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ORIGINAL RESEARCH

Coronary Artery Disease Risk Assessment by Coronary Artery Calcium Scoring in Asymptomatic Thai People with Diabetes Mellitus

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Background: People with diabetes mellitus (DM) remain at high risk of cardiovascular (CV) disease. The use of coronary artery calcium (CAC) has been demonstrated as the most powerful CV risk indicator and surrogate marker for the overall vascular health in the asymptomatic population.

Material and Methods: This study aimed to find the severity of CAC in asymptomatic Thai people with DM, evaluate the correlation of the severity CAC risk scoring system with different CV risk scores, and examine the impacts of CAC testing on patient managements. ABC control, defined as the proportion of individuals meeting glycemic, blood pressure, and LDL cholesterol targets together, was assessed at 6 months after the CAC measurement.

Results: A total of 157 patients (female 45.2%, T2D 93.0%, mean age 61.7±13.3 years, mean DM duration 12.4±10.6 years, BMI 26.4±4.8 kg/m^2, A1C 7.4±1.9%, insulin usage 28.7%) were included in the study. Zero calcium score was found in 24.2% and CAC score ≥100 AU was found in 40.3% of all patients. There was a weak to moderate significant positive correlation (correlation coefficients ranged from 0.311 to 0.449) between different CV risk scores with the presence of CAC score ≥100 AU. In those with CAC score ≥ 100 AU, aggressive lipid-lowering therapy, new prescription of SGLT2i or GLP-1 RA, new prescription of antiplatelet as primary prevention was all increased when compared with CAC <100 AU. At 6 months, achieved ABC target increased from 30.4% to 55.7% in patients with CAC ≥100 AU while achieved ABC target increased from 35.9% to 56.4% in patients with CAC < 100 AU.

Conclusion: CAC is an effective tool for CV risk stratification among asymptomatic people with DM and could improve metabolic target attainment rates. Currently available clinical risk assessment models including diabetes-specific risk scores correlated weakly with results from CAC testing among Thai people with DM.

Keywords: coronary artery calcium, CAC, cardiovascular risk assessment, asymptomatic, Thai, diabetes mellitus, DM

Introduction

Coronary artery disease (CAD) remains the leading cause of premature morbidity and mortality among individuals with diabetes mellitus (DM) and risk stratification is important in identifying those who might benefit the most from aggressive treatments to alleviate the cardiovascular (CV) disease morbidity and mortality. People with diabetes mellitus (DM) are at higher risk for CAD and often referred as CAD risk equivalent.[1] However, accumulating evidence indicates substantial heterogeneity in vascular risk within people with diabetes. Many people with DM have low CAD risk as with the general healthy population.[2,3] Various CV risk scores have been developed among people with type 2 diabetes (T2D) but they were not in widespread use.[4–6] Moreover, diabetes-specific risk scores which require many clinical and laboratory data did not appear to outperform scores derived for the general population.[7]

Since 2000, the landmark trial called "the Multi-Ethnic Study of Atherosclerosis" (MESA) demonstrated the impact and clinical utility of subclinical calcification assessed by coronary artery calcium (CAC) scoring on clinical outcomes in a cohort of asymptomatic adults from four ethnic groups across the United States.[8] A CAC score of zero confers a remarkably low risk

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of cardiovascular events,[9,10] whereas moderate-to-severe calcification markedly increases the likelihood of future Atherosclerotic Cardiovascular Disease (ASCVD) events and reclassifies risk beyond conventional prediction tools. Recent studies have shown that up to 40% of people with T2D have a CAC of zero and CAC risk scoring system has been shown to predict CV events during long-term follow-up in people with T2D more accurately than the UK Prospective Diabetes Study (UKPDS) and the Framingham risk scores.[11–13] Importantly, visualization of CAC may also influence both physician and patient behaviors, enhancing adherence to lipid-lowering medications and motivating intensification of preventive therapies.[14,15]

Nevertheless, clinical practice guidelines and standards of care regarding CAC did not endorse universal screening in asymptomatic people with DM, citing concerns regarding cost, radiation exposure, and uncertain incremental benefit over contemporary risk-factor–based care.[16] Furthermore, major risk engines such as the ASCVD pooled cohort equations, the Systematic Coronary Risk Evaluation 2 (SCORE2) model, and diabetes-specific tools like the UKPDS risk engine have shown variable accuracy in Asian. Diabetes in Thailand is a major public health concern but dedicated study among the role of cardiovascular tool assessment remained limited, especially the visualization tool like CAC measurement. Therefore, this study aimed to 1) examine subclinical CAD defined as a CAC score >0 Agatston units (AU) in asymptomatic Thai people with DM 2) find the correlation of the severity of subclinical CAD assessed by CAC risk scoring system with different CV risk scores 3) examine the impacts of CAC testing on patient managements including subsequent cascades of CAD screening tests, glucose-lowering treatment decisions, statin intensification, and also antiplatelet prescription 4) compare the metabolic risk factors control at 6 months after the CAC measurement.

Materials and Methods

Study Design and Population

We conducted a retrospective cohort study at Vimut–Theptarin Hospital, a tertiary endocrine center in Bangkok, Thailand. The study included individuals with diabetes who underwent clinically ordered CAC scoring between January 2020 and December 2022. Ethical approval was granted by the Theptarin Hospital Ethics Committee (EC No. 4-2021), and written informed consent for clinical data use was obtained at the time of evaluation. The study was conducted in accordance with the Declaration of Helsinki.

Eligible participants were adults (≥15 years old) with a confirmed diagnosis of DM who underwent CAC scanning for primary prevention and had no symptoms suggestive of CAD (eg, chest pain or dyspnea). We excluded individuals of non-Thai ethnicity, those who underwent CAC scanning for diagnostic purposes, and those with incomplete CAC data.

Coronary Artery Calcium Assessment

CAC scoring was performed using a standardized protocol with a 256-slice multidetector computed tomography scanner. Imaging acquisition followed the Society of Cardiovascular Computed Tomography (SCCT) recommendations, with electrocardiographic gating, heart-rate control (<80 beats/min), and uniform reconstruction parameters.[17] The vessels of interest included the left main (LM), left anterior descending (LAD), left circumflex (LCX), and right coronary arteries (RCA). The CAC results were quantified using the Agatston score.[18] The total Agatston score is the sum of all CAC lesions. Calcified lesions were identified using a threshold of ≥130 Hounsfield units and quantified using the Agatston method. CAC severity was categorized into standard clinical groups: Zero CAC (0 AU), Mild (1–99 AU), Moderate (100–399 AU), Severe (≥400 AU). For analytic purposes, CAC <100 AU and CAC ≥ 100 AU were compared to reflect clinically actionable treatment thresholds.

Cardiovascular Risk Assessment

Four risk engines were calculated using clinical and laboratory data obtained within six months of CAC measurement: Thai CV Risk Score (validated in Thai population), ASCVD Pooled Cohort Equations, SCORE2 model, UKPDS risk engine.[19–22] All cardiovascular risk scores assessment had been evaluated based on the recent clinical data before CAC testing. Risk categories were aligned with guideline-recommended thresholds for consideration of high-intensity statin therapy. Parameters included in the Thai CV risk score were: age, current smoking, presence of DM, systolic blood

pressure (BP), total cholesterol, waist circumference, and height. ABC control (A: hemoglobin A1C [A1C] <7.0%; B: blood pressure [BP] <140/90 mmHg; C: low-density lipoprotein [LDL] <100 mg/dL) which was defined as the proportion of individuals meeting glycemic, blood pressure, and LDL cholesterol targets together was assessed at within 6 months before and at 6 months after the CAC measurement.

Clinical Management and Outcomes

To examine the influence of CAC testing on clinical decision-making, we extracted data on: initiation/intensification of lipid-lowering therapy (statins, ezetimibe), new prescriptions of SGLT2 inhibitors or GLP-1 receptor agonists, initiation of antiplatelet therapy for primary prevention, downstream cardiac investigations (exercise stress testing, coronary computed tomography angiography (CCTA), coronary angiography, revascularization). Metabolic control was evaluated at two time points: within 6 months prior to CAC and within 6 months following CAC.

Statistical Analyses

Continuous variables were reported as means ± SD or medians with interquartile ranges. Between-group comparisons used Student's t-tests or chi-square tests, as appropriate. Spearman correlation coefficients quantified associations between CAC burden and each risk score. Various CV risk scores were also categorized as low-risk and higher risks for a 10-year cardiovascular morbidity and mortality risks based on the American College of Cardiology/American Heart Association guidelines for consideration of high-intensity statin use in those with diabetes.[23] Further analysis regarding the impacts of CAC testing on patient managements and achieved ABC control were done by dividing subjects into 2 groups (CAC < 100 AU versus CAC ≥ 100 AU). Analyses were conducted using SPSS version 25. Statistical significance was defined as *P-value* <0.05.

Results

Patient Characteristics

A total of 640 charts were reviewed and 157 participants met the inclusion criteria as shown in Figure 1. The baseline demographic and laboratory data are demonstrated in Table 1 (female 45.2%, T2D 93.0%, mean age 61.7±13.3 years, mean DM duration 12.4±10.6 years, BMI 26.4±4.8 kg/m^2, A1C 7.4±1.9%, insulin usage 28.7%). The prevalence of diabetic complications was retinopathy in 18.3% and nephropathy in 22.3% of the participants. The ASCVD risk score

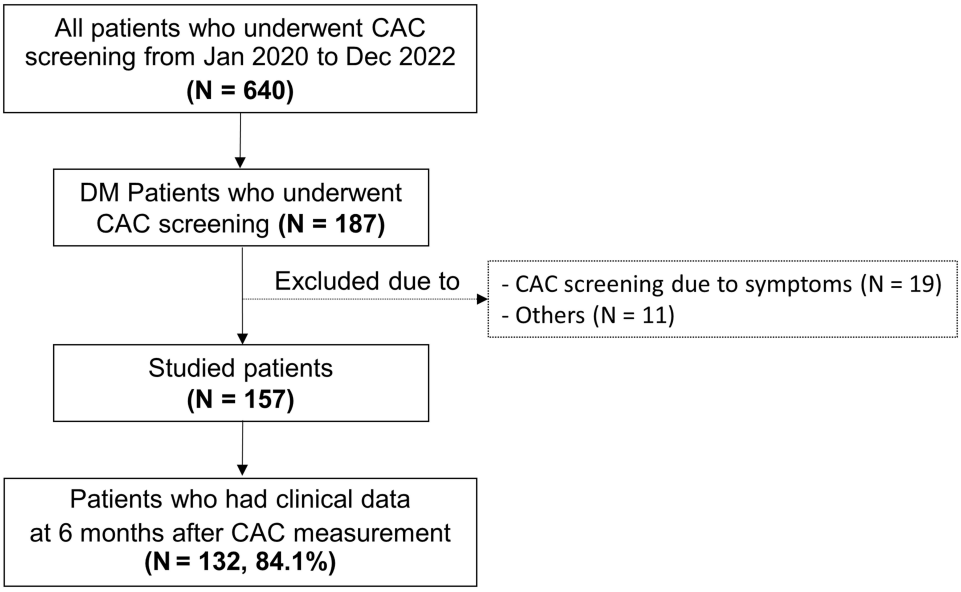

Figure 1 Flow selection diagram of studied patients (N=157).

Table 1 Characteristics of Studied Patients (N=157)

	Total patients (N = 157)	CACS <100 (N = 78, 49.7%)	CACS ≥100 (N = 79, 50.3%)	*P-value*
Age (years)	61.7±13.3	55.4±12.2	68.0±11.4	<0.001
Female (%)	45.2	50.0	40.5	0.263
BMI (kg/m^2)	26.4±4.8	25.5±5.2	26.4±4.4	0.869
Active smoking (%)	11.5	11.5	11.4	0.977
FH of ASCVD (%)	9.6	6.4	12.7	0.277
T2D (%)	93.0	88.5	97.5	0.082
Duration of DM (years)	12.4±10.6	8.7±8.6	16.0±11.1	<0.001
DM Duration ≥ 10 years	48.4	32.1	64.6	<0.001
Presence of DR (%)*	18.3	14.5	22.1	0.296
Presence of DKD (%)	22.3	16.7	27.8	0.092
HT (%)	54.1	35.9	72.2	<0.001
A1C (%)	7.4±1.9	7.4±1.9	7.4±1.9	0.939
Systolic BP (mmHg)	126±15	123±14	130±15	0.007
Diastolic BP (mmHg)	73±11	72±12	73±10	0.706
LDL (mg/dL)	99±42	106±48	93±33	0.051
Achieved ABC target (%)	33.1	35.9	30.4	0.501
Insulin usage (%)	28.7	29.5	27.8	0.861
Use of SGLT2i or GLP-1 RA (%)	29.3	25.6	32.9	0.317
Moderate to high intensity statin (%)	65.0	65.4	64.6	0.913

Note: *Available for diabetic retinopathy (DR) status = 153 cases.
Abbreviations: A1C, glycated hemoglobin; ASCVD, Atherosclerotic Cardiovascular Disease; BMI, Body mass index; BP, Blood Pressure; CACS, Coronary Artery Calcium Score; DM, Diabetes Mellitus; DR, Diabetic Retinopathy; DKD, Diabetic Kidney Disease; FH, Family History; GLP-1 RA, Glucagon-Like Peptide-1 Receptor Agonist; HT, Hypertension; LDL, Low-Density Lipoprotein; SGLT2i, Sodium-Glucose Cotransporter 2 Inhibitor.

classified the highest proportion of patients into high-risk category of CVD (67.4%), followed by Thai CV risk score (57.9%), SCORE2 (50.0%), and UKPDS (14.5%) as shown in Figure 2.

Patterns of Subclinical CAD and Degree of Calcification

As shown in Table 1, those with CAC ≥ 100 AU revealed older age, longer duration of DM, and higher rate of hypertension but no difference was observed in gender and glycemic control. Zero calcium score was found in 24.2% and CAC score ≥100 AU was found in 40.3% of all participants as revealed in Figure 3. Among those who had non-zero CAC score, triple or four vessels involvement was found in 49.6% as shown in Figure 4A. When stratified by age group, the prevalence of zero calcium score was observed in 66.7% of participants age under 40 years, compared with 10.4% participants age ≥65 years as demonstrated in Figure 4B. When stratified by CAC severity, almost three-fourths of CAC ≥400 AU was found in age ≥65 years as shown in Figure 4C. When stratified by duration of DM, higher CAC burdens were found increasingly with longer duration of DM as revealed in Figure 4D. But, zero calcium score was also found in 16.4% of patients with a duration of DM ≥10 years.

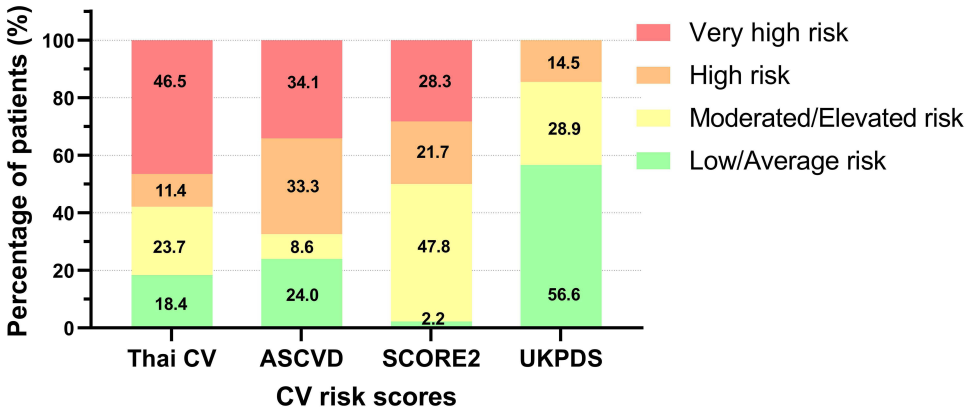

Figure 2 Proportion of patients into each category of cardiovascular diseases risk scores.

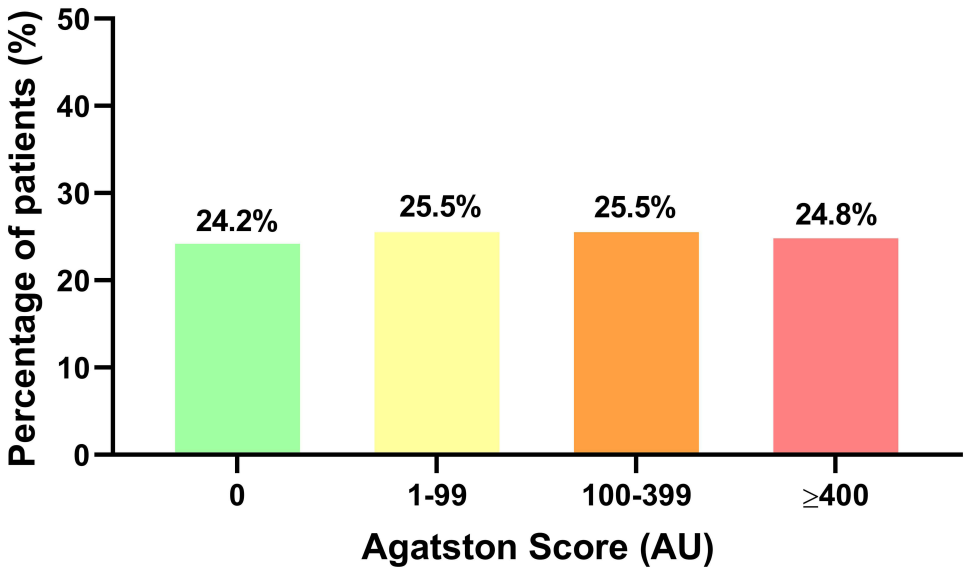

Figure 3 Distribution of coronary artery calcium (CAC) Agatston score among studied participants.

Predicting the Severity of Subclinical CAD from Different CV Risk Scores

The association between the severity of CAC and risk category from each CV score was demonstrated in Figure 5. According to Table 2, Spearman correlation coefficients for the presence or absence of CAC with various CV scores classified as low-risk ranged from 0.374 to 0.472 with UKPDS performed the best. When analyzing correlation coefficients between the presence of CAC ≥ 100 AU with various CV scores classified as higher risks, all CV scores yielded weak to moderate correlations with UKPDS performed the best (Spearman's Rho correlation coefficient at 0.449). The correlation between the Agatston score as a continuous data with different CV risk scores as a continuous data demonstrated only moderate relationship in all CV scores.

Impact of Coronary Artery Calcium Testing on Patient Management

CAC measurements influenced downstream cardiac investigations with 35.4% of patients with CAC ≥100 AU underwent imaging tests or coronary revascularizations within 6 months after having obtained the results. In those with diagnostic cardiac catheterization, revascularization intervention was performed in 80% of patients. Aggressive lipid-lowering therapy (statin intensification or adding ezetimibe), prescription of SGLT2i or GLP-1 RA, prescription of antiplatelet (aspirin or clopidogrel) as primary prevention, and achieved ABC target were all increased at 6 months post-CAC scoring

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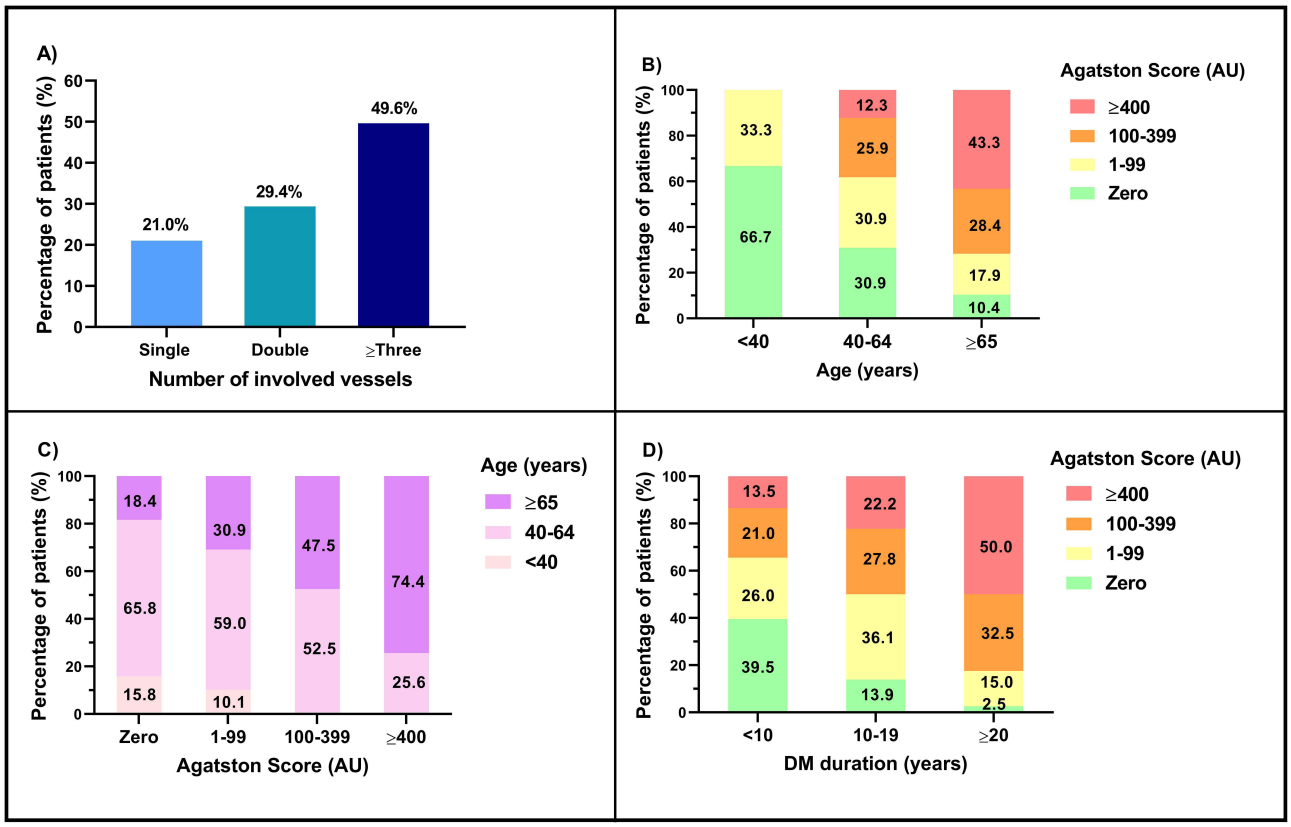

Figure 4 Patterns of subclinical coronary artery disease assessed by coronary artery calcium (CAC) (**A**) Number of vessels involvements in non-zero patients (**B**) Distribution of CAC scores stratified by age group (**C**) Distribution of age group stratified by severity of CAC burden (**D**) Distribution of CAC scores stratified by DM duration.

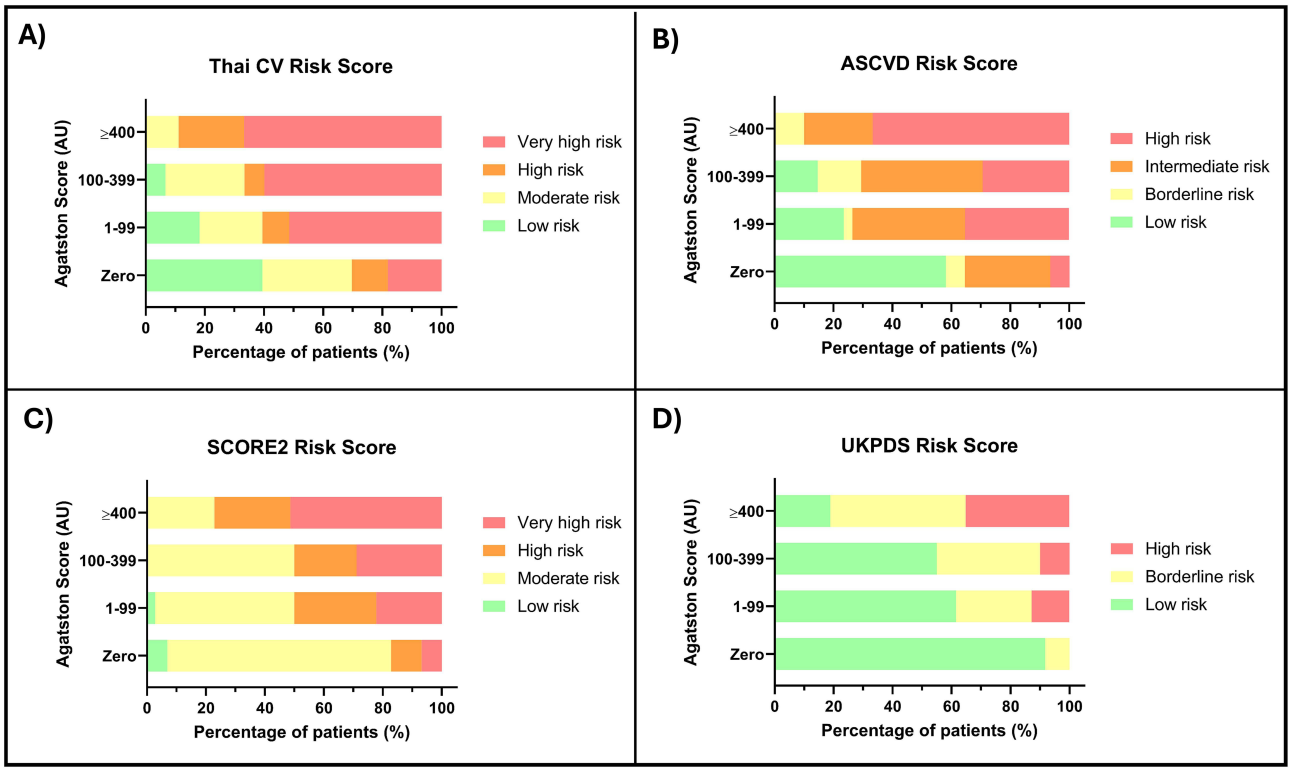

Figure 5 The association between the severity of CAC and risk category from each CV score (**A**) Thai Cardiovascular (CV) Risk Score (**B**) Atherosclerotic Cardiovascular Disease (ASCVD) Risk Score (**C**) Systematic Coronary Risk Evaluation 2 (SCORE2) Risk Score (**D**) UK Prospective Diabetes Study (UKPDS) Risk Score.

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Table 2 Spearman Correlation Coefficients for the Results from Coronary Artery Calcium (CAC) with Various Cardiovascular (CV) Scores

CV Risk score (CAC = 0)	**Spearman correlation coefficient**	***P-value***
Thai CV	0.374	<0.001
ASCVD	0.467	<0.001
SCORE2	0.408	<0.001
UKPDS	0.472	<0.001
CV Risk score (CAC≥100)	**Spearman correlation coefficient**	***P-value***
Thai CV	0.311	0.001
ASCVD	0.386	<0.001
SCORE2	0.385	<0.001
UKPDS	0.449	<0.001
CV Risk score (CAC as a continuous value)	**Spearman correlation coefficient**	***P-value***
Thai CV	0.396	<0.001
ASCVD	0.525	<0.001
SCORE2	0.483	<0.001
UKPDS	0.554	<0.001

Abbreviations: ASCVD, Atherosclerotic Cardiovascular Disease; CV, Cardiovascular; Thai CV, Thai Cardiovascular Risk Score; SCORE2, Systematic Coronary Risk Evaluation 2 mo UKPDS, United Kingdom Prospective Diabetes Study.

when compared with at 6 months before the CAC measurement. These trends were more pronounced in patients with CAC ≥100 AU when compared with CAC <100 AU as demonstrated in Figure 6. At 6 months, achieved ABC target increased from 30.4% to 55.7% in patients with CAC ≥100 AU while achieved ABC target increased from 35.9% to 56.4% in patients with CAC < 100 AU.

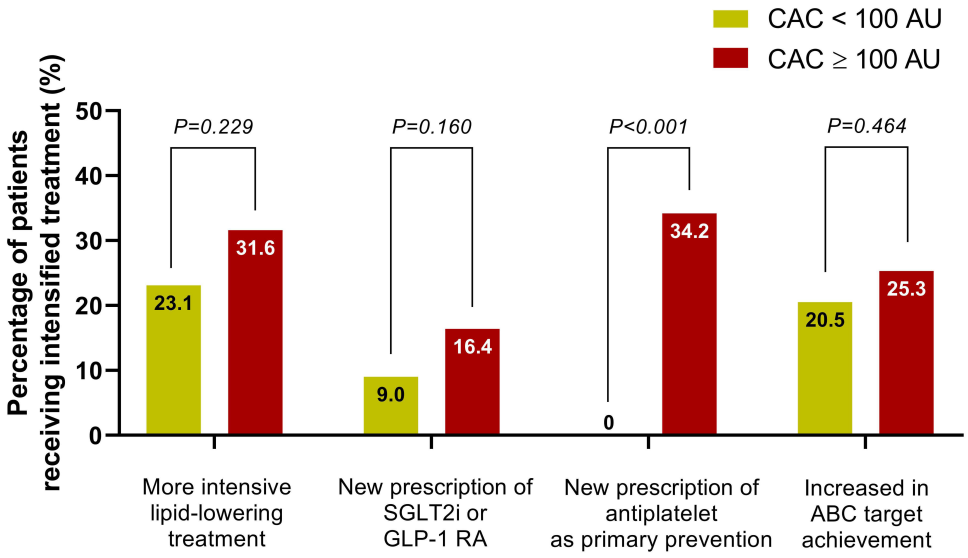

Figure 6 Impacts of coronary artery calcium (CAC) testing at 6 months after CAC measurement between patients with CAC < 100 AU and CAC ≥ 100 AU.

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Discussion

In this cohort of asymptomatic Thai adults with diabetes, we observed considerable heterogeneity in subclinical coronary atherosclerotic burden. Nearly one-quarter of participants had a CAC score of zero, demonstrating very low near-term ASCVD risk, whereas approximately 40% had CAC ≥100 AU, a threshold strongly associated with future adverse cardiovascular outcomes. This wide distribution reinforces that diabetes should not be uniformly treated as a CAD risk equivalent and underscores the need for individualized risk assessment in Asian populations. Subclinical atherosclerosis identified by CAC emerges as a promising reliable tool in general population and has been recommended as a "risk enhancing" factor among individuals who are at borderline or intermediate risk for ASCVD for statin eligibility.[24] Dedicated studies in people with DM also showed the similar results as in non-DM population.[25,26]

Our findings also highlight limitations of commonly used cardiovascular risk engines. All four assessed models (Thai CV Risk Score, ASCVD pooled equations, SCORE2, and UKPDS) showed only weak to moderate correlation with CAC burden. This is consistent with prior literature showing that traditional risk factors incompletely capture lifetime atherosclerotic exposure and that many diabetes-specific models were derived from Western cohorts with differing risk profiles. Importantly, the prevalence of zero CAC among individuals with long-standing diabetes in our study echoes emerging data suggesting that diabetes duration alone should not dictate escalation to high-intensity lipid-lowering or cardioprotective therapies. CAC screening may improve decision makings for preventive interventions by better delineating lifetime CV risk among people with DM and improved the attainment of multiple treatment targets.[27] Visualization of coronary calcium in high-risk patients would positively affect patients' adherence rates to medication and informed shared decision-making for glucose-lowering treatment decisions, statin intensification, and anti-platelet prescription.[28–30]

Improved utilization of anti-diabetic medications with CV benefits by CAC screening would lead to a novel opportunity to identify the most appropriate group of patients who should be allocated to this higher cost of medications.[31] Clinicians and patients may decide to be less aggressive strategy if zero CAC is present; by contrast, higher CAC scores may support a more aggressive approach from its association with higher CV events and long-term mortality. Future studies should evaluate the cost-effectiveness of SGLT2i or GLP-1 RA among patients who are at high risk for ASCVD defined by CAC scores. Several studies demonstrated it outperforming other non-invasive measures of subclinical atherosclerosis such as carotid plaque thickness measurement or ankle-brachial index.[32,33] A recent study demonstrated that CAC greater than 300 AU had an equivalent risk for major CV events as treated patients with established ASCVD.[34] The addition of CAC score to traditional risk assessment was associated with significantly improved CV risk classification in those with metabolic syndrome and DM even people with long-standing duration of DM.[12] This finding challenged a concept of longer duration of DM as a component of selecting treatment regimen.[35] Our present data also showed the same findings that calcium score of zero was found in more than one-fifth of patients with DM duration ≥20 years. Therefore, the application of CAC has the potential to accurately identify individuals who have not yet had a CV event to intervene with an appropriate intensity of treatments.

Current evidences showed moderate to poor discrimination ability for assessing 10-year ASCVD risk among people with DM.[7,36] Our present data were also in line with previous studies that all four CV risk scores did not accurately predict the severity of CAC burden.[37,38] Our results suggested that CAC scoring may provide important clinical value in Asian populations, particularly where traditional risk engines overestimate risk. Identifying individuals with zero CAC could prevent overtreatment and avoid unnecessary exposure to high-cost medications, while those with extensive calcification may benefit from intensified preventive therapy, including consideration of Proprotein Convertase Subtilisin/Kexin Type 9 (PCSK9) inhibitors, ezetimibe, or antiplatelet therapy in selected cases. Despite the concerns of cost, radiation exposure, and unnecessary invasive investigations from CAC screening, modern data suggest otherwise.[39] CAC also has the potential to identify individuals who might benefit from aspirin as primary prevention.[29,40] But it is important to note that CAC measurement could not identify non-calcified atherosclerotic plaque and CCTA is still required to identify early atherosclerotic disease especially in young patients.[41]

There are several limitations to this study. First, this is a retrospective analysis with its inherent biases and may not be generalizable to people with DM in other settings. Our studied cohort was relatively small due to incomplete data and short-term follow-up period to examine effects of CAC measurements. Nevertheless, the present study is the first cohort

to demonstrate the utility of CAC screening among asymptomatic Thai people with DM. Second, various CV risk scores are limited to subjects within the age range of risk engines. Application of CAC as a risk modifier in young-onset DM requires further validated studies for long-term outcomes. Third, CAC results were mostly studied to predict CV events but various CV risk scores include a composite vascular risk assessment. A score of zero does not imply zero ASCVD risk.[42] Fourth, the impacts of CAC testing on patient managements and metabolic controls might be confounded with many factors especially financial capability of patients in a private setting. Nonetheless, visualization of coronary calcium in high-risk patients could be used as a motivational tool to overcome the existence of therapeutic inertia among clinicians, and barriers among patients. Finally, there was no comparison with age-matched patients who did not undergo CAC measurements. Results of the present study should be interpreted with caution whether the improved metabolic outcomes were indeed an effect of high CAC burdens.

Conclusions

Our findings support the selective use of CAC scoring as a risk-stratification tool to guide personalized preventive strategies in asymptomatic individuals with diabetes, particularly in regions where conventional risk models show limited accuracy. It could also influence metabolic target attainment rates. The increasing accessibility and affordability of CAC testing could potentially play an important role in providing precision diagnoses and appropriate counseling for preventive therapies for individuals with diabetes.

Data Sharing Statement

The data that support the findings of this study are available from the corresponding upon reasonable request.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

No potential conflict of interest was reported by the authors.

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