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Correlation between 25-hydroxyvitamin D levels and remnant cholesterol in patients with type 2 diabetes

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Abstract

Background Remnant cholesterol (RC) is an independent predictor of cardiovascular events in type 2 diabetes mellitus (T2DM). Concurrently, vitamin D deficiency is a recognized risk factor for developing T2DM. However, the association between serum 25-hydroxyvitamin D (25(OH)D) levels and RC in patients with established T2DM remains incompletely elucidated. Specifically, potential non-linear relationships and modifications of this association by age and sex are unclear. This study investigates the relationship between 25(OH)D and RC in a cohort of 380 patients with T2DM.

Methods A total of 380 T2DM patients (283 men and 97 women) were evaluated. Demographic data were analyzed descriptively. Statistical tests assessed the association between 25(OH)D levels and RC, and piecewise linear regression was utilized to explore potential threshold effects.

Results Spearman correlation analysis revealed that female gender was significantly associated with higher RC levels ($\rho = 0.163$, $p = 0.002$). Piecewise linear regression identified a threshold effect at 18.8 ng/mL: below this threshold, each 1 ng/mL increase in 25(OH)D was associated with a decrease in RC of 0.01 mmol/L ($\beta = -0.01$, 95% CI: -0.02 to -0.00); above this threshold, it was associated with an increase of 0.02 mmol/L ($\beta = 0.02$, 95% CI: 0.00 to 0.03).Age significantly modified this association (interaction $p < 0.05$), suggesting an age-dependent inversion of the effect of vitamin D on RC.

Conclusion This study demonstrates a complex, non-linear relationship between 25(OH)D levels and Remnant cholesterol in patients with type 2 diabetes. Age significantly modifies this relationship, suggesting that tailored interventions based on vitamin D status may be warranted to inform future interventional studies targeting RC modulation.

Keywords Type 2 diabetes, 25-Hydroxyvitamin d, Remnant cholesterol, Non-linear relationship, Age, Threshold, Complex relationship

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Introduction

The global prevalence of type 2 diabetes mellitus (T2DM) is increasing, particularly among older adults, posing significant public health challenges due to increased morbidity, mortality, and healthcare costs [1]. Cardiovascular disease (CVD) is a leading cause of mortality in individuals with diabetes, underscoring the need for effective strategies to mitigate cardiovascular risk.Remnant cholesterol (RC), the cholesterol component of triglyceride-rich lipoproteins, has emerged as an important predictor of cardiovascular events and mortality in patients with T2DM. Several studies have identified RC as an independent risk factor for cardiovascular mortality [2] and incident T2DM [3]. Notably, elevated RC has been observed as a specific risk factor in diabetic, post-menopausal women with coronary artery disease [4].

Beyond its established role in calcium homeostasis and bone health, vitamin D has gained recognition for its broader metabolic effects, including potential influences on insulin resistance, inflammation, and glucose metabolism. Epidemiological studies have linked low 25-hydroxyvitamin D [25(OH)D] levels to an increased risk of T2DM and ischemic heart disease [5], suggesting a possible protective role for vitamin D in glucose regulation.

The interplay between vitamin D and lipid metabolism is of increasing interest [6]. Recent research suggests that alterations in vitamin D status may influence lipid profiles [7]. Given the established role of RC as an independent risk factor for cardiovascular mortality [2, 3], understanding the relationship between vitamin D and RC may be clinically relevant. As evidenced by, Turkes et al. [8] found that bioavailable vitamin D, rather than total 25(OH)D, was associated with elevated remnant cholesterol, independent of T2DM status. However, the precise mechanisms underlying the interaction between 25(OH)D levels and RC in patients with diabetes remain unclear. Factors such as age, sex, and body mass index (BMI) may further modulate this relationship.

Therefore, given the well-documented roles of both RC and vitamin D in cardiovascular health and diabetes pathophysiology, elucidating their relationship may contribute to the development of more effective strategies for cardiovascular risk mitigation in this high-risk population. This study aims to investigate the correlation between 25(OH)D levels and RC in patients with T2DM. Our goal is to characterize this association, exploring potential thresholds and effect modifiers, thereby informing the design of future interventional studies targeting RC reduction.

Methods

Study participants

This cross-sectional study included 380 patients with T2DM (283 males, 97 females; mean age 65.09 ± 8.20 years, range 55–92 years) who were consecutively admitted to the Department of Geriatric Endocrinology at The People's Hospital of Gansu Province between October 2019 and December 2021.

Inclusion Criteria: Patients were included if they had a confirmed diagnosis of T2DM according to established clinical and laboratory criteria, as determined by an endocrinologist.Diagnosis of type 2 diabetes followed the 2020 ADA Standards [9]: FPG ≥ 7.0 mmol/L, HbA1c ≥ 6.5%, random glucose ≥ 11.1 mmol/L with symptoms, or 2-h OGTT ≥ 11.1 mmol/L.

Exclusion criteria included: hepatorenal syndrome, hyperparathyroidism, malignancy, chronic digestive diseases, specific types of diabetes other than type 2, acute diabetic complications, active inflammation or infection, recent surgery, eGFR < 60 mL/min/1.73 m^2, use of glucocorticoids or anticonvulsants, and pre-hospitalization use of vitamin D supplements or complementary therapies.

Data collection and laboratory analyses

General information

The following data were collected for all participants: age, sex, height, and weight. BMI was calculated as weight (kg)/height $(m)^2$.

Laboratory measurements

After an 8–12 h overnight fast, venous blood samples were collected from all participants. The following parameters were measured: fasting blood glucose (FBG), lipid profile [TC, low-density lipoprotein cholesterol (LDL-C), HDL-C, triglycerides (TG)], blood urea nitrogen (BUN), serum creatinine (Scr), calcium, phosphate, 25(OH)D, and hemoglobin A1c (HbA1c). Blood biochemical analyses were performed using an Abbott C-1600 automated analyzer. Assay precision was rigorously monitored: Lipid profiles (TC, HDL-C, LDL-C, TG): Intra-assay CV < 3.0%, inter-assay CV < 5.0% at clinically relevant concentrations. FBG (glucose oxidase method): Intra-assay CV < 2.0%, inter-assay CV < 3.0%. 25(OH)D (chemiluminescent immunoassay; Abbott iSR-2000): Intra-assay CVs: 3.2% (15ng/mL), 4.1% (30ng/mL), 5.1% (60ng/mL); inter-assay CVs:4.8%(15ng/mL), 5.6% (30ng/mL), 6.5% (60ng/mL). HbA1c (ion-exchange HPLC): Intra-assay CV ≤ 1.5%, inter-assay CV ≤ 2.0%. Other parameters (BUN, Scr, calcium, phosphate): All intra-/inter-assay CVs < 5.0%. All laboratory analyses were performed by the certified clinical laboratory at The People's Hospital of Gansu Province, which adheres to standard quality control procedures and CLSI guidelines (EP05/EP15).

Diagnostic criteria and group assignment

Participants were categorized into subgroups based on sex (male, female) and vitamin D status, according to the Application Guidelines for Vitamin D [10]: vitamin D sufficiency [25(OH)D >30 ng/mL], insufficiency [25(OH)D >20 and ≤ 30 ng/mL], and deficiency [25(OH)D ≤ 20 ng/mL]. The distribution of participants within each vitamin D category was as follows: sufficiency (n = 8), insufficiency (n = 55), and deficiency (n = 317). Participants were also stratified by age (55–64 years [n = 204], 65–74 years [n = 120], and ≥ 75 years [n = 56]) and BMI, based on the 2024 Guidelines for the Treatment of Obesity [11]: normal weight (BMI ≥ 18.5 and < 24 kg/m² [n = 153]), overweight (BMI ≥ 24 and < 28 kg/m² [n = 186]), and obese (BMI ≥ 28 kg/m² [n = 41]).

RC was calculated using the following formula: RC = TC - HDL-C - LDL-C.

Statistical analysis

Descriptive statistics included frequencies (percentages) for categorical variables and median (interquartile range) for continuous variables, as the latter were all non-normally distributed based on graphical and statistical assessments. For comparisons across subgroups, continuous variables were analyzed using the Kruskal-Wallis rank-sum test, while categorical variables with expected cell counts below 10 were analyzed using Fisher's exact probability test. No post-hoc pairwise comparisons were conducted as analyses focused on detecting overall group differences rather than subgroup contrasts. Associations between RC and continuous biomarkers were assessed using Spearman's rank correlation coefficients, reported as the correlation coefficient (ρ) with p-values. Threshold effects of 25(OH)D on RC were identified and analyzed using piecewise linear regression models (threshold-stratified regression) implemented in R's 'segmented' package. These models identify breakpoints where the linear relationship between 25(OH)D and RC changes significantly. The association strength above and below the identified breakpoint is expressed as β coefficients with 95% confidence intervals. To account for potential confounding by lipid-lowering medications, all multivariate models adjusted for serum TC and HDL-C levels. Data were analyzed using R version 4.2.0 (R Foundation) and EmpowerStats (X&Y Solutions, Inc.), with two-sided p-values < 0.05 considered statistically significant.

Table 1 Characteristics of participants (N = 380)

	T1	T2	T3	*P*-value
No. of participants	317	55	8	
25(OH)D(ng/mL)	<=20	> 20, <=30	> 30	
Gender				NS
Male(%)	235 (74.13%)	40(72.73%)	8 (100.00%)	
Femal(%)	82 (25.87%)	15 (27.27%)	0 (0.00%)	
Age, y/o, median (IQR)	62(10.00)	66(11.00)	62.00 (9.00)	NS
BMI(kg/m^2)	24.49(2.86)	24.67(3.64)	25.34 (1.34)	NS
FBG(mmol/L)	8.9(3.87)	7.76(4.1)	7.04 (8.93)	0.03
PBG(mmol/L)	15.66(7.74)	15(8.24)	11.61 (7.70)	NS
HbA1c(%)	7.9(2.43)	7.4(2.65)	6.80 (2.00)	0.02
TG(mmol/L)	1.62(1.33)	1.52(1.06)	1.39 (2.43)	NS
TC(mmol/L)	4.35(1.3)	4.34(1.95)	5.09 (2.90)	NS
HDLC(mmol/L)	1.03(0.29)	1.06(0.37)	0.97 (0.45)	NS
LDLC(mmol/L)	2.62(1.03)	2.40(1.73)	1.98 (1.60)	NS
RC(mmol/L)	0.58(0.47)	0.60(0.49)	1.01 (1.45)	NS

Abbreviations: *25(OH)D* 25-hydroxyvitamin D, *BMI* body mass index, *FBG* fasting blood glucoser, *HbA1c* glycated haemoglobin, *TG* triglyceride, *TC* total cholesterol, *HDLC* high density lipoprotein cholesterol, *LDLC* low-density lipoprotein cholesterol, *RC* remnant cholesterol

Table Results: median (IQR)/N(%)

Values: Continuous variables were analyzed using the Kruskal-Wallis rank-sum test. Count variables with theoretical counts < 10 were analyzed using Fisher's exact probability test. This table was generated using EasyStat software (www.empowerstats.com) and R software

Result

Gender differences in RC levels: a descriptive analysis

Baseline characteristics of the participants are presented in Table 1. The cohort consisted of 283 males (74.5%) and 97 females (25.5%),with 83.4% exhibiting levels ≤ 20 ng/mL and merely 2.1% achieving sufficiency. Interestingly, the vitamin D insufficiency subgroup (> 20,≤30 ng/mL) demonstrated the most favorable glycemic parameters, with statistically significant differences in fasting blood glucose and HbA1c (p < 0.05). Despite varied vitamin D status, metabolic parameters remained homogeneous across groups.

Spearman correlations: RC with TG and sex differences

Spearman's rank correlation analysis (see Table 2) revealed significant correlations between RC and metabolic parameters, even when accounting for non-normal distributions. Strong positive correlations were observed with triglycerides (ρ = 0.697, p < 0.001) and total cholesterol (ρ = 0.561, p < 0.001).RC levels were higher in female participants (ρ = 0.163, p = 0.002). Weaker, yet still significant, associations were found with LDL-C (ρ = 0.243, p < 0.001) and HbA1c (ρ = 0.114, p = 0.027). However, no significant correlations were detected with 25(OH)D, age, fasting glucose or HDL-C.

Characterizing the Non-linear relationship between 25(OH)D and RC

A non-linear relationship was observed between 25(OH)D and RC. Although RC increased with rising 25(OH)D levels, the rate of increase appeared to plateau after reaching a certain threshold. This non-linearity suggests that the effect of 25(OH)D on RC is not consistent at higher concentrations and warrants further investigation

Table 2 Spearman's correlation matrix of clinical parameters with remnant cholesterol

Variable	GENDER	AGE	BMI	25(OH)D	FBG	PBG	HbA1c	TG	TC	HDL-C	LDL-C	RC
GENDER	—											
AGE	0.106*	—										
BMI	0.027	−0.086	—									
25(OH)D	−0.077	−0.100	−0.037	—								
FBG	−0.113	0.027	0.133*	−0.156**	—							
PBG	−0.042	−0.022	−0.048	−0.082	0.516***	—						
HbA1c	−0.026	0.089	−0.001	−0.223***	0.604***	0.526***	—					
TG	0.152**	−0.189***	0.206***	−0.131*	0.152**	0.107	0.102*	—				
TC	0.155**	−0.106*	−0.019	0.042	0.071	0.084	0.042	0.408***	—			
HDL-C	0.142**	0.099	−0.149**	0.067	−0.051	−0.029	−0.079	−0.236***	0.282***	—		
LDL-C	0.073	−0.135**	−0.017	0.055	0.015	0.051	0.013	0.241***	0.890***	0.177***	—	
RC	0.163**	−0.054	0.027	−0.061	0.107	0.069	0.114*	0.697***	0.561***	−0.055	0.243***	—

Abbreviations: *25(OH)D* 25-hydroxyvitamin D, *BMI* body mass index, *FBG* fasting blood glucose, *PBG* postprandial glucose, *HbA1c* glycated hemoglobin, *TG* triglycerides, *TC* total cholesterol, *HDL-C* high-density lipoprotein cholesterol, *LDL-C* low-density lipoprotein cholesterol, *RC* remnant cholesterol

Footnotes: Data are presented as Spearman's correlation coefficient (rho), *<0.05, **<0.01, ***<0.001

into the implications of these thresholds on patient health outcomes (see Fig. 1).

Threshold effects: understanding the non-linear relationship between 25(OH)D and RC

The threshold effect analysis, conducted using piecewise linear regression, revealed a significant non-linear relationship between 25(OH)D and remnant cholesterol (RC), identifying an inflection point at 18.8 ng/mL (Likelihood Ratio Test $P = 0.006$).Below this threshold, each 1 ng/mL increase in 25(OH)D was associated with a decrease in RC of 0.01 mmol/L (95% CI: −0.02 to −0.00, $p < 0.05$). Conversely, above this threshold, each 1 ng/mL increase was associated with an increase in RC of 0.02 mmol/L (95% CI: 0.00 to 0.03, $p < 0.05$).Conversely, each 1 ng/mL increase was associated with an increase in RC of 0.02mmol/L (95% CI: 0.00 to 0.03, $p < 0.05$). The difference between these two slopes was statistically significant ($p < 0.05$), suggesting a dual effect where insufficient 25(OH)D levels are associated with beneficial reductions in RC, whereas levels exceeding 18.8 ng/mL may contribute to elevated RC concentrations(see Table 3).

Age-dependent variations in the relationship between 25(OH)D and RC

In patients younger than 65 years, each 1 ng/mL increment in 25(OH)D was associated with a decrease in RC of 0.01 mmol/L (95% CI: −0.02 to −0.00, $p = 0.0151$). In contrast, patients aged 75 years and older experienced an increase in RC of 0.02 mmol/L for each 1 ng/mL increase in 25(OH)D (95% CI: 0.01 to 0.03, $p < 0.05$). Interaction analysis, after adjusting for confounding factors, indicated a significant influence of age on the relationship between 25(OH)D and RC ($p < 0.05$). However, the impacts of sex and BMI on this relationship were not found to be statistically significant (see Table 4).

Discussion

Our analysis reveals a significant non-monotonic relationship between serum 25(OH)D levels and remnant cholesterol (RC) in patients with type 2 diabetes mellitus (T2DM).This finding is consistent with previous research that observed similar trends between vitamin D levels and lipid profiles [12, 13].However, traditional multivariate linear regression failed to detect this association between 25(OH)D and RC due to unaccounted nonlinearity — a statistical limitation that was resolved through threshold analysis, which identified a U-shaped relationship with an inflection point at 18.8 ng/mL (95% CI: 16.3–22.6 ng/mL)(Supplementary Tables).This threshold's biological relevance is emphasised by its alignment with clinical deficiency cutoffs, its bootstrap-validated robustness and the cohort's high deficiency prevalence (80.5% had 25(OH)D below 18.8 ng/mL), which

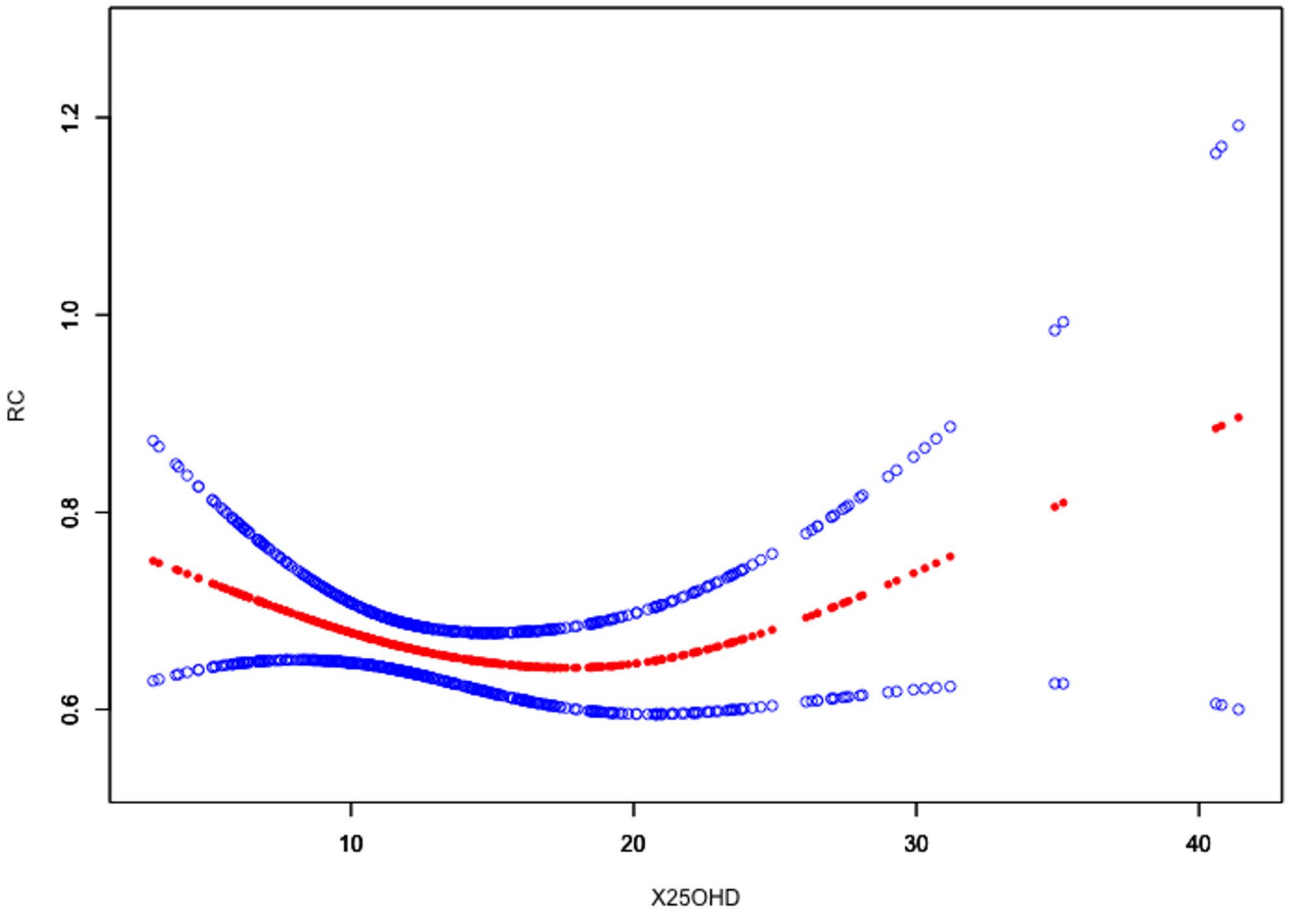


Fig. 1 Association between 25(OH)D and RC

Table 3 Threshold effect analysis of 25(OH)D and RC using Piece-wise linear regression

Models	Per-unit increase	
	β (95%CI)	*P* value
Model I		
One line effect	0.00 (−0.01, 0.01)	NS
Model II		
Turning point(K)	18.8	
25(OH)D < K	−0.01(−0.02, −0.00)	0.0367
25(OH)D >K	0.02 (0.00, 0.03)	0.0138
Predicted RC at K, mmol/L	0.583 (0.467, 0.699)	
P value for LRT test		0.006

Abbreviations: 25(OH)D:25-hydroxyvitamin D

Table Results:β (95% CI) P-value

Outcome Variable: RC

Exposure Variable: 25(OH)D

Adjustment Variables: GENDER; BMI; AGE; TC; HDLC; HbA1c

Table 4 Subgroup analysis of the association of 25(OH)D with RC

Characteristic	No.Of participants	β (95%CI)	*P* -value	*P* for interaction
Age (y/o)				0.0389
<=64	204	−0.01(−0.02,−0.00)	0.0151	
> 64, <=74	120	0.00 (−0.01,0.02)	NS	
> 75	56	0.02 (0.01, 0.03)	0.0033	
Sex				NS
Male	283	0.00 (−0.00, 0.01)	NS	
Female	97	−0.01 (−0.02,0.01)	NS	
BMI (kg/m^2)				NS
<24	153	0.00 (−0.01, 0.01)	NS	
>=24, < 28	186	0.00 (−0.01, 0.01)	NS	
>=28	41	−0.01 (−0.03,0.01)	NS	

Abbreviations: *BMI* body mass index

Table Results:β (95% CI) P-value

Adjusted for TC, HbA1c and HDLC except the subgroup variable

is consistent with regional epidemiology showing sufficiency rates in the adult population of Gansu Province [14]. Nevertheless, the limited sample in high 25(OH)D strata necessitates validation in larger cohorts. Notably, the inclusion of the vitamin D-sufficient subgroup (n = 8) — though limited by recruitment difficulties in this deficiency-prone demographic — was crucial for defining the supraphysiological part of the identified U-curve.This inverse U-shaped relationship has been documented previously, suggesting that, while vitamin D supplementation

can enhance lipid metabolism, excessive levels may disrupt this balance due to alterations in lipid transport or metabolism [15, 16].At low levels of 25(OH)D, deficiency may contribute to elevated RC through secondary hyperparathyroidism. Elevated parathyroid hormone (PTH), a well-known consequence of vitamin D deficiency, has been shown to stimulate hepatic very-low-density lipoprotein synthesis and secretion, leading to increased levels of triglyceride-rich lipoproteins and consequently RC [16].Conversely, In contrast, activation of the vitamin D receptor (VDR) represses hepatic small heterodimer partner (SHP), thereby increasing levels of cholesterol 7α-hydroxylase (CYP7A1) in both mice and humans and reducing cholesterol [17]. It is plausible that this reduction in cholesterol subsequently contributes to decreased levels of RC.

Our study identified a threshold effect of 25(OH)D on RC at 18.8 ng/mL. Below this threshold, increasing 25(OH)D was associated with reduced RC, whereas above it, RC significantly increased. This biphasic pattern aligns with emerging evidence of non-linear vitamin D-health associations [12]. Crucially, our findings provide a mechanistic bridge between vitamin D status and cardiovascular outcomes.Large-scale genetic studies have confirmed nonlinear inverse relationships between 25(OH)D and cardiovascular endpoints with risk that started to increase at 25(OH)D concentrations < 30ug/mL [18].Similarly, a non-linear relationship between vitamin D and blood lipid parameters has also been reported in the Chinese population [12]. RC, as a key driver of coronary heart disease, may be one of the mediators of cardiovascular damage caused by vitamin D excess.This aligns with recent studies that emphasize the role of remnant cholesterol as a significant independent risk factor for coronary artery disease [19].

Our study highlights a clinically significant finding in younger T2DM patients (≤ 64 years): over 80% had vitamin D deficiency (25(OH)D ≤ 20ng/mL), mirroring the overall cohort. Crucially, in this younger subgroup, each 1 ng/mL increase in 25(OH)D was associated with a significant 0.01 mmol/L reduction in RC (β = −0.01, 95% CI: −0.02 to −0.00, p = 0.015), suggesting targeted vitamin D repletion may optimize lipids in young, deficient diabetics. However, age emerged as a critical modifier of this relationship. While protective in the young, we observed a detrimental reversal in older patients (≥ 75 years), where rising 25(OH)D levels were associated with increased RC. This age-dependent reversal aligns with Cheng et al.'s findings [20], which show vitamin D deficiency linked to hypertriglyceridemia primarily in individuals under 65 years old but not in those over 65, highlighting the need for age-tailored supplementation strategies. The protective effect in youth versus the detrimental effect in the elderly may reflect age-related vitamin D receptor (VDR) dysfunction [21]. Given RC's role as an independent CVD risk factor [2],its elevation at even modest vitamin D levels (>18.8 ng/mL) in the elderly could initiate vascular damage decades before clinical events manifest.

Additionally, our study revealed significant gender differences in RC levels, with female patients displaying higher RC levels relative to males. This finding is consistent with previous studies that report gender-specific variations in lipid profiles and vitamin D status among populations with T2DM [22]. Hormonal differences, particularly the role of estrogen in lipid metabolism, may partially explain this disparity. Estrogen is known to modulate cholesterol transport and metabolism, and its decline in postmenopausal women could contribute to higher RC levels and altered responses to vitamin D [23]. Supporting this, Ooi et al. [24] demonstrated that genetically elevated RC is associated with low 25(OH)D levels, particularly in women. These gender-specific responses emphasize the importance of considering sex as a variable in clinical interventions, as individualized approaches may enhance the effectiveness of vitamin D supplementation and improve metabolic health [25].

While our cross-sectional design limits definitive mechanistic insights, the observed non-linear relationship between vitamin D levels and lipid metabolism reveals potentially significant biological interactions. The robust association suggests that both vitamin D deficiency and excess may adversely impact cholesterol regulation in patients with T2DM. Although causation cannot be conclusively established, our findings highlight the complex, age-dependent modulation of lipid profiles by vitamin D status. These results challenge the traditional linear supplementation paradigm and underscore the importance of precision medicine approaches. Specifically, our data suggest an optimal therapeutic window for vitamin D, where levels neither too low nor too high may optimize cholesterol regulation. Future research should employ longitudinal and mechanistic approaches to validate the proposed non-linear relationship between vitamin D status and lipid metabolism, delineate the molecular mechanisms underlying vitamin D-mediated cholesterol regulation, and establish precision medicine-based, age-stratified vitamin D supplementation strategies that mitigate cardiovascular risk associated with cholesterol dysregulation in type 2 diabetes mellitus.

Limitations

This study provides valuable insights into the relationship between 25(OH)D and RC, yet several limitations must be acknowledged. First, the cross-sectional design precludes causal inference. Second, unmeasured confounders—including disease duration, dietary habits, physical activity, and genetic predispositions—may

influence observed associations, while residual confounding from lifestyle factors persists despite excluding renal/liver dysfunction. Third, although glucocorticoid/anticonvulsant users were excluded and adjustments for TC/HDL-C addressed lipid-lowering effects, the lack of specific statin/fibrate data remains a gap. Fourth, while total 25(OH)D was appropriately used (given exclusion of hepatorenal impairment where it reliably reflects status), emerging evidence suggests bioavailable/free 25(OH)D may better capture physiological activity in subpopulations [26]. Fifth, the vitamin D-sufficient subgroup (>30 ng/mL) comprised only 8 participants, all of whom were male. This small sample size may affect the effect estimates in the high concentration range and limits the generalizability of sex-stratified analyses, particularly regarding the relationship between optimal vitamin D status and remnant cholesterol in women with T2DM. Finally, the biological mechanisms underlying non-linear, age- and gender-dependent relationships remain unclear. Therefore, future longitudinal studies should integrate disease duration, granular organ metrics, and medication specifics; mechanistic work must elucidate vitamin D-cholesterol interplay in T2DM (including direct measurement of vitamin D-binding protein/albumin to calculate bioavailable vitamin D); and randomized trials should establish optimal vitamin D levels for cardiovascular risk reduction.

Conclusion

This study identifies a nonlinear threshold effect of 25-hydroxyvitamin D on RC in type 2 diabetes, with a critical inflection point at 18.8 ng/mL. Below this threshold, increasing 25(OH)D concentrations associate with reduced RC, whereas higher levels correlate with elevated RC. Crucially, this relationship undergoes a directional reversal by age: beneficial RC reduction in younger patients (≤64 years) contrasts with adverse elevation in older adults (≥75 years). Sex significantly influences baseline RC levels but does not moderate the association between vitamin D and RC.Collectively, these mechanistic insights compel a redefinition of clinical vitamin D targets for cardiovascular risk mitigation in diabetes.

Instead of pursuing traditional sufficiency (>30ng/mL), maintaining 25(OH)D concentrations near 18.8 ng/mL maximizes remnant cholesterol control. This approach is particularly beneficial for younger individuals requiring vitamin D repletion, while cautious dosing is essential for elderly patients (>75 years) to prevent adverse lipid effects. This dual-strategy approach (combining biological threshold targeting and age stratification) establishes a mechanistic framework for personalized interventions targeting remnant cholesterol reduction.Future trials should validate these thresholds in prospective cohorts and investigate vitamin D receptor pathway modulation across age groups.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12902-025-02062-4.

Supplementary Material 1.

Supplementary Material 2.

Supplementary Material 3.

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Authors' contributions

L.:Conceptualization, Formal analysis, Writing Original Draft; L.and Y.: Data curation; C.:Methodology; Q.: Funding acquisition; L.:Supervision, Review, Editing.All authors reviewed the manuscript.

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Data availability

All data generated or analyzed during this study are included in this published article and its supplementary information files.

Declarations

Ethics approval and consent to participate

The experimental protocol was established, according to the ethical guidelines of the Helsinki Declaration and was approved by the Human Ethics Committee of the People's Hospital of Gansu Province, the number was 2024 – 845.Written informed consent was obtained from each participant before data collection.Due to the impact of the epidemic, the upload of the original file was delayed.

Consent to publication

Not Applicable.

Competing interests

The authors declare no competing interests.

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