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Association of renal impairment gradient with coronary plaque burden assessed by intravascular ultrasound in patients with type 2 diabetes: a single-center retrospective study

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Abstract

Background

Type 2 diabetes mellitus (T2DM) and chronic kidney disease (CKD) frequently coexist and jointly increase cardiovascular risk. Whether worsening renal impairment is associated with graded increases in coronary plaque burden on intravascular ultrasound (IVUS) in patients with T2DM—and whether metabolic, inflammatory, and nutritional markers attenuate this association—remain unclear.

Methods

This single-center retrospective cross-sectional study included 129 adults with T2DM who underwent coronary IVUS between January 2022 and May 2026. Using KDIGO principles and dialysis status, we defined a three-level renal gradient: T2DM alone (n = 64), non-dialysis CKD (n = 31), and dialysis-dependent CKD (n = 34). We used linear trend tests and stepwise multivariable regression for plaque burden (primary outcome) and minimum lumen area (key secondary outcome), Firth penalized logistic regression for binary outcomes, restricted cubic splines for continuous eGFR, and multiple imputation for missing covariates.

Results

Plaque burden increased across the renal gradient (unadjusted β 1.63% per category, 95% CI 0.47 to 2.79; $P = 0.006$) and remained associated after adjustment for conventional cardiometabolic risk factors (β 1.49%, 95% CI 0.05 to 2.93; $P = 0.042$). Additional adjustment for phosphorus, high-sensitivity C-reactive protein, hemoglobin, albumin, calcium, and target vessel location attenuated the association toward the null (β − 0.20%, 95% CI − 2.08 to 1.68; $P = 0.833$). Minimum lumen area did not differ across groups ($P = 0.708$). Each one-category increase in renal impairment was associated with higher odds of high plaque burden (≥ 80%) (adjusted OR 2.27, 95% CI 1.28 to 4.03; $P = 0.005$). Phosphorus and hs-CRP increased and hemoglobin and albumin decreased across the gradient (all $P < 0.05$), whereas glucose and lipid indices showed no gradient.

Conclusions

In patients with T2DM, greater renal impairment was associated with higher coronary plaque burden on IVUS, independent of conventional cardiometabolic risk factors. This association was substantially attenuated by further adjustment for phosphorus, inflammatory, and nutritional markers—a hypothesis-generating finding that warrants prospective confirmation.

Background

Type 2 diabetes mellitus (T2DM) and chronic kidney disease (CKD) frequently coexist and jointly amplify cardiovascular risk [1, 2]. Cardiovascular disease is the leading cause of death among patients with CKD, and T2DM is a major cause of CKD; their coexistence further increases all-cause and cardiovascular mortality [1, 2]. As kidney function deteriorates, disturbances in calcium–phosphorus metabolism, chronic inflammation, anemia, and malnutrition become more pronounced and may accelerate coronary calcification and plaque accumulation [3], placing these patients within the broader cardiovascular–kidney–metabolic framework.

Intravascular ultrasound (IVUS) enables precise, quantitative measurement of coronary plaque burden, morphology, and vessel remodeling [4, 5]. Intracoronary imaging studies suggest that CKD is associated with more rapid coronary calcification [7] and with plaque composition that differs across CKD stages [8], and that renal dysfunction increases cardiovascular risk in intermediate coronary lesions [10]. In patients with diabetes, thin-cap fibroatheroma—a high-risk plaque phenotype identifiable by intracoronary imaging—predicts clinical events even when fractional flow reserve is normal [9]. Most prior work, however, has analyzed CKD as a binary or single category rather than a spectrum, and has seldom focused specifically on patients with T2DM across the full range from normal kidney function to dialysis dependence. In addition, the gradients of metabolic, inflammatory, and nutritional markers across renal strata, and whether these markers accompany the association between renal impairment and plaque burden, remain poorly characterized.

We therefore conducted a single-center retrospective cross-sectional study of patients with T2DM undergoing coronary IVUS to evaluate (i) whether a worsening gradient of renal impairment is associated with coronary plaque phenotype on IVUS and (ii), through a prespecified exploratory attenuation analysis, whether additional adjustment for metabolic–inflammatory–nutritional indicators attenuates this association.

Methods

Study design and setting

This single-center retrospective cross-sectional study was conducted at Hangzhou Hospital of Traditional Chinese Medicine affiliated to Zhejiang Chinese Medical University. The study protocol was approved by the institutional ethics committee (approval number: 2024KLL216), and the requirement for informed consent was waived because of the retrospective design. The study was reported in accordance with the STROBE statement [19].

Study population

We screened T2DM patients (WHO 1999 criteria) who underwent coronary IVUS between January 2022 and May 2026. Eligible patients were aged ≥ 18 years, had a confirmed diagnosis of T2DM, and had IVUS images of sufficient quality for quantitative analysis with complete core IVUS measurements. Exclusion

criteria were: type 1 diabetes or other specific types of diabetes; acute kidney injury rather than CKD; poor-quality IVUS images; primary percutaneous coronary intervention for ST-segment elevation myocardial infarction; previous coronary artery bypass grafting; in-stent restenosis as the target lesion; active malignancy; severe valvular disease or cardiomyopathy; and missing core IVUS outcome measures. Missing covariates were not used as exclusion criteria and were handled by multiple imputation.

Of 210 screened patients, 81 were excluded because IVUS image quality was inadequate for quantitative analysis or the target segment record was incomplete, leaving 129 patients for the final analysis.

Renal impairment groups

Patients were categorized into three prespecified groups according to the KDIGO 2024 CKD classification principles [11] and dialysis status, using eGFR (CKD-EPI equation) as the core criterion combined with urinalysis protein results and clinical renal diagnoses. T2DM alone (n = 64): eGFR ≥ 60 mL/min/1.73 m² with no evidence of kidney damage (negative urine protein; no clinical diagnosis of CKD, diabetic kidney disease, persistent proteinuria, or chronic nephritis; no structural renal abnormality). Non-dialysis CKD (n = 31): no maintenance hemodialysis or peritoneal dialysis, and any of the following: (a) eGFR 15–59 mL/min/1.73 m²; (b) eGFR ≥ 60 mL/min/1.73 m² with definite evidence of kidney damage (proteinuria or documented diabetic kidney disease/chronic nephritis); or (c) eGFR < 15 mL/min/1.73 m² (CKD stage 5) not yet receiving maintenance dialysis. Dialysis-dependent CKD (n = 34): eGFR < 15 mL/min/1.73 m² or end-stage kidney disease receiving maintenance dialysis.

Clinical and laboratory variables

Variables extracted from the electronic medical record system included age, sex, body mass index (BMI), diabetes duration, history of hypertension, history of dyslipidemia, smoking status (never/former/current), and prior myocardial infarction or percutaneous coronary intervention, as well as glucose-lowering medication use (insulin therapy and oral antidiabetic agents). Laboratory variables (fasting venous blood within 24 h before the procedure) included hemoglobin, serum albumin, high-sensitivity C-reactive protein (hs-CRP), calcium, phosphorus, fasting plasma glucose, glycated hemoglobin (HbA1c, within 3 months before the procedure), low-density lipoprotein cholesterol (LDL-C), total cholesterol, triglycerides, and high-density lipoprotein cholesterol (HDL-C). Apolipoprotein B, lipoprotein(a), and intact parathyroid hormone were excluded from regression analyses because of missingness > 65%. Target vessel location (left main, left anterior descending, left circumflex, right coronary artery and major branches) and qualitative lesion phenotype (calcified, lipid-rich, fibrous) were recorded from grayscale IVUS.

IVUS acquisition and measurements

IVUS was performed with the Boston Scientific iLab system using automated pullback at 0.5 mm/s. Two physicians blinded to clinical group assignment independently performed all measurements, and the mean value was used. A random 20% sample was used to assess intraobserver and interobserver reproducibility; intraclass correlation coefficients for all core parameters exceeded 0.90. Measurements followed ACC IVUS consensus definitions [12]: minimum lumen area (MLA, mm^2), maximum lumen area (mm^2), maximum plaque thickness (mm), and plaque burden (PB) = (EEM CSA − MLA)/EEM CSA ×100%. High plaque burden was defined as PB ≥ 80%, a cutoff validated against fractional flow reserve < 0.75 in the IDEAS study (sensitivity 87.9%, specificity 78.9%) [13]. Lesions were qualitatively classified on grayscale IVUS as calcified (echogenic with acoustic shadowing), lipid-rich (echolucent), or fibrous (intermediate echogenicity without shadowing) [6, 12], with disagreements resolved by consensus.

Outcomes

The primary outcome was coronary plaque burden. The key secondary outcome was minimum lumen area. Additional secondary outcomes included maximum lumen area, maximum plaque thickness, calcified plaque phenotype, and high plaque burden (≥ 80%).

Statistical analysis

Descriptive statistics were based on observed data. Regression and trend analyses were conducted on the multiply imputed datasets. Continuous variables were presented as mean ± standard deviation or median (interquartile range), as appropriate; categorical variables were presented as counts and percentages. Group comparisons used one-way analysis of variance, the Kruskal–Wallis test, the chi-square test, or Fisher's exact test, as appropriate. The three renal groups were modeled as an ordinal exposure representing the renal impairment gradient (T2DM alone → non-dialysis CKD → dialysis-dependent CKD). Continuous outcomes were assessed by one-degree-of-freedom linear trend tests and categorical outcomes by Cochran–Armitage trend tests.

Multivariable linear regression models were constructed for plaque burden and minimum lumen area. Model 1 adjusted for age and sex. Model 2 additionally adjusted for BMI, diabetes duration, HbA1c, fasting glucose, hypertension, dyslipidemia, smoking history, LDL-C, total cholesterol, triglycerides, and HDL-C, and served as the primary inferential model. Model 3 further adjusted for hs-CRP, calcium, phosphorus, hemoglobin, albumin, and target vessel location. Because several of these variables may lie on, or be close to, the causal pathway between renal dysfunction and coronary plaque burden, Model 3 was prespecified as an exploratory model to assess attenuation of the association after additional adjustment, rather than to estimate the principal independent effect; no formal mediation analysis was performed, and the attenuation pattern should not be interpreted causally. Multicollinearity was assessed by variance inflation factors (VIF), and ridge regression ($\lambda = 10$, standardized scale) was used as a sensitivity check on coefficient stability.

Binary outcomes (calcified plaque phenotype, high plaque burden) were analyzed using Firth penalized logistic regression. The covariate set for the binary models was prespecified and restricted according to

event counts, with covariate numbers guided by events-per-variable principles [14]. eGFR was additionally analyzed as a continuous exposure using restricted cubic splines with four knots at the 5th, 35th, 65th, and 95th percentiles; this analysis also served to assess the equal-spacing assumption underlying the ordinal exposure, and its conclusions were interpreted together with the ordinal trend estimates. Missing covariates were handled by multiple imputation by chained equations (20 imputed datasets, 10 iterations; predictive mean matching for continuous variables and logistic/polytomous regression for categorical variables) under an assumption compatible with missing at random, pooled by Rubin's rules [15–17]. Sensitivity analyses included: exclusion of the dialysis group; reclassification using an eGFR cutoff of 45 mL/min/1.73 m²; complete-case analysis; age-adjusted trend analysis; and inverse probability weighting (IPW) to assess potential selection bias related to exclusion of patients with non-analyzable IVUS images [18]. Plaque burden was the prespecified primary outcome; analyses of all secondary outcomes were considered exploratory, and no adjustment for multiple comparisons was performed. All tests were two-sided, and $P < 0.05$ was considered statistically significant. Analyses were performed using R version 4.4.

Results

Patient selection and baseline characteristics

Of 210 screened patients, 129 were included in the final analysis: 64 in the T2DM-alone group, 31 in the non-dialysis CKD group, and 34 in the dialysis-dependent CKD group (Fig. 1). Baseline characteristics are summarized in Table 1. The three groups differed significantly in age, diabetes duration, eGFR, HbA1c, hs-CRP, phosphorus, hemoglobin, albumin, prevalence of hypertension, urine protein positivity, and insulin use (all $P < 0.05$). Notably, the non-dialysis CKD group was older than the dialysis-dependent CKD group (73.58 ± 9.85 vs 61.26 ± 12.37 years), suggesting heterogeneity in disease trajectories across renal impairment strata. In descriptive group comparisons, median plaque burden (78%, 80%, and 81%; $P = 0.018$) and maximum plaque thickness ($P = 0.019$) differed significantly across groups, whereas minimum lumen area was broadly similar ($P = 0.844$); trend tests for these IVUS outcomes are presented below.

Table 1
Baseline clinical characteristics and IVUS findings according to renal impairment group

Variable	T2DM alone (n = 64)	Non-dialysis CKD (n = 31)	Dialysis-dependent CKD (n = 34)	F/χ^2/H	*P* value
Age, years	66.92 ± 10.71	73.58 ± 9.85	61.26 ± 12.37	10.208	< 0.001
BMI, kg/m²	23.57 (21.78, 25.28)	23.83 (22.42, 26.13)	23.36 (21.82, 26.37)	1.254	0.534
Diabetes duration, years	8.00 (3.00, 12.00)	10.00 (8.00, 20.00)	15.00 (10.00, 20.00)	18.798	< 0.001
eGFR, mL/min/1.73 m²	92.43 (84.48, 100.89)	51.50 (41.52, 63.61)	8.00 (4.91, 12.46)	101.965	< 0.001
HbA1c, %	7.00 (6.65, 7.85)	7.40 (7.00, 8.30)	6.50 (5.80, 8.10)	6.437	0.040
Fasting glucose, mmol/L	6.20 (5.43, 7.50)	6.89 (5.98, 7.68)	6.76 (4.76, 8.06)	1.004	0.605
hs-CRP, mg/L	1.27 (0.50, 3.48)	0.50 (0.50, 3.20)	8.32 (3.26, 15.14)	17.912	< 0.001
Calcium, mmol/L	2.19 ± 0.10	2.18 ± 0.15	2.16 ± 0.18	0.377	0.687
Phosphorus, mmol/L	1.04 ± 0.14	1.05 ± 0.19	1.40 ± 0.51	18.226	< 0.001
Hemoglobin, g/L	137.58 ± 17.74	125.48 ± 23.02	102.76 ± 23.09	31.797	< 0.001
Albumin, g/L	38.45 (36.68, 41.45)	36.00 (33.95, 38.35)	30.60 (27.07, 35.45)	43.219	< 0.001
LDL-C, mmol/L	2.20 (1.55, 2.64)	2.02 (1.56, 2.62)	1.79 (1.56, 2.26)	3.910	0.142
Total cholesterol, mmol/L	3.62 (2.96, 4.21)	3.63 (2.71, 4.26)	3.17 (2.63, 3.83)	2.743	0.254
Triglycerides, mmol/L	1.33 (0.97, 2.05)	1.34 (0.98, 1.83)	1.44 (1.01, 2.24)	0.336	0.845
HDL-C, mmol/L	0.92 (0.79, 1.13)	0.89 (0.77, 1.01)	0.81 (0.74, 0.96)	2.809	0.245
Minimum lumen area, mm²	2.42 (2.01, 2.92)	2.40 (1.94, 3.47)	2.69 (2.00, 3.12)	0.339	0.844
Maximum lumen area, mm²	11.63 (8.82, 16.25)	13.36 (10.04, 16.47)	14.25 (10.95, 18.21)	4.419	0.110
Plaque burden, %	78 (73, 82)	80 (74, 82)	81 (78, 85)	7.985	0.018

Variable	T2DM alone (n = 64)	Non-dialysis CKD (n = 31)	Dialysis-dependent CKD (n = 34)	F/χ²/H	*P* value
Maximum plaque thickness, mm	1.60 (1.40, 1.93)	1.59 (1.34, 1.97)	1.90 (1.60, 2.24)	7.908	0.019
Male, n (%)	48 (75.0)	23 (74.2)	29 (85.3)	1.609	0.447
Hypertension, n (%)	48 (75.0)	23 (74.2)	34 (100.0)	10.362	0.006
Dyslipidemia, n (%)	36 (56.2)	17 (54.8)	17 (50.0)	0.355	0.837
Smoking history, n (%)	11 (17.2)	9 (29.0)	9 (26.5)	2.298	0.317
Insulin therapy, n (%)	15 (23.4)	11 (36.7)	26 (76.5)	26.144	< 0.001
Urine protein positive, n (%)	0 (0.0)	13 (41.9)	34 (100.0)	96.407	< 0.001
High plaque burden (≥ 80%), n (%)	25 (39.1)	16 (51.6)	24 (70.6)	8.852	0.012
Target vessel, n (%)				5.220	0.516
Left anterior descending	31 (48.4)	13 (41.9)	21 (61.8)		
Left circumflex	10 (15.6)	2 (6.5)	4 (11.8)		
Right coronary artery	19 (29.7)	13 (41.9)	9 (26.5)		
Left main and branches	2 (3.1)	1 (3.2)	0 (0.0)		
Lesion phenotype, n (%)				5.181	0.269
Calcified	43 (67.2)	23 (74.2)	29 (85.3)		
Lipid-rich	16 (25.0)	7 (22.6)	5 (14.7)		
Fibrous	5 (7.8)	1 (3.2)	0 (0.0)		

Normally distributed continuous variables were expressed as mean ± SD (one-way ANOVA, F); skewed variables as median (IQR) (Kruskal–Wallis test, H); categorical variables as n (%) (chi-square test, χ²). Target vessel location was missing in 4 patients (2 in the T2DM-alone group and 2 in the non-dialysis CKD group) and was not included in the corresponding test. Insulin therapy data were missing in 1 patient (non-dialysis CKD group); the percentage for that group was calculated on the available denominator (n = 30). Differences in eGFR, urine protein positivity, and the prevalence of hypertension (100% in the dialysis-dependent CKD group) were expected by group definition. Apolipoprotein B, lipoprotein(a), and intact parathyroid hormone (missingness > 65%) were not included in regression analyses. BMI body mass index, eGFR estimated

glomerular filtration rate, HbA1c glycated hemoglobin, hs-CRP high-sensitivity C-reactive protein, LDL-C low-density lipoprotein cholesterol, HDL-C high-density lipoprotein cholesterol.

Trends in IVUS phenotypes across renal impairment groups

Plaque burden increased significantly across the renal impairment gradient (unadjusted β 1.632% per category, 95% CI 0.474 to 2.791; *P* = 0.006; Table 2, Fig. 2). In contrast, minimum lumen area showed no significant gradient (β 0.037 mm² per category, 95% CI − 0.156 to 0.229; *P* = 0.708). Among additional IVUS parameters, maximum lumen area (β 1.162 mm² per category, *P* = 0.018) and maximum plaque thickness (β 0.127 mm per category, *P* = 0.009) increased significantly. The proportion of calcified plaques increased numerically across groups (67.2%, 74.2%, and 85.3%; overall χ^2 *P* = 0.269; Cochran–Armitage trend Z = 1.93, *P* = 0.054), a non-significant upward trend (Fig. S1).

Table 2
Linear trends in IVUS parameters and metabolic-inflammatory-nutritional markers across the renal impairment gradient

Outcome	β per category	95% CI	t	*P* value
Plaque burden, %	1.632	0.474 to 2.791	2.761	0.006
Minimum lumen area, mm²	0.037	−0.156 to 0.229	0.377	0.708
Maximum lumen area, mm²	1.162	0.200 to 2.125	2.366	0.018
Maximum plaque thickness, mm	0.127	0.032 to 0.221	2.634	0.009
HbA1c, %	−0.120	−0.471 to 0.231	−0.670	0.501
Fasting glucose, mmol/L	0.224	−0.279 to 0.726	0.874	0.383
hs-CRP, mg/L	3.408	1.066 to 5.751	2.852	0.004
Calcium, mmol/L	−0.011	−0.039 to 0.017	−0.770	0.438
Phosphorus, mmol/L	0.169	0.107 to 0.232	5.300	< 0.001
Hemoglobin, g/L	−16.986	−21.221 to − 12.751	−7.861	< 0.001
Albumin, g/L	−4.401	−5.644 to − 3.157	−6.937	< 0.001
LDL-C, mmol/L	−0.167	−0.351 to 0.016	−1.784	0.074
Total cholesterol, mmol/L	−0.152	−0.408 to 0.105	−1.161	0.246
Triglycerides, mmol/L	0.266	−0.123 to 0.656	1.339	0.180
HDL-C, mmol/L	−0.035	−0.090 to 0.021	−1.236	0.225

Estimates and standard errors were pooled across 20 imputed datasets using Rubin's rules; t = β/SE. Descriptive group comparisons in Table 1 *were based on observed data. Abbreviations as in* Table 1.

Trends in metabolic, inflammatory, and nutritional indicators

Across the renal impairment gradient, hs-CRP (β 3.408 mg/L per category, *P* = 0.004) and phosphorus (β 0.169 mmol/L per category, *P* < 0.001) increased significantly, whereas hemoglobin (β − 16.986 g/L per category, *P* < 0.001) and albumin (β − 4.401 g/L per category, *P* < 0.001) decreased significantly (Table 2, Fig. S2). In contrast, HbA1c, fasting glucose, LDL-C, total cholesterol, triglycerides, and HDL-C showed no significant trends.

Multivariable association between renal impairment gradient and plaque burden

The association between the renal impairment gradient and plaque burden remained significant in Model 1 (β 1.487% per category, 95% CI 0.320 to 2.654; *P* = 0.013) and in the primary inferential Model 2 (β 1.494%, 95% CI 0.053 to 2.934; *P* = 0.042; Table 3, Fig. 3). In the exploratory Model 3, which further adjusted for hs-CRP, calcium, phosphorus, hemoglobin, albumin, and target vessel location, the coefficient was markedly attenuated toward the null (β − 0.203%, 95% CI − 2.083 to 1.677; *P* = 0.833). VIFs indicated no meaningful multicollinearity involving the main exposure (VIF 3.1); VIFs were higher for total cholesterol (8.8) and LDL-C (7.2) owing to the algebraic relationship between lipid components, which affects their own coefficients but not that of the main exposure, and both were retained. In a ridge regression sensitivity analysis (λ = 10, standardized scale), the standardized coefficient for the renal impairment gradient was near zero, consistent in direction and magnitude with the ordinary least squares estimate of Model 3. Minimum lumen area was not significantly associated with the renal impairment gradient in any model (all *P* > 0.3).

Table 3
Multivariable linear regression of IVUS outcomes on the renal impairment gradient (β per one-category increase)

Outcome	Model	β (95% CI)	*P* value
Plaque burden, %	Model 1 (age, sex)	1.487 (0.320 to 2.654)	0.013
Plaque burden, %	Model 2 (primary inferential model; + glycemic, lipid and traditional risk factors)	1.494 (0.053 to 2.934)	0.042
Plaque burden, %	Model 3 (exploratory; + hs-CRP, calcium, phosphorus, hemoglobin, albumin, target vessel)	−0.203 (− 2.083 to 1.677)	0.833
Minimum lumen area, mm²	Model 1	0.039 (− 0.156 to 0.234)	0.697
Minimum lumen area, mm²	Model 2	0.034 (− 0.204 to 0.272)	0.781
Minimum lumen area, mm²	Model 3	0.151 (− 0.178 to 0.480)	0.370

Binary outcomes

In Firth penalized logistic regression, each one-category increase in renal impairment was associated with higher odds of high plaque burden (≥ 80%) in Model 1 (OR 1.78, 95% CI 1.14 to 2.77; *P* = 0.011) and in Model 2 (OR 2.27, 95% CI 1.28 to 4.03; *P* = 0.005; Table 4). For calcified plaque phenotype, the direction of association was similar but not statistically significant after multivariable adjustment (Model 2 OR 1.45, 95% CI 0.79 to 2.68; *P* = 0.233).

Table 4
Firth penalized logistic regression for calcified plaque phenotype and high plaque burden (OR per one-category increase)

Outcome	Model	OR (95% CI)	*P* value
Calcified plaque	Model 1	1.62 (0.98 to 2.68)	0.058
Calcified plaque	Model 2	1.45 (0.79 to 2.68)	0.233
High plaque burden (≥ 80%)	Model 1	1.78 (1.14 to 2.77)	0.011
High plaque burden (≥ 80%)	Model 2	2.27 (1.28 to 4.03)	0.005

Dose–response analysis using continuous eGFR

Restricted cubic spline analysis of eGFR as a continuous exposure (knots at the 5th, 35th, 65th, and 95th percentiles: 4.55, 47.26, 86.53, and 105.04 mL/min/1.73 m²; reference at the median, 65.9 mL/min/1.73 m²), fitted on the Model 2 covariate set, detected no significant nonlinearity for plaque burden (*P* for nonlinearity = 0.347) or minimum lumen area (*P* = 0.678). The plaque burden curve suggested a steeper

increase at eGFR values below approximately 60 mL/min/1.73 m², consistent with the clinical CKD stage 3 threshold (Fig. 4).

Sensitivity analyses

The association between the renal impairment gradient and greater plaque burden was broadly consistent across sensitivity analyses (Table 5, Fig. S3). After exclusion of the dialysis group, the point estimate was essentially unchanged (β 1.638% per category) but statistical significance was lost (*P* = 0.192), likely reflecting reduced power. Reclassification using an eGFR cutoff of 45 mL/min/1.73 m² (groups 64/22/43) preserved a significant trend (β 1.486% per category, *P* = 0.007). Complete-case analysis (n = 79) yielded a comparable trend (β 1.806%, *P* = 0.008; Model 2 *P* = 0.080). IPW produced estimates highly similar to the primary analysis (β 1.593%, 95% CI 0.410 to 2.775; *P* = 0.008). Age-adjusted trend analysis remained significant (β 1.549%, 95% CI 0.377 to 2.722; *P* = 0.011), indicating that the non-monotonic age distribution across groups does not explain the primary finding.

Table 5
Sensitivity analyses for the association between the renal impairment gradient and plaque burden

Analysis scenario	Estimate	95% CI	*P* value
Exclusion of dialysis group (n = 95), trend β, %	1.638	−0.846 to 4.121	0.192
Reclassification at eGFR 45 mL/min/1.73 m² (n = 64/22/43), trend β, %	1.486	0.387 to 2.585	0.007
Complete-case analysis (n = 79), trend β, %	1.806	0.485 to 3.126	0.008
Complete-case analysis (n = 79), Model 2 β, %	1.493	−0.183 to 3.170	0.080
Inverse probability weighting, trend β, %	1.593	0.410 to 2.775	0.008
Age-adjusted trend β, %	1.549	0.377 to 2.722	0.011

eGFR estimated glomerular filtration rate, IPW inverse probability weighting. Estimates are β coefficients (percentage points of plaque burden per one-category increase in the renal impairment gradient).

Discussion

In this single-center retrospective cross-sectional study of patients with T2DM who underwent coronary IVUS, worsening renal impairment across a three-level gradient (T2DM alone → non-dialysis CKD → dialysis-dependent CKD) was associated with greater coronary plaque burden. This association persisted after adjustment for demographic characteristics, glycemic and lipid variables, and

conventional cardiovascular risk factors, but was substantially attenuated after additional adjustment for phosphorus, inflammatory, and nutritional indicators. Minimum lumen area did not show a significant gradient.

These findings extend previous intracoronary imaging observations linking CKD to more advanced coronary atherosclerosis and calcification [7, 8, 10] by focusing specifically on patients with T2DM and by separating non-dialysis CKD from dialysis-dependent CKD. Rather than treating CKD as a binary exposure, the ordinal renal impairment gradient may better reflect the progressive cardiovascular burden associated with worsening kidney dysfunction, consistent with the cardiovascular-kidney-metabolic framework in which diabetes, CKD, and cardiovascular disease interact closely [2, 3].

A key observation was that the association between the renal impairment gradient and plaque burden persisted after adjustment for conventional cardiometabolic variables but was markedly attenuated after further adjustment for phosphorus, hs-CRP, hemoglobin, and albumin. This pattern should be interpreted cautiously: it does not establish mediation or causality, particularly given the cross-sectional design. Rather, it suggests that disturbances in mineral metabolism, inflammation, anemia, and nutritional status may statistically accompany the relationship between worsening renal dysfunction and greater plaque burden—an interpretation that is biologically plausible, because these abnormalities progress with declining renal function [2, 3]. The consistency of the attenuation pattern across model specifications, together with collinearity diagnostics and ridge regression, indicates that this attenuation was not a multicollinearity artifact.

Notably, glucose and lipid indices showed no significant gradient across renal impairment categories, whereas phosphorus, inflammatory, and nutritional indicators did. A possible explanation is a "ceiling" effect of treatment: all three groups received routine glucose-lowering and lipid-lowering therapy, compressing intergroup differences in glycemic and lipid parameters toward target ranges, whereas CKD-related disturbances such as phosphorus retention, chronic inflammation, anemia, and hypoalbuminemia remain more tightly linked to the severity of renal dysfunction and are less amenable to routine pharmacological correction. If confirmed, this would help explain why conventional metabolic control alone does not fully capture cardiovascular vulnerability in T2DM patients with CKD. Consistent with this interpretation, glucose-lowering medication data collected in this cohort showed that insulin use increased across the renal impairment gradient (23.4%, 36.7%, and 76.5% in the T2DM-alone, non-dialysis CKD, and dialysis-dependent CKD groups, respectively), alongside oral antidiabetic agents, whereas glycemic indices showed no corresponding gradient (Table 1), lending direct support to the treatment ceiling-effect interpretation.

The non-monotonic age distribution across groups deserves comment. The younger age in the dialysis-dependent CKD group may reflect selection of patients referred for IVUS-guided coronary evaluation rather than the age distribution of the broader dialysis population, and potential survivor or referral bias cannot be excluded. From a clinical perspective, these findings suggest that T2DM patients with impaired renal function—particularly those with advanced CKD or dialysis dependence—may carry a

greater coronary plaque burden detectable by IVUS, supporting refined imaging-based risk stratification in this high-risk subgroup. Comprehensive cardiovascular risk assessment in this population should extend beyond glucose and lipid management to include attention to phosphorus balance, inflammatory activity, anemia, and nutritional status.

Several strengths of this study should be noted. First, IVUS provided quantitative coronary phenotyping with blinded image assessment and high interobserver agreement. Second, the use of an ordinal renal impairment gradient allowed assessment of dose–response patterns rather than binary contrasts. Third, the consistency of the primary plaque burden finding across multiple sensitivity analyses, including IPW to address selection bias, supports the robustness of the observation.

This study also has several limitations. First, the single-center retrospective design limits generalizability. Second, the cross-sectional analysis precludes temporal or causal inference, and the attenuation observed in Model 3 should be regarded as hypothesis-generating. Third, a substantial proportion of screened patients (81 of 210, 38.6%) were excluded because IVUS images were inadequate for quantitative analysis or target segment records were incomplete; the study cohort therefore represents a selected IVUS-analyzable subset of T2DM patients undergoing coronary evaluation, and although IPW analysis suggested that this exclusion did not fully account for the findings, residual selection bias and limited external validity cannot be excluded. Fourth, grayscale IVUS has limited ability to characterize plaque composition compared with newer multimodality intracoronary imaging. Fifth, the sample size was modest (n = 129), which limited statistical power—particularly after exclusion of the dialysis group, in which the association was no longer significant—and the primary adjusted association was of borderline significance (Model 2 $P = 0.042$); the findings should therefore be regarded as exploratory, and residual confounding remains possible.

Conclusions

In patients with T2DM, worsening renal impairment was associated with greater coronary plaque burden assessed by IVUS. This association persisted after adjustment for conventional cardiometabolic risk factors, but additional adjustment for phosphorus, inflammatory, and nutritional markers substantially attenuated the observed association. These findings are hypothesis-generating and warrant confirmation in larger prospective studies.

Abbreviations

ACC American College of Cardiology; BMI body mass index; CKD chronic kidney disease; CKD-EPI Chronic Kidney Disease Epidemiology Collaboration; eGFR estimated glomerular filtration rate; HDL-C high-density lipoprotein cholesterol; hs-CRP high-sensitivity C-reactive protein; IPW inverse probability weighting; IVUS intravascular ultrasound; LDL-C low-density lipoprotein cholesterol; MLA minimum lumen area; PB plaque burden; T2DM type 2 diabetes mellitus; VIF variance inflation factor.

Declarations

Ethics approval and consent to participate

The study was conducted in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of Hangzhou Hospital of Traditional Chinese Medicine Affiliated to Zhejiang Chinese Medical University (approval number: 2024KLL216). The requirement for informed consent was waived by the ethics committee because of the retrospective, observational design of the study, which posed minimal risk to participants.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Author Contribution

YY contributed to conceptualization, methodology, formal analysis, and writing—original draft. SQ contributed to investigation (IVUS image measurement). LW contributed to data curation and formal analysis. CT contributed to conceptualization, supervision, and writing—review and editing. All authors read and approved the final manuscript.

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Not applicable.

Data Availability

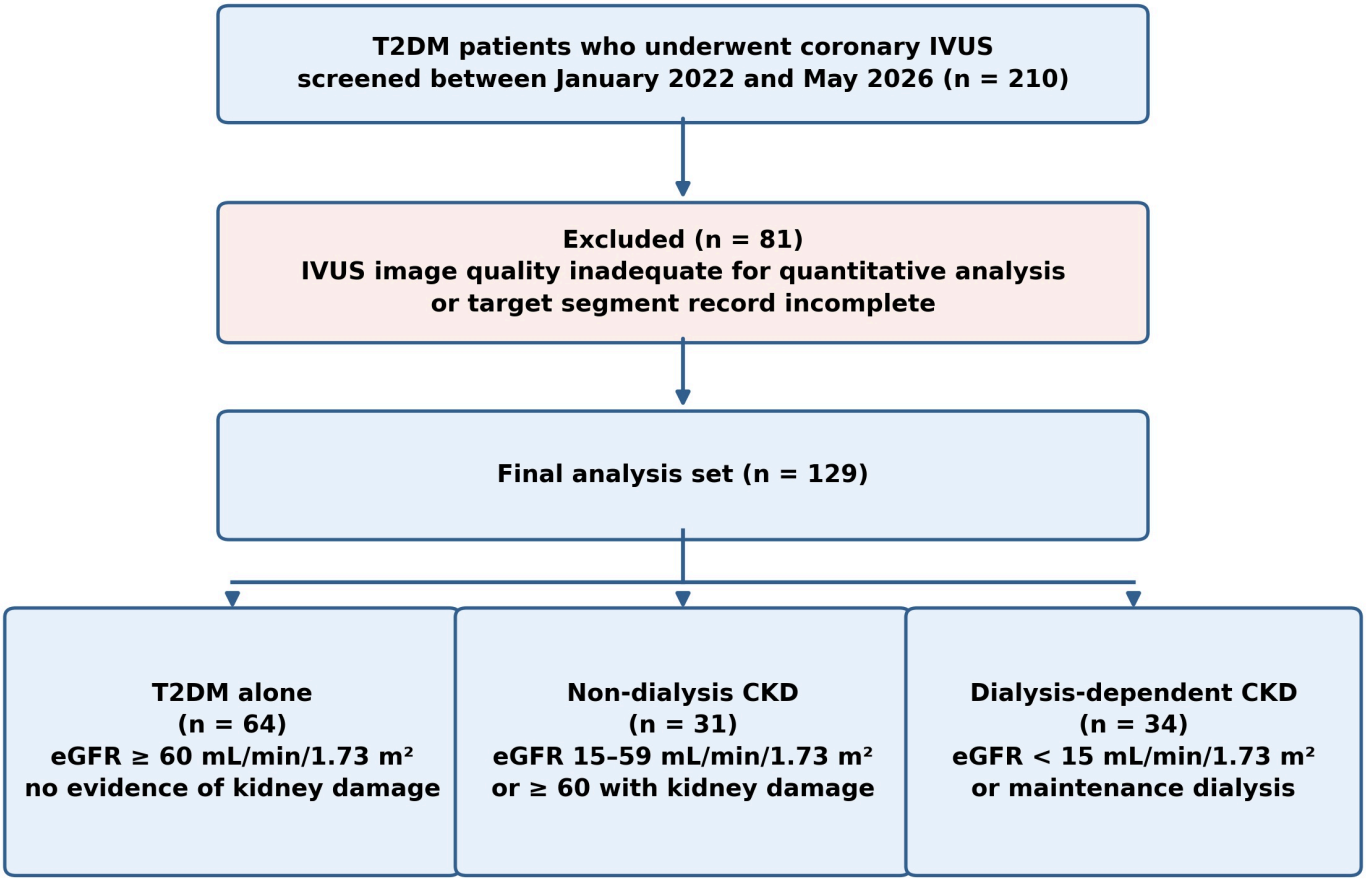
he data that support the findings of this study are not openly available owing to patient-privacy-related ethical restrictions. De-identified datasets are available from the corresponding author upon reasonable request.

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Figures



Renal impairment gradient (ordinal exposure): T2DM alone → non-dialysis CKD → dialysis-dependent CKD

Figure 1

Study flow diagram (STROBE). Of 210 screened patients with T2DM who underwent coronary IVUS, 81 were excluded because of inadequate IVUS image quality or incomplete target segment records, leaving 129 patients in the final analysis.

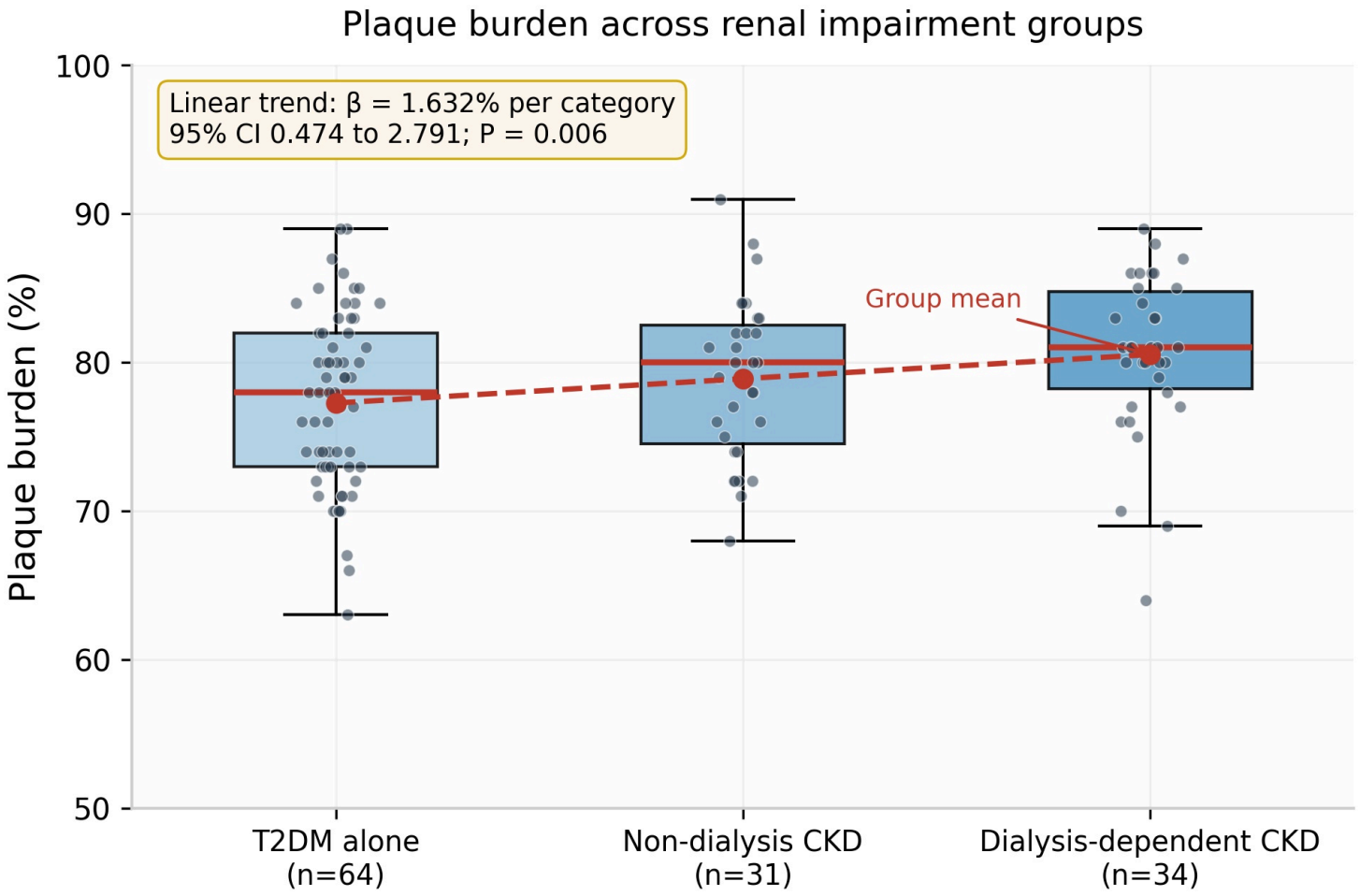


Figure 2

Plaque burden across renal impairment groups (box plots with individual data points and group means). Plaque burden increased significantly across the gradient (unadjusted β 1.632% per category, 95% CI 0.474 to 2.791; *P* = 0.006).

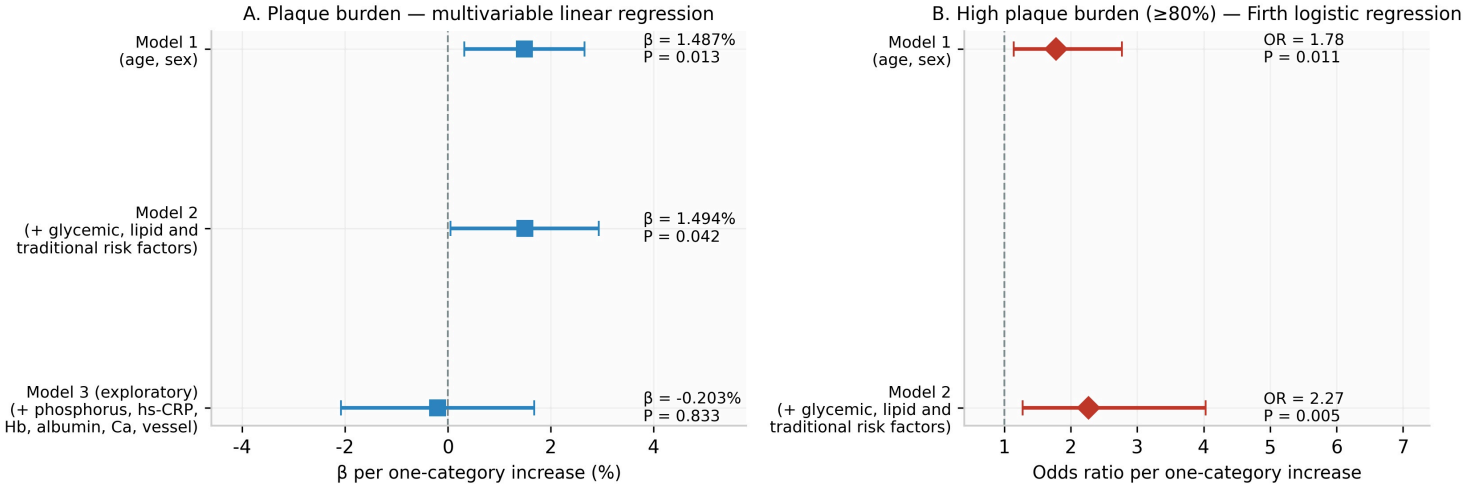
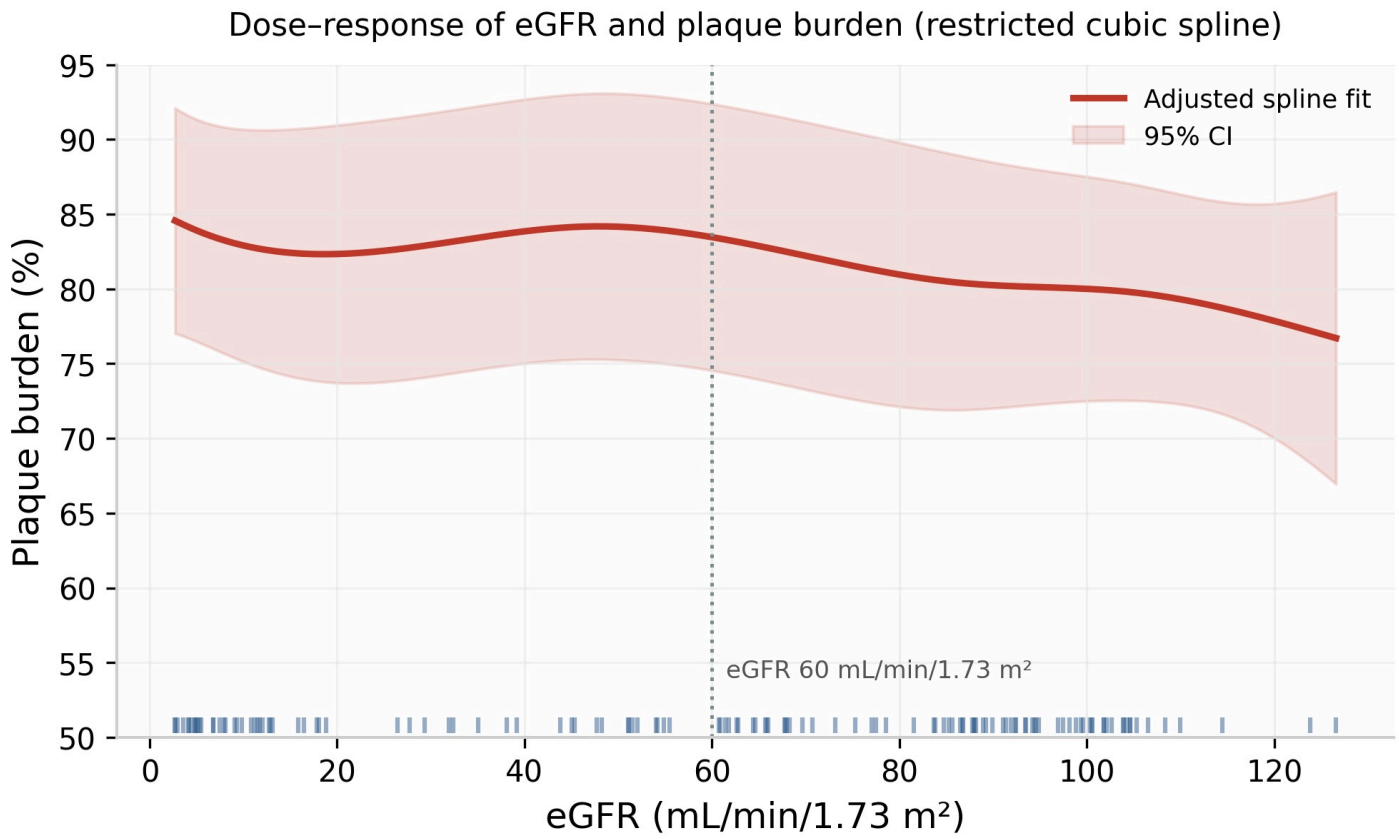


Figure 3

Multivariable associations of the renal impairment gradient with plaque burden. (A) Linear regression models with stepwise adjustment; (B) Firth penalized logistic regression for high plaque burden (≥80%).



Adjusted for the Model 2 covariate set; no significant nonlinearity (P = 0.347). Vertical ticks: observed eGFR distribution.

Figure 4

Restricted cubic spline analysis of eGFR and plaque burden (adjusted for the Model 2 covariate set). No significant nonlinearity was detected (*P* for nonlinearity = 0.347); the curve suggests a steeper increase in plaque burden below approximately 60 mL/min/1.73 m². Vertical ticks along the bottom indicate the distribution of observed eGFR values.

Supplementary Files

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- FigureS1.jpeg
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