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Low-density lipoprotein cholesterol predicts coronary artery calcification events in patients with type 2 diabetes: a longitudinal study

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Abstract

Background Coronary Artery Calcification (CAC) is a major risk factor for various cardiovascular diseases. Low-Density Lipoprotein Cholesterol (LDL-C) is a significant factor in atherosclerotic cardiovascular diseases and is usually elevated in patients with Type 2 Diabetes Mellitus (T2DM). However, the association between LDL-C levels and incident CAC in asymptomatic T2DM patients remains unclear.

Methods This study is a single-center retrospective cohort study conducted from January 2018 to December 2023, including 2,631 asymptomatic T2DM patients who underwent regular health screenings. All participants were confirmed to be free of CAC at baseline by computed tomography (CT). Based on baseline LDL-C levels, participants were divided into three groups (T1: 0.66–2.43 mmol/L; T2: 2.44–3.18 mmol/L; T3: 3.19–7.21 mmol/L). The follow-up endpoint was the occurrence of incident CAC, with a total follow-up period of 72 months. Kaplan-Meier survival curves were used for analysis, followed by log-rank tests. Univariate and multivariate Cox proportional hazards regression models were employed to investigate the relationship between LDL-C and incident CAC, and subgroup analysis was performed to test the robustness of the LDL-C and CAC relationship.

Results During a median follow-up period of 29.9 months, 885 (33.64%) participants developed incident CAC occurred. The cumulative incidence of incident CAC increased progressively with higher LDL-C levels (log-rank test, $P < 0.001$). After adjusting for confounding factors, multivariable Cox proportional hazards regression results showed a significant association between LDL-C and incident CAC (hazard ratio [HR], 1.77; 95% confidence interval [CI], 1.64–1.92). When LDL-C was treated as a categorical variable, elevated levels in T2 (adjusted HR, 1.62; 95% CI, 1.36–1.93; $P < 0.001$) and T3 (adjusted HR, 3.38; 95% CI, 2.84–4.03; $P < 0.001$) were significantly associated with the risk of incident CAC. Additionally, subgroup analysis demonstrated a consistent association between LDL-C and incident CAC.

Conclusion High LDL-C levels are associated with incident CAC in asymptomatic T2DM patients, suggesting that LDL-C may be useful for risk stratification in this population.

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Keywords Coronary artery calcification, Low-density lipoprotein cholesterol, Type 2 diabetes mellitus, Kaplan-Meier survival curves

Introduction

Coronary Artery Calcification (CAC) refers to the build-up of calcium in the walls of the coronary arteries, causing them to harden and narrow [1]. CAC is a key pathological feature of coronary artery disease and is closely linked to various cardiovascular diseases [2]. Patients with T2DM demonstrate a higher incidence of CAC and earlier age of onset compared to non-diabetic individuals [3]. Currently, computed tomography (CT) serves as a crucial tool for CAC detection, and clinical guidelines acknowledge CT-confirmed CAC as a validated risk prediction tool [4, 5]. The European Society of Cardiology (ESC) and the European Association for the Study of Diabetes recommend CAC assessment for asymptomatic T2DM patients to better evaluate their cardiovascular risk [6–8]. However, routine CT assessments of CAC may expose diabetic patients to radiation [9]. Therefore, finding easily usable biomarkers for CAC risk in asymptomatic T2DM patients is highly important.

Low-density lipoprotein cholesterol (LDL-C), a crucial cholesterol carrier in the bloodstream, has been well-established to be strongly associated with atherosclerotic cardiovascular disease when elevated. High levels of LDL-C can lead to the build-up of cholesterol in the arterial walls, forming atherosclerotic plaques and increasing the risk of cardiovascular diseases [10]. Recent studies have demonstrated that T2DM patients frequently present with elevated LDL-C levels, which significantly increases their risk of all-cause mortality [11, 12]. Although the relationship between LDL-C and cardiovascular disease in patients with T2DM has attracted considerable interest from researchers, the predictive role of LDL-C in CAC events among asymptomatic T2DM patients remains unclear.

Therefore, this study aims to investigate the association between LDL-C levels and incident CAC among asymptomatic T2DM patients, potentially providing a novel reference indicator for clinical risk assessment.

Materials and methods

Participants and the criteria for inclusion

This retrospective cohort study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of Henan Provincial People's Hospital (Approval Code: 2021-68). The requirement for informed consent was waived by the ethics committee due to the retrospective nature of the study and the use of de-identified data. We analyzed data from adult patients with T2DM who underwent regular annual health examinations at the Health Management Center of Henan Provincial People's Hospital between January 2018 and December 2023. These examinations were conducted as part of corporate health programs, ensuring systematic and standardized data collection. All patient data were anonymized before analysis. All participants were diagnosed without incident CAC by coronary CT during their first examination. Exclusion criteria included: absence of coronary CT in follow-up examinations; less than six months between two health examinations; patients with heart disease, including coronary artery disease, congenital heart disease, or previous cardiac surgery; history of any form of cancer; mental or cognitive disorders in women; immobility; pregnant or breastfeeding women; use of antiplatelet drugs; missing lipid profile data; and incomplete or extreme values in other laboratory indicators. Ultimately, 2,631 participants were selected for the final analysis, with 1,746 participants free of CAC at the end of the follow-up period and 885 participants experiencing incident CAC. General demographic information, medical history, and medication history of the participants were collected through face-to-face interviews by professional researchers. The specific case selection flowchart is shown in Fig. 1.

Definition of variables

The diagnosis of T2DM was based on the American Diabetes Association criteria [13]: a previous physician diagnosis of diabetes or current treatment with hypoglycemic medications, or fasting plasma glucose ≥ 7.0 mmol/L, or glycosylated hemoglobin (HbA1c) level ≥ 6.5%, or 2-hour oral glucose tolerance test (OGTT) blood glucose ≥ 11.1 mmol/L, or use of insulin or oral hypoglycemic agents. Asymptomatic specifically refers to the absence of cardiac symptoms (such as chest pain or shortness of breath) at baseline, rather than the absence of all diabetes-related complications. All participants underwent comprehensive health examinations at our Health Management Center, which included standardized clinical assessments and laboratory tests.

Hypertension was defined as a systolic blood pressure (SBP) ≥ 140 mmHg or diastolic blood pressure (DBP) ≥ 90 mmHg on two consecutive measurements, self-reported hypertension, taking antihypertensive medication, or undergoing antihypertensive treatment [14]. Hypotension was defined as SBP ≤ 90 mmHg or DBP ≤ 60 mmHg. Blood pressure within these ranges was considered normal.

All T2DM patients were categorized into three groups based on LDL-C levels: T1 (0.66–2.43 mmol/L), T2 (2.44–3.18 mmol/L), and T3 (3.19–7.21 mmol/L).

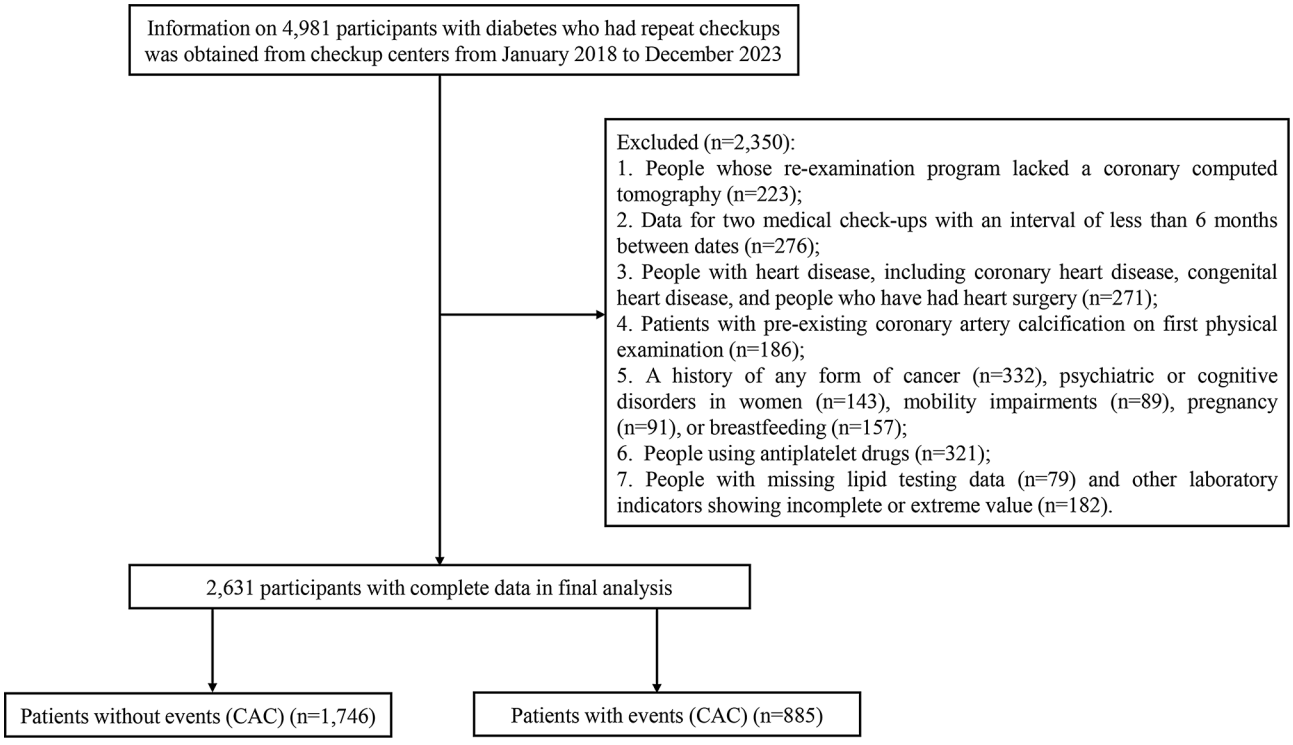

Fig. 1 Flowchart of participants selection

Current smoking was defined as self-reported smoking by the participants. Current drinking was defined as consuming at least one alcoholic beverage per week in the 12 months before the health examination.

Laboratory measurements

All researchers received standardized training to ensure impartiality and accuracy. Before the examination, researchers used standardized questionnaires to collect necessary information from all participants, including medical history, such as current diabetes, history of various cancers, heart surgeries, and current medications. After completing the questionnaires, researchers organized, summarized, and verified the data.

Venous blood samples were collected from all participants at 8 a.m. after an overnight fast to measure various biochemical markers, including total protein, total bilirubin, alanine aminotransferase (ALT), aspartate transaminase (AST), glutamyl transpeptidase (GGT), creatinine, uric acid, total cholesterol (TC), LDL-C, triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), fasting plasma glucose, and HbA1c. Blood glucose levels were measured using the Olympus® AU 5400 automatic biochemical analyzer (Olympus Corporation, Shizuoka, Japan). Other indicators were assessed following standard laboratory procedures.

SBP and DBP were measured by researchers using an electronic sphygmomanometer (OMRON U30, Omron Corporation, Kyoto, Japan) with the right arm in a semi-flexed position at heart level.

Study endpoints and definitions

The primary endpoint was the occurrence of an incident CAC more than six months after the baseline health screening. All coronary CT examinations were performed as part of a standardized cardiovascular risk assessment protocol in our corporate health examination program. These examinations were conducted based on clinical indications and standardized protocols, not individual requests.

All scans were performed using 256-slice CT scanners with radiation dose optimization following the ALARA (As Low As Reasonably Achievable) principle, ensuring minimal radiation exposure while maintaining diagnostic image quality. The mean effective radiation dose was 2.4 ± 1.4 mSv, which is within the recommended range for coronary CTA examinations. Incident CACs were determined by coronary CT results. The scan results were independently read at a centralized reading center, and the calcification amount was quantified using the Agatston scoring method by imaging radiologists [15]. An Agatston score of 0 was defined as without incident CAC, indicating no detectable calcified deposits in the coronary arteries. An Agatston score greater than 0 was defined as having incident CAC.

All incident CACs were judged and confirmed by an independent imaging radiologist using predefined criteria and then reviewed and confirmed by another senior imaging radiologist who was blinded to the study. Any discrepancies were resolved by consulting a third, more experienced senior imaging radiologist. If a participant had consecutive examinations showing incident CAC, the time of the first occurrence was recorded.

Statistical analysis

All statistical analyses were performed using R version 4.2.0 (R Foundation) and EmpowerStats (http://www.empowerstats.com, X&Y Solutions, Inc., Boston, MA). All statistical tests were two-tailed with a significance level of $P < 0.05$.

Normality tests were conducted on all datasets to assess continuous variables. Normally distributed continuous variables were described as mean ± standard deviation, while skewed continuous variables were presented as median (interquartile range). Group differences for continuous variables were evaluated using t-tests or rank-sum tests. Categorical variables were expressed as frequencies and percentages, and comparisons were conducted using chi-square tests or Fisher's exact tests. Kaplan-Meier survival curves were employed to illustrate the occurrence of incident CAC during follow-up among different LDL-C groups, with comparisons made using the log-rank test. The variance inflation factor (VIF) was calculated to detect multicollinearity among variables in the model, with VIF < 10 indicating no multicollinearity. Univariate and multivariate Cox proportional hazards regression models were used to examine the association between LDL-C and CAC, providing hazard ratios (HR) and 95% confidence intervals (CI). The univariate Cox model explored relationships between various variables and CAC risk, while the multivariate Cox model assessed the relationship between LDL-C levels and incident CAC after adjusting for demographic factors (sex, age, ethnic group), lifestyle factors (current smoking, current drinking, BMI), medical conditions and medications (hypertension status, antidiabetic medications, statins), and laboratory parameters (total protein, total bilirubin, ALT, AST, GGT, creatinine, uric acid). Subgroup analyses investigated the association between LDL-C and incident CAC across different subgroups, including sex, age, BMI, blood pressure status, hypertension treatment, diabetes medications, and statin use. Interaction P-values were determined using the multivariate Cox regression model. All analyses were based on baseline participant data.

Results

Baseline characteristics according to incident CAC at follow-up

A total of 2,631 T2DM participants free of CAC at baseline were included in this study. Table 1 presents the baseline characteristics of all participants divided into two groups (without and with incident CAC) based on CAC status at the follow-up endpoint. Over a median follow-up of 29.9 months (range: 6.07-69.00 months), 588 (66.44%) of the 1,649 male participants and 297 (33.56%) of the 964 female participants developed CAC. Those with CAC were generally older, predominantly male, had higher rates of hypertension, lower ALT levels, and higher TC and LDL-C levels (all $P < 0.05$). No significant differences were found in other variables between the two groups (all $P > 0.05$).

Baseline characteristics by LDL-C classification

Baseline characteristics by LDL-C classification: Compared to patients with lower LDL-C levels, those with higher LDL-C levels were more likely to be female and had higher levels of total protein, ALT, AST, GGT, uric acid, TG, and HDL-C, but were younger and had lower Cre levels (all $P < 0.05$). No significant differences were observed among the three groups for other variables (all $P > 0.05$, Supplementary Table 1).

Univariate cox regression analyses for CAC

Univariate Cox regression analyses for incident CAC: Univariate Cox proportional hazards regression analysis indicated that age, male gender, TP, GGT, UA, TC, HDL-C, and LDL-C were significant risk factors for incident CAC during follow-up (all $P < 0.05$). Other variables did not show significant statistical differences (all $P > 0.05$, Table 2).

LDL-C and CAC risk

The occurrence of CAC at follow-up for T2DM patients in the T1, T2, and T3 LDL-C groups were 282 (31.86%), 269 (30.40%), and 334 (37.74%), respectively (Table 3). Kaplan-Meier survival analysis revealed significant differences in CAC development among the three LDL-C groups over the 6-year follow-up, with the T3 group showing the highest cumulative incidence of CAC (Log-rank $P < 0.001$, Fig. 2) and the lowest CAC-free survival rate (Log-rank $P < 0.001$, Supplementary Fig. 1).

Multivariate Cox proportional hazards regression analysis was utilized to examine the relationship between LDL-C and incident CAC (Table 3). In the univariate model, the HR for CAC was 1.69 (95% CI: 1.57–1.83, $P < 0.001$). This association remained significant after adjusting for sex, age, ethnicity, hypertension medication, antidiabetic medication, statins, current smoking, current drinking, BMI, hypertension status, total protein, total bilirubin, ALT, AST, GGT, creatinine, and uric acid. When LDL-C was categorized, compared to the T1 group, the risk of CAC was higher in the T2 group (adjusted HR, 1.62; 95% CI, 1.36–1.93; $P < 0.001$) and

Table 1 Baseline characteristics stratified by the occurrence of CAC

Variables	Overall	Non-CAC	CAC	*P*-value
N	2631	1746	885	
Age, years	56.62 ± 12.33	55.62 ± 12.84	58.59 ± 11.00	< 0.001
Sex, n (%)				0.020
Female	964 (36.64)	667 (38.20)	297 (33.56)	
Male	1667 (63.36)	1079 (61.80)	588 (66.44)	
Ethnic group, n (%)				0.781
Non-han	105 (3.99)	71 (4.07)	34 (3.84)	
Han	2526 (96.01)	1675 (95.93)	851 (96.16)	
BMI, kg/m^2	26.27 ± 3.35	26.28 ± 3.36	26.24 ± 3.34	0.742
Current smoking, n (%)				0.843
No	2452 (93.20)	1626 (93.13)	826 (93.33)	
Yes	179 (6.80)	120 (6.87)	59 (6.67)	
Current drinking, n (%)				0.495
No	2333 (88.67)	1543 (88.37)	790 (89.27)	
Yes	298 (11.33)	203 (11.63)	95 (10.73)	
Blood pressure status, n (%)				0.031
Normobaric blood pressure	1415 (53.78)	966 (55.33)	449 (50.73)	
Hypertension	1208 (45.91)	773 (44.27)	435 (49.15)	
Hypotension	8 (0.30)	7 (0.40)	1 (0.11)	
Hypertensive medication, n (%)				0.548
No	2572 (97.76)	1709 (97.88)	863 (97.51)	
Yes	59 (2.24)	37 (2.12)	22 (2.49)	
Medications for diabetes, n (%)				0.764
No	2534 (96.31)	1683 (96.39)	851 (96.16)	
Yes	97 (3.69)	63 (3.61)	34 (3.84)	
Statins, n (%)				0.219
No	2586 (98.29)	1720 (98.51)	866 (97.85)	
Yes	45 (1.71)	26 (1.49)	19 (2.15)	
Total protein, g/L	72.01 ± 4.47	72.09 ± 4.64	71.85 ± 4.12	0.204
Total bilirubin, μmol/L	11.66 ± 4.61	11.64 ± 4.55	11.70 ± 4.72	0.739
ALT, U/L	22.10 (16.45–32.70)	22.60 (16.40–34.00)	21.50 (16.60–30.00)	0.004
AST, U/L	20.80 (17.05–26.30)	20.80 (17.00-26.58)	20.80 (17.10–25.90)	0.125
GGT, U/L	28.90 (20.10–46.20)	28.90 (20.40–46.00)	29.00 (19.80–46.60)	0.879
Creatinine, μmol/L	62.18 ± 16.94	62.03 ± 16.74	62.47 ± 17.33	0.538
Uric acid, μmol/L	324.12 ± 88.66	322.91 ± 88.92	326.51 ± 88.16	0.326
Fasting plasma glucose, mmol/L	8.16 ± 2.48	8.23 ± 2.52	8.03 ± 2.41	0.051
HbA1C, %	7.45 ± 1.39	7.42 ± 1.37	7.49 ± 1.42	0.437
TC, mmol/L	4.99 ± 1.17	4.95 ± 1.16	5.08 ± 1.19	0.008
TG, mmol/L	1.89 (1.33–2.76)	1.87 (1.34–2.75)	1.93 (1.31–2.78)	0.520
HDL-C, mmol/L	1.20 ± 0.27	1.20 ± 0.27	1.21 ± 0.26	0.419
LDL-C, mmol/L	2.85 ± 0.87	2.81 ± 0.84	2.91 ± 0.92	0.006

BMI, body mass index; ALT, alanine aminotransferase; AST, aspartate transaminase; GGT, glutamyl transpeptidase; HbA1c, Glycosylated hemoglobin; TC, total cholesterol; TG, triglycerides; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol

Except for the AST, ALT, GGT, and TG variables, which are expressed as medians (upper and lower quartiles), all other variables are expressed as mean ± standard deviation or counts (percentages)

the T3 group (adjusted HR, 3.38; 95% CI, 2.84–4.03; $P < 0.001$). In a subgroup analysis with available waist circumference data ($n = 588$), a stronger association was observed between LDL-C and CAC development, with increased risks in the T2 group (adjusted HR, 1.84; 95% CI, 1.23–2.77; $P = 0.003$) and the T3 group (adjusted HR, 4.61; 95% CI, 2.97–7.13; $P < 0.001$) compared to the T1 group (Supplementary Table 2).

Subgroup analysis

Subgroup analyses were conducted based on sex (male/female), age (< 40/≥40, < 60/≥60 years), BMI (< 24/≥24, < 28/≥28 kg/m^2), blood pressure status (normal/hypertension/hypotension), diabetes medication use (yes/no), and statin use (yes/no). Interaction *P*-values were calculated to explore the impact of each subgroup on the outcomes. The results consistently showed an association

Table 2 Univariate Cox regression analyses for incident CAC

Variables	HR	95%CI	*P*-value
Age, years	1.009	(1.003, 1.014)	0.003
Sex, n (%)			
Female		1.0	
Male	1.180	(1.026, 1.357)	0.020
Ethnic group, n (%)			
Non-han		1.0	
Han	1.521	(1.079, 2.145)	0.017
BMI, kg/m^2	1.011	(0.991, 1.030)	0.294
Current smoking, n (%)			
No		1.0	
Yes	1.014	(0.778, 1.320)	0.919
Current drinking, n (%)			
No		1.0	
Yes	0.885	(0.715, 1.095)	0.261
Blood pressure status, n (%)			
Normobaric blood pressure		1.0	
Hypertension	1.130	(0.990, 1.289)	0.070
Hypotension	0.317	(0.044, 2.255)	0.251
Hypertensive medication, n (%)			
No		1.0	
Yes	1.068	(0.700, 1.631)	0.759
Medications for diabetes, n (%)			
No		1.0	
Yes	0.969	(0.688, 1.366)	0.859
Statins, n (%)			
No		1.0	
Yes	1.550	(0.983, 2.444)	0.059
Total protein, g/L	0.982	(0.967, 0.998)	0.026
Total bilirubin, μmol/L	1.010	(0.996, 1.024)	0.159
ALT, U/L	0.999	(0.995, 1.002)	0.437
AST, U/L	0.999	(0.993, 1.004)	0.616
GGT, U/L	1.002	(1.000, 1.003)	0.028
Creatinine, μmol/L	1.002	(0.999, 1.006)	0.201
Uric acid, μmol/L	1.001	(1.000, 1.002)	0.003
Fasting plasma glucose, mmol/L	0.964	(0.937, 0.992)	0.012
TC, mmol/L	1.215	(1.157, 1.276)	< 0.001
TG, mmol/L	0.992	(0.965, 1.021)	0.591
HDL-C, mmol/L	1.312	(1.032, 1.667)	0.027
LDL-C, mmol/L	1.693	(1.565, 1.832)	< 0.001

BMI, body mass index; ALT, alanine aminotransferase; AST, aspartate transaminase; GGT, glutamyl transpeptidase; HbA1c, Glycosylated hemoglobin; TC, total cholesterol; TG, triglycerides; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; HR, hazard ratios; CI, confidence intervals

between elevated LDL-C and CAC development in T2DM patients across different subgroups (Fig. 3, all *P* for interaction > 0.05).

Discussion

This study analyzed data from 2,631 asymptomatic patients with T2DM undergoing regular health screenings. We observed that LDL-C levels were significantly higher in patients who developed CAC compared to those who remained CAC-free. Using a multivariable Cox proportional hazards model adjusting for potential confounding factors, we found that each unit increase in LDL-C levels was associated with a 1.77-fold higher risk of CAC development. Subgroup analyses demonstrated consistent associations across various population strata including sex, age, BMI, blood pressure status, antidiabetic medication use, and statin use, with no significant effect modification observed (all interaction $P > 0.05$). These findings highlight LDL-C as a potential marker for predicting CAC risk in asymptomatic T2DM patients, suggesting its utility in cardiovascular risk stratification for this population.

Previous research has extensively documented the role of LDL-C in atherosclerosis and CAC development.

Table 3 Multivariate cox regression analysis for incident CAC

	Events (%)	HR (95%CI)		
		Non-adjusted *P*-value	Adjust I *P*-value	Adjust II *P*-value
LDL-C	885 (33.64)	1.69 (1.57, 1.83) < 0.001	1.74 (1.61, 1.89) < 0.001	1.77 (1.64, 1.92) < 0.001
LDL-C tertile				
T1	282 (31.86)	Reference	Reference	Reference
T2	269 (30.40)	1.51 (1.27, 1.80) < 0.001	1.60 (1.34, 1.90) < 0.001	1.62 (1.36, 1.93) < 0.001
T3	334 (37.74)	3.07 (2.59, 3.65) < 0.001	3.30 (2.78, 3.92) < 0.001	3.38 (2.84, 4.03) < 0.001
P for trend		1.76 (1.62, 1.92) < 0.001	1.83 (1.67, 1.99) < 0.001	1.85 (1.69, 2.02) < 0.001

Non-adjusted model adjusts for: None

Adjust I model adjust for: sex, age, and ethnic group

Adjust II model adjust for: sex, age, ethnic group, hypertensive medication; medications for diabetes; statins; current smoking; current drinking; BMI; blood pressure status; total protein; total bilirubin; ALT; AST; GGT; creatinine; uric acid. HR, hazard ratio; CI, confidence interval

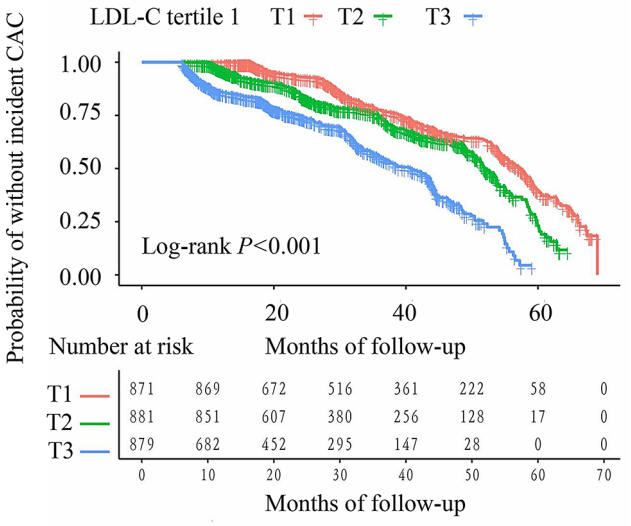

Fig. 2 Kaplan-Meier curves for LDL-C tertiles and incident CAC. CAC, coronary artery calcification

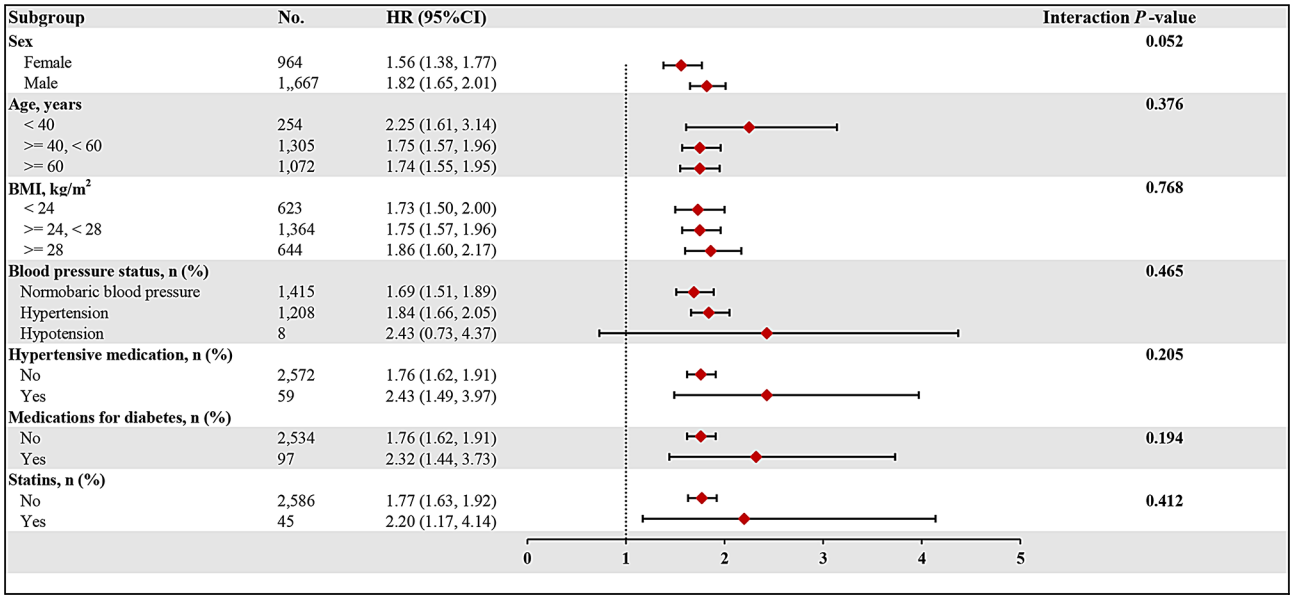

Fig. 3 The forest plot shows LDL-C levels and incident CAC in different subgroups of T2DM patients. Models adjusted for all confounders except for this subgroup variable. Red dots indicate HR values and bars indicate 95% CI. HR: risk ratio; CI, confidence interval

Animal studies have demonstrated that elevated LDL-C levels significantly contribute to the initiation and progression of atherosclerosis [16]. Clinical and experimental studies have revealed that LDL-C accumulation in the arterial wall triggers a series of pathological changes leading to plaque formation and subsequent calcification [17, 18]. In the context of T2DM, research has shown that insulin resistance fundamentally alters lipid metabolism, particularly affecting LDL-C metabolism through hepatic pathways [19]. Studies have also established that diabetic patients with elevated LDL-C levels face a higher risk of vascular calcification compared to those with normal LDL-C levels [20]. These findings from previous research provide a strong theoretical foundation for our observation that LDL-C serves as a predictor of CAC development in T2DM patients, suggesting its potential value in cardiovascular risk stratification.

This study monitored the health status of asymptomatic T2DM patients over six years and found a progressive increase in CAC risk with higher LDL-C levels, consistently observed across various subgroups. A prior multicenter prospective study with 259 asymptomatic T2DM patients highlighted LDL-C as a significant predictor of coronary artery disease severity and adverse cardiovascular events [21]. Longitudinal data from 208 diabetic patients in China indicated that poorly controlled LDL-C levels may exacerbate coronary plaque instability and CAC [22]. Another retrospective analysis from China involving 935 acute coronary syndrome patients underscored the significant impact of LDL-C and HDL-C on multivessel coronary disease occurrence [23]. The 2023 CAC guidelines emphasize lowering LDL-C as a preventive strategy against atherosclerotic cardiovascular diseases linked to CAC [24]. These findings demonstrate that elevated LDL-C levels are independently associated with increased risk of CAC development in patients with T2DM. Recognizing waist circumference as a crucial indicator of abdominal fat accumulation [25], we adjusted for it in the multivariable Cox proportional hazards model, confirming a robust association between LDL-C and CAC risk.

However, recent findings from the Danish Heart Registry, involving 23,132 symptomatic coronary artery disease patients, demonstrated a significant association between LDL-C and ASCVD in patients who developed CAC. In contrast, traditional risk factors including smoking, diabetes, and low HDL-C levels showed stronger associations with cardiovascular outcomes in patients without CAC [26]. Zaid et al. [27] reported that in a community sample of 870 Japanese men aged 40–79 without cardiovascular disease, LDL-P demonstrated an independent association with CAC development, whereas LDL-C showed no significant relationship. These discrepancies may be attributed to several factors: (i) differences in study populations, as our investigation specifically targeted asymptomatic T2DM patients; (ii) methodological differences in confounder adjustment and statistical analyses, with our study incorporating a broader range of potential confounders; and (iii) potential ethnic variations in the relationship between LDL-C and CAC development.

Several limitations of our study should be acknowledged. First and foremost, the absence of apoB measurements represents a significant limitation, as recent

studies have demonstrated that apoB serves as a more precise marker for cardiovascular risk assessment than traditional lipid parameters [28], particularly in metabolically complex patients where significant discordance between cholesterol content and atherogenic particle numbers may exist [29]. This limitation is especially relevant in T2DM patients, where relying solely on LDL-C measurements might underestimate the actual cardiovascular risk due to the potential presence of elevated apoB-containing particles despite normal LDL-C levels [30]. Additionally, our study has several methodological limitations: being a single-center study focusing on asymptomatic T2DM patients in China limits the generalizability of our findings, although our study population's characteristics were comparable to those reported in other Asian diabetes cohorts; the cross-sectional design precludes the establishment of causal relationships; and the study did not assess the number of calcified coronary arteries, which limits our understanding of the relationship between lipid parameters and CAC severity. Moreover, some potential confounding factors, such as high-sensitivity C-reactive protein and inflammatory markers, were not collected. Future multicenter prospective studies incorporating both apoB and traditional lipid measurements are needed to validate our findings and provide more comprehensive cardiovascular risk assessment in diverse T2DM populations.

Conclusion

In this study, we demonstrated a significant independent association between elevated LDL-C levels and CAC development in asymptomatic T2DM patients. These findings suggest that LDL-C could serve as a valuable marker for CAC risk assessment in this population, potentially enabling early cardiovascular risk stratification. However, our findings need validation through prospective multicenter studies in diverse populations, including non-diabetic individuals, to establish optimal risk stratification thresholds. Future research should investigate the molecular mechanisms underlying the LDL-C-coronary calcification relationship and evaluate how lipid-lowering interventions affect CAC progression.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s13098-025-01625-8 .

Supplementary Table 1

Supplementary Fig. 1

Supplementary Table 2

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Author contributions

ZZ, YS and YL contributed the central idea, YS and LZ analyzed most of the data. ZZ wrote the initial draft of the paper. YZ, XL, JZ, and ZL contributed to the data collection, and XW, LW, Xiaodong Li, YW, YH, FL, and JZ contributed to the opinion refinement, supplementary analysis, and finalization of this paper. The author(s) 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

The study was approved by the Ethics Committee of Henan Provincial People's Hospital (Approval Code: 2021-68).

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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