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The utility of Vitamin D levels in predicting the severity of coronary artery disease in obese patients

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ABSTRACT

Objectives: This study aimed to investigate the relationship between Vitamin D (25-hydroxy [OH]D, 25[OH]D) levels and the severity of coronary artery disease (CAD), as measured by the SYNTAX score, in obese patients undergoing angiography for stable angina pectoris.

Patients and methods: This retrospective study included 120 obese patients (61 males, 59 females; mean age: 61.7±10.5 years) who underwent coronary angiography between May 2012 and June 2023. Obesity was defined as a body mass index >30 kg/m^2. Serum Vitamin D levels were measured within six months before angiography, and CAD severity was assessed using the SYNTAX score. Patients were categorized into three groups based on their SYNTAX scores: <23, 23-32, and ≥33.

Results: The 25(OH)D levels were significantly lower in the group with the highest SYNTAX scores. Multivariable regression analysis identified 25(OH)D levels as an independent predictor of the SYNTAX score (odds ratio=0.809, 95% confidence interval 0.743-0.881, p<0.001). A strong negative correlation was observed between 25(OH)D levels and SYNTAX scores (r=0.77, p<0.001). Additionally, a serum 25(OH)D level of 13.87 ng/mL could predict high SYNTAX scores with 81% sensitivity and 80.6% specificity.

Conclusion: This study demonstrates a significant association between low 25(OH)D levels and higher SYNTAX scores, indicating more severe CAD in obese individuals. Vitamin D deficiency may be an independent predictor of CAD severity in this population.

Keywords: Coronary artery disease, obesity, SYNTAX score, Vitamin D, 25(OH)D

Obesity is a growing global health issue, defined by a body mass index (BMI) over 30 kg/m^2. According to World Health Organization data, 16% of adults were obese in 2022. Its prevalence has more than doubled compared to 1990. Obesity is well-known to contribute to coronary artery disease (CAD) by accelerating atherosclerosis through mechanisms such as insulin resistance and inflammation.[1] It raises the risk of CAD by contributing to other traditional cardiovascular risk factors, such as diabetes and hypertension.[1]

Vitamin D deficiency is another significant public health issue due to its widespread prevalence.[2] The serum 25-hydroxy (OH)D (25[OH]D) level is measured to assess Vitamin D status, and low levels of 25(OH)D can lead to a range of health issues, mainly bone disorders. Beyond skeletal problems, low 25(OH)D levels have been associated with an increased risk of chronic diseases, such as cardiovascular diseases and the severity of CAD.[3,4] Importantly, Vitamin D deficiency is more prevalent among obese individuals, who are already at a heightened risk for CAD.[5]

Both obesity and Vitamin D deficiency may independently contribute to an increased risk of cardiovascular disease. The coexistence of these two conditions may further exacerbate the severity of CAD. It is known that Vitamin D deficiency is more common in obese people than in those with normal BMI. Therefore, this study aimed investigate the relationship between Vitamin D status and the severity of CAD, as measured by the SYNTAX score, in obese

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patients who underwent angiography for stable angina pectoris.

PATIENTS AND METHODS

In this study, files of patients who underwent angiography due to stable angina pectoris at the Gazi University Faculty of Medicine between May 2012 and June 2023 were retrospectively scanned. One hundred twenty patients (61 males, 59 females; mean age: 61.7±10.5 years) who had their 25(OH)D levels tested within six months before coronary angiography for various reasons, such as general health check-ups or osteoporosis risk evaluation, and who were classified as obese (BMI >30 kg/m^2) were included. Serum 25(OH)D levels were measured from venous blood samples using the Architect 25(OH) Vitamin D analysis kit (Abbott Laboratories, Chicago, United States of America). The SYNTAX score was calculated to determine the extent of CAD from the angiography images of the patients. The SYNTAX score calculation was performed using the international calculation method (www.syntaxscore.com). Patients were divided into three groups based on their SYNTAX score: a score of ≤22 was classified as mild disease, a score between 23 and 32 as moderate disease, and a score ≥33 as severe disease. Exclusion criteria were age under 18 years, acute coronary syndrome, evidence of acute or chronic infection, systemic inflammatory or autoimmune disease, history of using glucocorticoid therapy within the past three months, trauma, recent major surgery, active malignancy, hypo-or hyperthyroidism, hematological diseases, and severe liver or renal failure. None of the patients had a genetic condition that would affect their 25(OH)D levels, and it was also confirmed that no patient was receiving oral Vitamin D therapy. Patients without documented 25(OH)D levels within the last six months were excluded from the study. The study protocol was approved by the Gazi University Faculty of Medicine Ethics Committee (date: 10.09.2024, no: 2024-1441). Written informed consent was acquired from all participants. The study was conducted in accordance with the criteria of the Declaration of Helsinki.

Statistical analysis

All statistical analyses were performed using IBM SPSS version 25.0 software (IBM Corp., Armonk, NY, USA). The normality of the distribution of the data was assessed using a Kolmogorov-Smirnov test. Data were presented as frequency (percentage), median and interquartile range, (IQR) or mean ± standard deviation (SD). Categorical variables were subjected to comparison using the chi-square test. Continuous variables between study groups were compared using one-way analysis of variance or the Kruskal-Wallis test. Multivariable logistic regression analysis was utilized to identify factors contributing to the SYNTAX score. The correlation between 25(OH)D levels and the SYNTAX score was evaluated using Pearson's test. The capacity of 25(OH)D value in predicting a high SYNTAX score was analyzed using receiver operating characteristic curve analysis. All statistical analyses were performed two-sided, and a p-value <0.05 was considered statistically significant.

RESULTS

Forty-five of the patients had a SYNTAX score ≤22, 38 had a score between 22 and 32, and 37 had a score ≥33. Age, sex, BMI, hypertension, and diabetes rates were similar between the groups (p>0.05 for all parameters). In addition, no statistical difference was found between the groups in terms of hemogram and biochemistry values. Moreover, 25(OH)D levels were the lowest in the group with the highest SYNTAX score, while 25(OH)D levels were the highest in the group with the lowest SYNTAX score (34.7±3.9 ng/mL *vs.* 17.5±7.5 ng/mL *vs.* 11.6±6.5 ng/mL; Table 1).

In the multivariable regression analysis, 25(OH)D levels were found to be an independent predictor of the SYNTAX score (odds ratio=0.809, 95% confidence interval 0.743-0.881, p<0.001; Table 2). There was a strong negative correlation between the SYNTAX score and 25(OH)D levels (r=0.77, p<0.001; Figure 1). Additionally, a serum 25(OH)D level of 13.87 ng/mL could predict a SYNTAX score with 81% sensitivity and 80.6% specificity (Figure 2).

DISCUSSION

This study revealed a significant relationship between 25(OH)D levels and the severity of CAD in obese patients. Our findings suggest that lower 25(OH)D levels are associated with increased coronary lesion complexity and severity. Furthermore, 25(OH)D levels were an independent predictor of SYNTAX scores in obese patients.

Table 1
Baseline clinical and laboratory parameters of the study population (n=120)

	SYNTAX score <22 (n=45)					SYNTAX score 22-32 (n=38)					SYNTAX score ≥33 (n=37)					
	n	%	Mean±SD	Median	IQR	n	%	Mean±SD	Median	IQR	n	%	Mean±SD	Median	IQR	*p*
Age (year)			61.7±1.5					61.2±1.7					62.2±1.8			0.914
Sex Male	23	51				22	58				16	43				0.447
BMI (kg/m^2)			34.7±2.2					35.2±2.2					34.6±2.1			0.490
Smokers	11	24				9	24				10	27				0.940
Hypertension	19	42				15	40				188	49				0.712
Diabetes mellitus	15	33				12	32				16	43				0.521
Glucose (mg/dL)				106	89.5-145				99	88.7-157				107	89.2-132.5	0.944
Urea (mg/dL)			18±5.4					18.3±7.2					17.4±5.1			0.831
Creatinine (mg/dL)			0.9±0.2					0.8±0.2					0.9±0.2			0.620
Sodium (mEq/L)			140.2±3.1					140.1±2.3					140.3±2.2			0.936
Potassium (mmol/L)			4.2±0.3					4.3±0.3					4.2±0.3			0.243
Total cholesterol (mg/dL)			178.6±65					193.5±60.3					192.9±50.8			0.433
Triglyceride (mg/dL)			48.5±10.8					50.7±16.7					48.6±13.4			0.828
HDL (mg/dL)				47	41-55.5				47.5	38.7-59.5				45	37-60.5	0.734
LDL (mg/dL)			93.6±44.5					103.2±43.6					106.5±38.1			0.348
Hemoglobin (g/dL)			13.8±1.8					13.4±1.5					13.6±1.6			0.586
Platelet count (×10^3)			258.9±92.8					242.1±77.5					228.5±58.9			0.286
White blood cells (×10^3)			7.5±1.8					7.8±2.3					7.6±2.8			0.693
25(OH)D (ng/mL)			34.7±3.9					17.5±7.5					11.6±6.5			<0.001
Ejection fraction (%)			63.8±3.9					63.2±5.7					61.5±7.1			0.177

SD: Standard deviation; IQR: Interquartile range; BMI: Body mass index; HDL: High-density lipoprotein; LDL: Low-density lipoprotein; 25(OH)D: Vitamin D.

Table 2
Multivariable logistic regression analyses showing the independent predictors of the presence of a SYNTAX score ≥33 in obese patients

	Multivariable analysis			
		95% CI		
	OR	Lower	Upper	*p*
Age	1.057	0.999	1.119	0.054
Sex	0.345	0.114	1.047	0.060
Hypertension	1.310	0.438	3.916	0.630
Diabetes mellitus	1.494	0.473	4.716	0.494
Smoking	1.205	0.332	4.370	0.776
Low-density lipoprotein	1.002	0.989	1.016	0.750
25(OH)D	0.809	0.743	0.881	<0.001

CI: Confidence interval; OR: Odds ratio; 25(OH)D: Vitamin D.

Previous studies have shown an inverse relationship between serum 25(OH)D levels and obesity.[5-8] Several hypotheses have been proposed to explain how obesity leads to Vitamin D deficiency. The most likely mechanism is believed to be the volumetric distribution of Vitamin D. Since adipose tissue acts as a reservoir for Vitamin D, obese patients tend to have lower serum concentrations compared to lean individuals, even when their overall 25(OH)D levels are similar.[9,10] Additionally, obese individuals tend to respond less effectively to Vitamin D supplements.[11] Another possible mechanism is the impairment of 25-hydroxylation caused by hepatic steatosis, a condition commonly observed in obese individuals. This impairment leads to a reduction in the conversion of Vitamin D into its active form.[9] Other hypotheses include poor dietary habits, reduced sun exposure, and variations in gene expression that affect Vitamin D metabolism.[9]

Our results also align with observational studies identifying a link between serum 25(OH)D levels and CAD.[12,13] A comprehensive meta-analysis of prospective studies involving over 18,000 participants demonstrated that the serum 25(OH)D level was

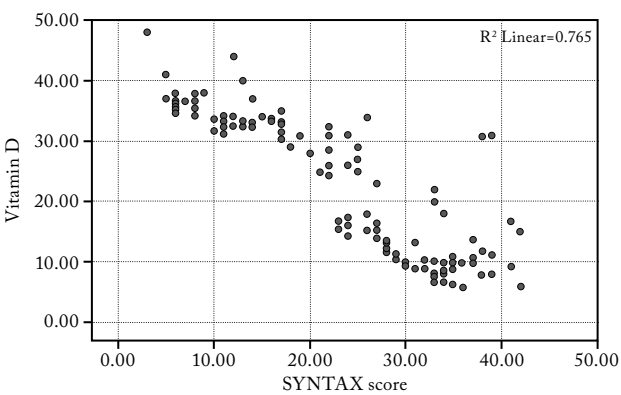

Figure 1. Correlation between 25(OH)D levels and SYNTAX scores in the study population.
25(OH)D: Vitamin D.

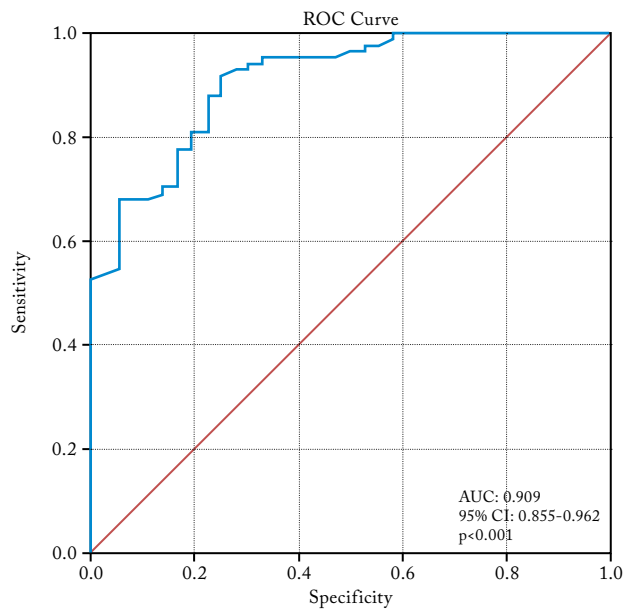

Figure 2. Receiver operating characteristic curve analysis of the 25(OH)D level for the detection of high SYNTAX scores (<33 *vs.* ≥33 comparison).
25(OH)D: Vitamin D.

inversely associated with the risk of cardiovascular events and cardiovascular mortality.[14] Verdoia et al.[4] demonstrated that lower 25(OH)D levels were associated with the severity of CAD. Similarly, a study involving 348 patients undergoing coronary angiography found that lower serum 25(OH)D levels were independently associated with higher SYNTAX scores, indicating more severe coronary lesions.[15] Notably, our findings extend these observations specifically to obese patients, confirming that low 25(OH)D levels are associated with increased coronary lesion complexity and severity.

Vitamin D appears to play a protective role in atherosclerosis through multiple mechanisms. It prevents endothelial dysfunction by increasing nitric oxide production, reducing oxidative stress, and inhibiting inflammatory cytokines and adhesion molecules.[16] Vitamin D also regulates vascular tone and angiogenesis.[16] In vascular smooth muscle cells, it has antiproliferative effects and impacts processes such as cell migration and fibrosis.[16] Another potential mechanism by which Vitamin D might influence myocardial infarction risk is through its effect on vascular calcification, as evidenced by the negative relationship between levels of 1,25-dihydroxyvitamin D and vascular calcification.[17] Vitamin D modulates immune responses by shifting the balance from proatherogenic T helper 1 cells to antiatherogenic T helper 2 profiles.[16] It also influences atherosclerosis by improving systemic conditions that contribute to it, such as insulin sensitivity, beta cell function, and lipid profiles.[16] Furthermore, it suppresses the renin-angiotensin-aldosterone system.[16]

Obesity is associated with a chronic, low-level inflammatory state that affects several metabolic and vascular pathways, such as insulin resistance, endothelial function, and lipid metabolism, all of which are also influenced by Vitamin D.[18] Additionally, obesity has been linked to increased inflammation in epicardial adipose tissue, which significantly correlates with the pathogenesis of CAD.[19] In obese individuals, low 25(OH)D levels can worsen these conditions, leading to increased atherosclerosis and higher cardiovascular risk. This is primarily assumed to be because low 25(OH)D levels fail to counteract oxidative stress.[20] However, it is unclear whether these factors are impaired simultaneously or whether there is a causal relationship.

There were some limitations to this study. First, as a cross-sectional study, the causal relationship between 25(OH)D levels and the severity of coronary artery stenosis could not be established. Second, 25(OH)D levels were measured only once within six months before angiography, which might not reflect seasonal or lifestyle changes. Third, the number of patients in the study was relatively low.

In conclusion, this study demonstrates a significant association between low serum 25(OH)D levels and higher SYNTAX scores, indicating more severe CAD in obese individuals. Additionally, in obese patients, Vitamin D levels were an independent predictor of SYNTAX scores.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions: Conceptualization, investigation, writing-original draft, review, and editing: B.C.; Data curation, investigation, methodology, review and editing: B.A.Y.; Methodology, formal analysis, supervision, writing-review and editing: M.C.

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