval.

CCTA image interpretation

All cardiac images were retrospectively analyzed on an offline workstation (EBW 4.4, Philips Medical Systems, Best, The Netherlands). The total calcium burden in the coronary arteries was quantified using the scoring algorithm [18], and the predefined calcium score (CACS) categories (0, 1-100, 101-400, and >400) were employed [19].

The coronary artery tree was divided into 16 segments according to the Society of Cardiovascular Computed Tomography guidelines [20]. The degree of stenosis was classified as obstructive if the patient had >50% diameter stenosis on the longitudinal images. We evaluated the plaque extent and stenosis rate by summing the number of epicardial vessels with obstructive stenosis (i.e., no plaque, no obstruction, 1-vessel disease, 2-vessel disease, 3-vessel disease). Atheroma burden obstructive score (ABOS), segment involvement score (SIS), and segment stenosis score (SSS) were measured [9]. ABOS was defined as the number of plaques with >50% stenosis in the entire coronary artery tree. SIS was calculated as the total number of coronary artery segments that exhibited plaque, irrespective of the degree of luminal stenosis within each segment (minimum=0; maximum=16). SSS was used as a measure of the overall extent of coronary atherosclerosis. To determine the SSS, the degree of stenosis of each coronary segment was graded based on Coronary Artery Disease - Reporting and Data System (scores ranged from 0 to 5) [21]. The extent scores of all 16 segments were then summed to yield a total score ranging from 0 to 80.

Moreover, coronary plaques were classified as calcified

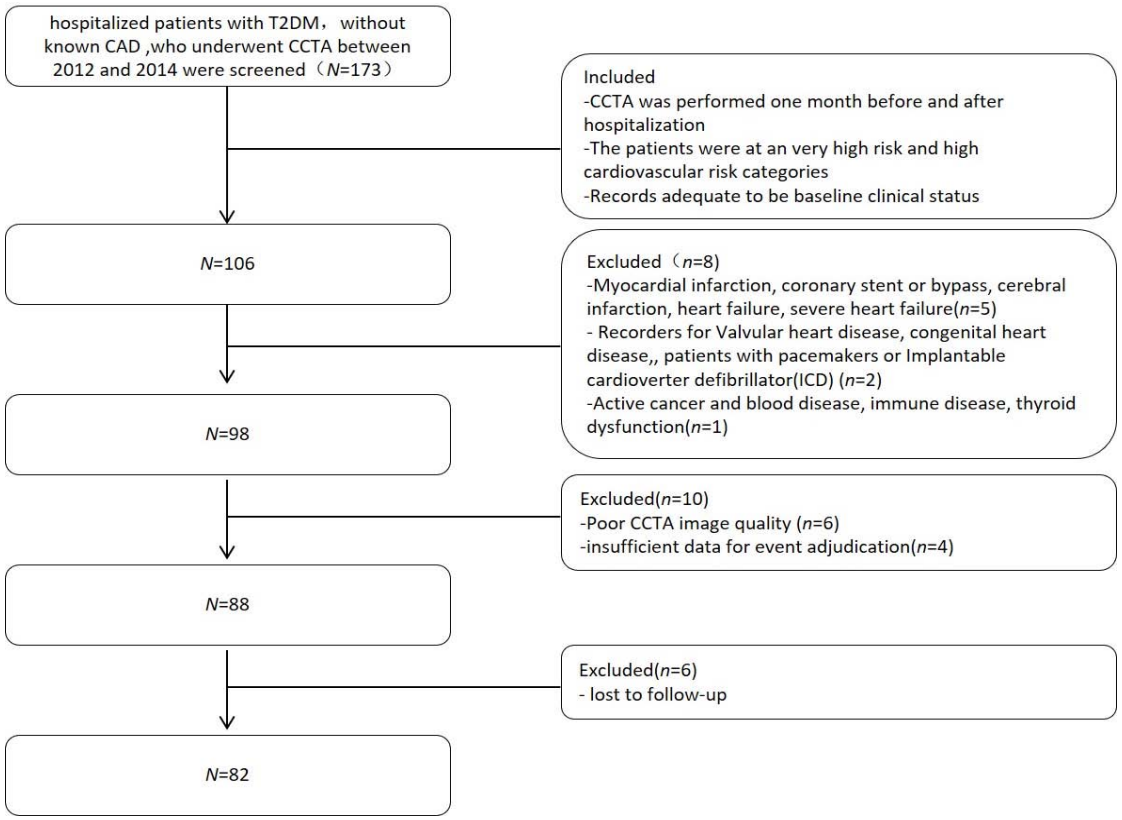

Figure 1: Flowchart of study design. CCTA indicates computed tomography coronary angiography.

(composed exclusively of a high-density material >130 HU), non-calcified (composed exclusively of a material with a density ≤130 HU), and mixed (with components of both calcified and non-calcified plaques) [22]. Vulnerable plaques were confirmed by the following characteristics: positive remodeling, low-attenuation plaque, spotty calcification, and the napkin-ring sign [23].

EAT depot was defined as the fat tissue between the outer wall of the myocardium and the visceral layer of the pericardium [24]. The epicardial fat volume was assessed using a dedicated workstation (Advantage Workstation 4.6; GE Healthcare). The pericardium was manually traced from the right pulmonary artery to the diaphragm to determine a region of interest. Within the region of interest, fat was defined as pixels with CT attenuation values within a window of -190 to -30 HU. Overall, only pixels with Hounsfield units equivalent to fat within the pericardial sac were counted as EAT (Figure 1). Reproducibility was excellent (for interobserver variability, intraclass correlation coefficient=0.889, $p<0.05$; for intraobserver variability, intraclass correlation coefficient=0.814, $p<0.05$).

Two experienced computed tomography readers who were blinded to the clinical characteristics and procedural outcomes and each other's assessment measured the characteristics of CCTA and EAT volume separately. In cases of discrepancy, the consensus was reached by discussion (Figure 2).

Statistical analysis

Patient characteristics were expressed as mean±standard deviation for continuous data and counts and proportions for categorical data. Kolmogorov-Smirnov test was used to test the normal distribution of the continuous variables. Chi-square test, Student's *t*-test, and non-parametric equivalent tests were employed when appropriate. A comparative analysis of diabetes with and without CVEVs was performed to evaluate potential predictors. The independent predictors of CVEVs were identified by univariable and multivariate logistic regression analysis. The increased discriminative value after the addition of CAD features and EAT volume to the established clinical risk factors were estimated using the area under a receiver-operating characteristic curve (AUC) between individual predicted probabilities and incidence of events, and was compared in a clinical risk factors model and an enriched model with coronary artery disease features, EAT volume, and both. SPSS Statistics for Windows v18.0 (SPSS Inc., Chicago, USA) and MedCalc Statistical Software version 13.0 (MedCalc Software bvba, Ostend, Belgium; http://www.medcalc.org; 2014) were used for data analysis. A two-tailed p-value <0.05 indicated statistical significance.

Results

Study endpoints

A total of 82 asymptomatic type 2 diabetes patients without known CAD before coronary CTA were analyzed in this study. During a mean follow-up period of 4.7±1.5 years, 22 CVEVs (26.8%) were reported. As follow, one cardiac death (1.2%), four non-fatal MI (4.9%), two coronary revascularizations (2.4%), five non-fatal strokes (6.1%), and ten hospitalizations for unstable angina (12.2%).

Table 1: Baseline characteristics Between Subjects With and Without a CVEVs.

Characteristic	Overall (n=82)	No CVEVs (n=60)	CVEVs (n=22)	*P*-value
Risk factors				
Age (yrs)	59±8.0	58.8±7.7	62.3±8.1	0.083
Male*	48(58.5)	34(56.7)	14(63.4)	0.621
Mean BMI (kg/m^2)	24.6±2.7	24.8±2.6	24.2±3.1	0.376
Hypertension*	31(37.8)	18(30.0)	13(59.1)	0.016
Family history of CAD*	11(13.4)	7(11.7)	4(18.2)	0.332
Hyperlipidemia*	44(53.7)	32(53.3)	12(54.5)	0.532
smoking*	30(36.6)	23(38.3)	7(31.8)	0.392
Diabetic characteristics				
Duration of diabetes (yrs)	6.7±6.0	5.6±4.5	9.7±8.3	0.004
Mean HbA1c level (%)	7.5±1.4	7.9±1.5	7.2±1.3	0.058
Fasting blood glucose(mmol/L)	8.0±2.1	7.9±1.9	8.4±52.6	0.498
Postprandial plasma glucose(mmol/L)	13.1±3.4	12.9±3.2	13.4±3.9	0.572
Mean creatinine level (μmol/L)	59.6±14.5	57±13.4	66.1±15.7	0.013
Treatment after CCTA				
Insulin therapy*	24(29.3)	16(26.7)	8(36.4)	0.421
Oral hypoglycaemic agents*	71(86.6)	54(90.0)	17(77.3)	0.136
Antiplatelet*	66(80.5)	46(76.7)	20(90.1)	0.152
Statins*	67(81.7)	50(83.3)	17(77.3)	0.532
ACEI/ARB*	21(25.6)	10(16.7)	11(50.0)	0.002
Beta-blocker*	25(30.5)	20(33.3)	5(22.7)	0.358
Percutaneous revascularization*	2(2.4)	1(1.7)	1(4.5)	0.457

Except where indicated, data are means ± standard deviations, *Data are numbers of patients, with percentages in parentheses. CAD: Coronary Artery Disease; BMI: Body Mass Index; ACEI: Angiotensin-Converting Enzyme Inhibition; ARB: Angiotensin Receptor Blocker.

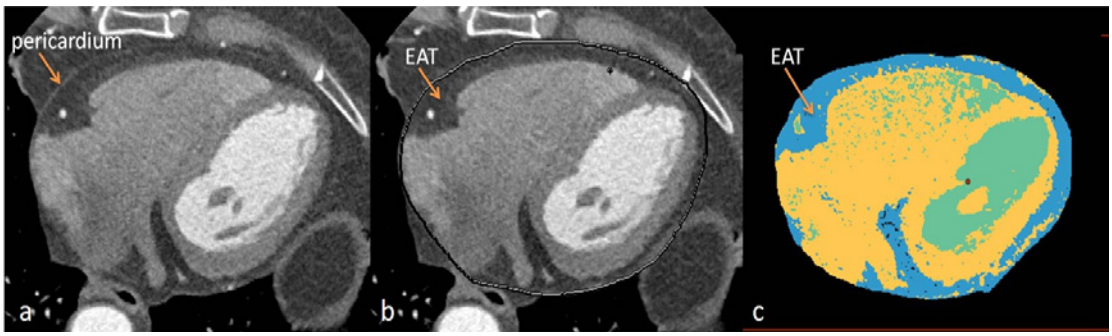

Figure 2: Epicardial adipose tissue (EAT) total volume measurement. (a) Identify the pericardium at each slice of volume data; (b) Segmentation of EAT was obtained by manually tracing the pericardium on axial images; (c) After segmentation, a threshold of -190 to -30 Hounsfield units was applied to isolate the adipose tissue.

Patient characteristics

The mean age of the study population was 59±8.0 years, and 48 (58.5%) patients were men. Mean diabetes mellitus duration was 6.7±6.0 years, and the mean HbA1c value was 7.5±1.4%. The demographic, clinical, and laboratory characteristics and therapeutic approach at baseline were compared between patients with and without CVEVs (Table 1). Patients with CVEVs had significantly longer diabetes duration and higher serum creatine levels than those without CVEVs. The patients with a CVEV were more likely to have hypertension and be treated with ACE inhibitor/ARB.

Coronary computed tomography angiography findings

The participants with a CVEV had a higher EAT volume than those without a CVEV (P=0.007). Obstructive CAD, which was defined as >50% luminal stenosis, and vulnerable plaque were found more frequently in those with a CVEV (obstructive, P=0.013; vulnerable, P=0.029). Compared to those without a CVEV, those with a CVEV had a significantly higher ABOS (P=0.016) and SSS (P=0.049). The lesion characteristics assessed by CCTA are summarized in Table 2.

Table 2: Differences in Cardiac CT findings between Subjects with and without a CVEV.

Finding	Overall (n=82)	No CVEV (n=60)	CVEV (n=22)	*P*-value
Total Agatston score*	101.6±290.9	72.2±261.9	181.8±352.9	0.194
Calcium score categories				0.072
0	44(53.6)	35((58.3)	10((45.5)	
0-100	21((25.6)	16((26.7)	4((18.2)	
101-400	11(13.4)	6(10.0)	5(22.7)	
>400	6(7.3)	3(5.0)	3(13.6)	
Presence of plaque	63(76.8)	44(73.3)	19(86.4)	0.254
SIS*	2.4±2.3	2.1±2.1	3.0±2.8	0.222
Plaque range				0.369
1-vessel	22(26.8)	14(23.3)	8(36.4)	
2-vessel	25(30.5)	20(33.3)	5(22.7)	
3-vessel	16(19.5)	10(16.7)	6(27.3)	
Character of plaque				
Calcified plaque	38(46.3)	25(41.7)	13(59.1)	0.213
Non-calcified	46(56.1)	33(55.0)	13(59.1)	0.805
Mixed plaque	13(15.8)	7(11.7)	6(27.3)	0.1
Stability of plaque				0.029
Vulnerable plaque	8(9.8)	3(5.0)	5(22.7)	
Stable plaques	74(91.2)	57(95.0)	17(77.3)	
Stenosis Severity				0.013
Obstructive plaques	25(30.5)	12(20.0)	13(59.1)	
Nonobstructive plaques	57(69.5)	48(80.0)	9(40.1)	
ABOS*	0.48±1.0	0.25±0.65	1.09±1.5	0.016
SSS*	4.6±5.1	3.27±3.2	8.23±7.3	0.049
EAT volume*	147.3±41.9	139.9±37.8	167.5±44.5	0.007

Except where indicated, data are numbers of patients, with percentages in parentheses. *Data are means ± standard deviations. SIS: The Segment Involvement Score; ABOS: The Atheroma Burden Obstructive Score; SSS: The Segment Stenosis Score; EAT: Epicardial Adipose Tissue.

Predictors of CVEVs by univariable and multivariate regression

All the differences factors between CVEVs and no-CVEVs and clinical cardiovascular risk factors were included in the multivariate logistic regression analysis. Hypertension (odds ratio (OR) 3.844, 95%confidence interval [CI] 1.000-10.056; P=0.020), diabetes duration (OR 1.129, 95% CI (0.986-1.293); P=0.049), creatinine (OR 1.072, 95% CI 1.010-1.138; P=0.022), ABOS (OR 1.729, 95% CI 1.112-6.217; P=0.031), SSS (OR 1.213, 95% CI 0.955-1.988; P=0.021), and EAT volume (OR 1.025, 95% CI1.005-1.045; P=0.012) were independently associated with CVEVs (Table 3).

The clinical risk factors model for the AUC included age, male sex, smoking, hypertension, hyperlipidemia, BMI, family history of CAD, creatinine, and duration of diabetes. The model showed a good power for forewarning of CVEVs (AUC: 0.821, 95% CI: 0.721-0.897). When ABOS and SSS were added, or EAT was added, the AUC increased (AUC: 0.895, 95% CI: 0.808- 0.952; AUC: 0.885, 95% CI: 0.795 to 0.945). Whereas adding ABOS, SSS, and EAT volume showed significant improvement to AUC (AUC: 0.955, 95% CI: 0.885 to 0.989) beyond the risk factors (Figure 3 and Table 4).

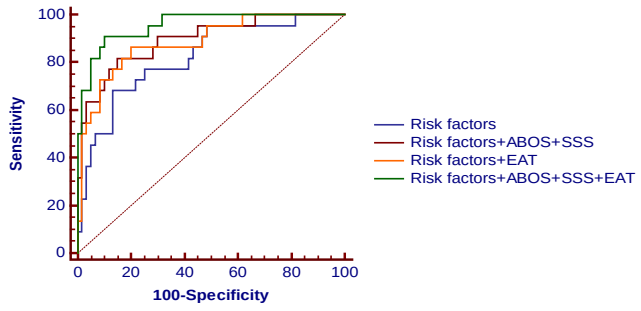

Figure 3: Incremental value of CCTA to identify patients with CVEVs.
The risk factors included the following variables: Age, male sex, smoking, hypertension, hyperlipidemia, BMI, family history of CAD, creatinine and duration of diabetes.

Discussion

The main findings of this study were as follows: (1) CVEVs were more likely to occur in patients with T2DM at high/very high cardiovascular risk who had longer diabetes duration, higher creatinine levels, and combined hypertension. (2) ABOS, SSS, and EAT volume were the independent risk factors for cardiac events in

Table 3: Univariable and multivariable analysis for predictors of CVEVs.

	Univariate Analysis		Multivariable Analysis	
	OR (95% CI)	P-value	OR (95% CI)	P-value
Age	1.059(0.992-1.131)	0.086		
Male	1.338(0.489-3.666)	0.571		
BMI	0.919(0.764-1.106)	0.372		
Hypertension	3.370(1.223-9.286)	0.019	3.844(1.000-10.056)	20
Family history of CAD	1.114(0.411-3.017)	0.832		
Smoking	1.751(0.897-2.318)	0.588		
Duration of diabetes	1.125(1.027-1.232)	0.011	1.129(0.986-1.293)	0.049
Mean HbA1c level	1.395(0.981-1.983)	0.064		
Creatinine	1.059(1.020-1.100)	0.003	1.072(1.010-1.138)	0.022
Hyperlipidemia	1.129(0.874-1.944)	0.528	2.034(1.466-7.657)	0.342
Vulnerable plaque	5.588(1.210-25.818)	0.028	4.225(0260-68.660)	0.311
Obstructive plaques	5.778(2.003-16.068)	0.001	1.485(0.127-17.317)	0.752
ABOS	2.523(1.263-5.043)	0.009	1.729(1.112-6.217)	0.031
SIS	1.158(0.944-1.420)	0.159		
SSS	1.240(1.086-1.415)	0.002	1.213(0.955-1.988)	0.021
EAT volume	1.017(1.004-1.030)	0.01	1.025(1.005-1.045)	0.012
Statins	0.680(0.204-2.272)	0.531		
ACEI/ARB	5.000(1.703-14.676)	0.003	5.330(0.924-30.735)	0.061

Table 4: Receiver operating characteristic (ROC) curve evaluation for CVEV prediction.

Prediction of CVEV	AUC	95% CI	Specificity	Sensitivity
Risk factors	0.821	0.721 to 0.897	75	76.4
Risk factors+ABOS+SSS	0.895	0.808 to 0.952	85	81.8
Risk factors+EAT	0.885	0.795 to 0.945	80	85.5
Risk factors+ABOS+SSS+EAT	0.955	0.885 to 0.989	90	90
ROC comparisons *vs.* Risk factors	**AUC (difference)**	**95% CI**	***P***	**-**
Risk factors+ABOS+SSS	0.074	-0.012to 0.160	0.09	-
Risk factors+EAT	0.064	-0.003 to 0.131	0.06	-
Risk factors+ABOS+SSS+EAT	0.134	0.042 to 0.226	0.004	

Areas under ROC curves (AUC), 95% confidence intervals (CI), and the significance level (P) are presented. The results presented in this table are related to the curves shown in Figure 3.

type 2 diabetic patients with high/very high cardiovascular risk. (3) Addition of the ABOS, SSS, and EAT volume assessed by CCTA to the existing clinical risk prediction model significantly increased the predictive ability for CVEVs in these patients.

In previous studies on high-risk diabetes patients, the methods of risk stratification are diverse [5,6,25], which will lead to differences in research results. In our study, the definition of high/very high cardiovascular risk in our study was based on the 2019 ESC guidelines, including a comprehensive assessment of T2DM target organ damage, age, hypertension, dyslipidemia, smoking, obesity and other risk factors and diabetes duration, which was more accurate and more referential. In our study, T2DM patients at high/very high risk had high CVEVs (26.8%) during a long-term follow-up, with cardiac events (i.e., cardiovascular death, non-fatal myocardial infarction, unstable angina requiring hospitalization, or late coronary revascularization) [26] accounting for 20.7%. The incidence of long-term cardiac events is nearly 5 times in these patients than in a holistic asymptomatic cohort of patients with T2DM [26]. Therefore, it is necessary to study the forewarning factors of adverse events in these patients.

Duration of diabetes, mean creatinine level, and hypertension were the independent predictor of CVEVs. These findings suggest that a long course of diabetes, impairment of renal function, and poor blood pressure control may contribute to the poor prognosis in T2DM patients, which is similar to some previous studies [27,28]. Therefore, to prevent future cardiac events in these patients, more effort should be made to protect kidney function and reduce complications.

A comprehensive analysis of CCTA was used in our study, including the CAC score, plaque location, lumen stenosis, plaque characteristics, plaque stability, and EAT volume. The results showed

obstructive CAD in patients with T2DM were associated with a poor prognosis, which is consistent with the findings of previous studies [29]. Moreover, ABOS, which represents the involvement of coronary obstructive stenosis, showed the highest OR (14.060) among all risk factors and was an independent predictor of CVEVs. This suggests that patients with multiple coronary obstructive stenoses should be recommended to undergo diagnostic coronary angiography and evaluation of coronary hemodynamics. Also, the SSS, which represents the overall extent of coronary atherosclerotic stenosis, was higher in patients with CVEVs than those without. It shows that these two scores can fully reflect the characteristics of CAD in high-risk diabetic patients, that is, multi-segments involvement and multiple stenoses [3]. These results suggest that the overall atherosclerotic burden of coronary arteries has a greater long-term prognostic value than obstructive CAD in type 2 diabetic patients with high/very high risk. This is also one of the reasons why the FACTOR-64 study [5] has negative results in terms of CCTA benefits. In the treatment of CAD of type 2 diabetes, more attention should be paid to how to reduce the burden of overall coronary atherosclerotic lesions, which is better than the intervention of a certain lesion. Furthermore, ABOS and SSS could be used in future research as indicators for treatment effects in plaque. It is noteworthy that quantitative measurement of EAT volume which is indicated as a coronary inflammatory biomarker was added to the CCTA analysis in our study. It showed that the EAT volume was an independent predictor of CVEVs in diabetic patients at high/very high risk. Moreover, the results implied that excessive visceral obesity and low-grade systemic vascular inflammation were closely associated with the rising incidence of CVEVs in these patients. In diabetic patients at high/very high risk, more attention should monitor the distribution of visceral adipose tissue, and CCTA is a convenient method. Although the previous evidence would support the use of coronary artery calcium (CAC) score scanning for risk stratification and to guide management in the asymptomatic DM patient, as recommended with a Class IIb indication in the 2019 ESC guidelines [2,30,31], However, CAC score and categories were not associated with subsequent cardiovascular events in our study. It may be attributes to the widespread use of statins in these individuals, which can lead to plaque calcification progression [32].

In this study, ABOS, SSS, and EAT volume from CCTA were used as forewarning indicators for CVEVs, which improved the sensitivity and specificity. This indicates that CCTA has a potential incremental prognostic value of predictors and may be used to guide an intensified secondary prevention strategy for T2DM patients with a higher cardiovascular risk.

This study has some limitations. This was an observational retrospective study with a limited number of enrolled patients, and whether to perform CCTA examination depended on the judgment of the clinician; thus, selection bias was possible. Furthermore, the outcomes might be confounded by the efficacy of treatment decisions and the patients' attitude towards treatment, compliance, and self-management. In the future, a large-sample randomized controlled prospective study is needed for verification.

Conclusion

The extent and severity of overall coronary atheroma burden and EAT volume based on CCTA are associated with long-term CVEVs for type 2 diabetic patients at high/very high cardiovascular risk. CCTA has incremental value in evaluating the heterogeneity of such subclinical patients and beneficial forewarning for these individuals with CVEVs.

Ethics Approval and Consent to Participate

Approved by the Institutional Review Board of the First Affiliated Hospital of Xi'an Jiaotong University with a waiver of informed consent due to the retrospective nature of this investigation.

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