Int Cardiovasc Res J.2023;**17**(2):39-43.icrj.139878

International Cardiovascular Research Journal

www.ircrj.com

Roles of Serum Parathyroid Hormone and Vitamin D Levels in Severity of Coronary Artery Disease and Left Ventricular Systolic Function

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ARTICLE INFO

Article Type:
Research Article

Article History:
Received: 8 Aug 2023
Revised: 12 Nov 2023
Accepted: 25 Dec 2023

Keywords:
Cardiovascular Diseases
Parathyroid Hormone
25-Hydroxyvitamin D
Left Ventricular Systolic Function
Coronary Artery Disease

ABSTRACT

Background: Vitamin D and parathyroid hormone (PTH) are related but impact cardiovascular functions differently.

Objectives: This study investigated the roles of PTH and vitamin D serum levels in the severity of coronary artery disease and left ventricular systolic function (LVSF).

Methods: This cross-sectional study was conducted on 271 participants who underwent elective coronary angiography at Dr. Heshmat Hospital, selected by convenience sampling over four months. 25-hydroxyvitamin D (25 (OH) D) and PTH levels were obtained from patients' blood samples. Vitamin D levels were categorized into three categories. The SYNTAX score was used to evaluate the severity of coronary artery disease (CAD), classified across three categories. The chi-squared test, independent samples t-test, and multivariable logistic regression were used for statistical analysis. Data were analyzed by SPSS ver.21.

Results: Diabetes, hypertension, dyslipidemia, and lower vitamin D levels were independent variables affecting patients' high-risk conditions. The highest SYNTAX score was in patients with vitamin D deficiency ($P < 0.001$). Patients with different ejection fractions did not have statistically significant differences in vitamin D (25.38 ± 14.23) and PTH levels (66.62 ± 17.39) ($P = 0.4$). The severity of CAD in patients with PTH > 40 was higher than in patients with PTH ≤ 40, but this was not statistically significant ($P = 0.06$).

Conclusion: Our results showed an inverse relation between CAD and vitamin D. However, the CAD risk did not change with PTH levels.

1. Introduction

Cardiovascular diseases (CVDs) are the most common cause of death worldwide (1), accounting for 32% (17.9 million) of deaths worldwide every year (2). The incidence and prevalence of CVDs have increased in recent years in Iran, and about 43% of all mortalities in this country are caused by CVDs (1). Coronary artery diseases (CADs), as a subset of CVD, remain the main reason for morbidity and mortality in the world (3). In low- and middle-income countries, rates of CAD are increasing, and this change is occurring rapidly and at an alarming rate (4, 5).

Vitamin D insufficiency is related to many health conditions and chronic conditions (6) like hypertension (HTN) and mortality. Vitamin D deficiency is linked with different CVDs, like CAD, heart failure (HF), and HTN (3, 7), mediated by the renin-angiotensin-aldosterone system (RAAS) (8). Vitamin D affects different stages of CAD pathogenesis because its receptors are in disparate tissues. They regulate blood pressure (BP) and replication by affecting vascular smooth muscle cells and cardiomyocytes (9). Vitamin D deficiency plays a significant role in CAD pathogenesis (4, 10-12). Bahrami et al. suggested that using vitamin D correlates with improved cardiac outcomes in CAD patients with vitamin D deficiency (13).

Despite the mentioned evidence, the impact of vitamin D on the prevention of CVDs is unclear (14). Vitamin D plays

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a vital role in calcium and bone metabolism. Meanwhile, the vitamin D mechanism in CVDs has not been revealed completely. Based on basic studies, Tsugawa's study showed that vitamin D has a protective effect on CVDs. In contrast, randomized control trials have not validated the effect of this supplement (14). The serum 25-hydroxyvitamin D (25(OH)D) level is a significant indicator of vitamin D status (13, 15). A study showed that vitamin D supplementation prevented left ventricular hypertrophy and reduced fibrosis (16). Vitamin D is associated with both the healthy population's ventricular dilation degree in HF and left ventricular geometry (17). Some have reported that vitamin D deficiency impairs left heart function (18).

Vitamin D has pivotal impacts on parathyroid cells, prohibiting parathyroid hormone (PTH) secretion and parathyroid cell proliferation through its receptors (19). Hypothesized mechanisms have been reported in suppressing PTH modulation (14). PTH, a mineral and bone metabolism regulator, has an adverse cardiovascular (CV) correlation, which is increasingly reported (20). Production of PTH happens by parathyroid cells, which is a vital regulator of Ca, P, and vitamin D metabolism (21), and its receptors are present in vascular smooth muscle cells, endothelial cells, and cardiomyocytes, which indicates that PTH may have a significant role in CAD pathophysiology (22). PTH is thought to be associated with the RAAS and directly affects the CV system (21). A study indicated that PTH serum levels were associated with CV mortality in diabetic patients (23). PTH's effects on the CV system are known (21).

Chen et al. found that vitamin D and PTH levels in serum and CAD risks in the elderly Chinese population independently correlate with each other (3). At the same time, another study demonstrated that 25(OH)D, Ca, and PTH levels in the serum may not be correlated with the risk of CAD in patients with diabetes (24).

2. Objectives

Building on recent studies, we aimed to investigate the correlation of PTH and vitamin D serum levels with the severity of coronary artery disease and left ventricular systolic function (LVSF) in Rasht, Iran.

3. Material and Methods

3.1. Participants

This cross-sectional study was conducted on 271 patients who underwent elective coronary angiography at Dr. Heshmat Hospital, the only CVD center in Guilan province, Iran, by convenience sampling between October 2016 and February 2017.

Patients without kidney failure, chronic liver disease, systemic infections, bone disorders, trauma, thyroid disease, recent major surgery, bisphosphonate use, vitamin D or calcium supplements, angina in the 48 hours before admission, history of angioplasty or CABG, or history of thyroid/parathyroid surgery were included.

3.2. Data Collection

Data were gathered after explaining the study's main aim and obtaining informed consent from the participants. Demographic characteristics (sex, age, history of smoking, underlying diseases, drug history, and family history of CVDs) were collected through interviews and patient records. 25(OH)D, Ca, PTH, and P levels were obtained from patients' blood samples. Levels of vitamin D were categorized into three categories (sufficient ≥ 30 ng/mL, insufficient 20 – 30 ng/mL, deficient < 20 ng/mL), while PTH levels were divided into ≥ 40 pg/mL and < 40 pg/mL groups. SYNTAX score was used for evaluation of CAD severity and classified into three categories (high ≥ 33, intermediate 23-32, low < 22), and echocardiography was divided into EF ≥ 50% and EF < 50%). A cardiologist calculates these variables. The LVSF was determined by EF obtained from echocardiography.

3.3. Statistical Analysis

Data on a total of 271 patients were analyzed in this study. The frequency (percent), median (interquartile range (IQR)), or mean (standard deviation (SD)) of data are presented. The chi-squared test was used to survey the relationship between qualitative characteristics (PTH, vitamin D, coronary artery disease involvement, and left ventricular systolic function). An independent samples t-test was used to investigate the relation between quantitative characteristics. Multiple logistic regression method was used to investigate the impact of variables on the intensity of CADs. P-values below 0.05 were considered significant, and SPSS software v. 21 was used for all analyses.

4. Results

Demographic information of patients, history of diseases, and laboratory indices are shown in Table 1. Of all 271 participants, 51.6 % were males. The mean age of patients was 60.8 ± 11.8 years.

Descriptive patient characteristics showed that 40.9% of cases had a deficiency of vitamin D (25.38 ± 14.23), 70.84% had a low level of PTH (66.62 ± 17.39), 63.46% had a SYNTAX index < 22 (16.30 ± 8.41), and 65.1% had an EF ≥ 50 (46.71 ± 10.16) (Table 2).

Based on the chi-squared test, the EF did not correlate with the vitamin D level (P = 0.4). In vitamin D deficiency, a greater risk of CVDs was observed (P < 0.001). Hence, an inverse relationship was recorded between vitamin D and SYNTAX criteria. Pearson correlation also showed a similar result ($R_{Pearson}$: -0.32).

Based on independent t-test results, the severity of CAD in patients with PTH > 40 was higher than in patients with PTH ≤ 40, but this was not statistically significant (P = 0.06). PTH serum levels in different SYNTAX categories were not significantly different (P = 0.1) (Table 3). Patients with EF less than or greater than 50% did not significantly differ in PTH levels (P = 0.5). Although the average vitamin D level in people with normal EF was higher than that of low EF, this was not statistically significant (P = 0.1) (Table 4).

The data in Table 5 show that diabetes (OR = 2, 95% CI (1.4 - 2.4), P = 0.03), hypertension (OR = 2.6, 95% CI (1.1 - 8.1), P = 0.01), dyslipidemia (OR = 3.3, 95% CI (1.2 - 10.2), P = 0.02) and vitamin D deficiency (OR = 3.4, 95% CI (1.7 - 6.7), P = 0.001) were risk factors of high SYNTAX scores.

Table 1. Demographics, History of Diseases, and Laboratory Indices of Patients.

Variables	N (%)	Mean (SD)
Age		60.8 (11.8)
Sex		
Male	140 (51.66)	
Female	131 (48.33)	
Diabetes	98 (36.2)	
Hypertension	165 (60.9)	
Dyslipidemia	161 (59/4)	
Smoking	58 (21.4)	
Systolic BP (mm Hg)		122.54 (14.12)
Diastolic BP (mm Hg)		74.84 (10.06)
Total cholesterol (mg/dL)		159.04 (53.51)
LDL (mg/dL)		87.34 (31.33)
HDL (mg/dL)		43.42 (13.81)
Hb (g/L)		12.8 (1.5)

Abbreviations: BP; Blood pressure, LDL; Low-density lipoprotein, HDL; High-density lipoprotein, Hb; Hemoglobin

Table 2. Patients' Characteristics Categorized by Study Variables

Variable		N (%)	Mean ± SD
	Deficient	111 (40.95%0)	
Vitamin D level	Insufficient	74 (27.3%)	25.38 ± 14.23
	Sufficient	86 (31.7%)	
PTH level	< 40	79 (29.1%)	66.62 ± 17.39
	≥ 40	192 (70.84%)	
	< 22	172 (63.46%)	
SYNTAX score	23-32	48 (17.71%)	16.30 ± 8.41
	≥ 33	51 (18.81%)	
Ejection fraction	≥ 50	176 (65.1%)	46.71 ± 10.16
	< 50	95 (35.05%)	

Abbreviations: PTH; parathyroid hormone

Table 3. Frequency of SYNTAX Score Groups in Different Vitamin D and Parathyroid Hormone Levels.

Variables	SYNTAX Category N (%)			P-value*
Vitamin D	≥ 33	23 - 32	≤ 22	< 0.001
< 20	30 (65.2)	24 (57.1)	48 (28.9)	
20-30	6 (13)	10 (23.8)	52 (31.3)	
> 30	10 (21.7)	8 (19)	66 (39.8)	
PTH				0.1
≤ 40	9 (19.6)	9 (20.9)	54 (32.7)	
> 40	37 (80.4)	34 (79.1)	111 (67.3)	

Abbreviations: PTH; parathyroid hormone, *Chi-squared test

Table 4. Comparison of Mean Vitamin D Levels based on Ejection Fraction

Ejection fraction (%)	Vitamin D (Mean ± SD)	P-value*
≥ 50	25.1 ± 10.8	0.1
< 50	22.3 ± 11.6	

*Independent T-test

5. Discussion

Little was found in the recent literature to determine the effects of vitamin D and PTH on coronary artery disease involvement and LVSF. Our study's most important finding was that the CAD risk in patients with vitamin D deficiency significantly differed from other groups. Moreover, CAD risk and PTH level were not related.

Our findings align with those of Chen et al., who concluded that vitamin D and PTH levels are independently associated with CAD in the Chinese elderly population (3). However, another study demonstrated that serum 25 (OH) D, PTH, and Ca levels were not associated with CAD risk (24).

The findings in this study mirror those of a previous study that linked lower levels of free 25 (OH) D with the prevalence of CV mortality independent of other CV risk factors (25). Other researchers linked PTH serum levels with CV mortality in patients with diabetes (23). Also, Palmeri et al. associated PTH levels with longer QT intervals in ACS survivors, independent of Ca concentration (20).

Table 5. Factors Affecting High SYNTAX Score (≥ 33) based on Logistic Regression

Variable		OR (CI 95%)	P-value
Age		1.03 (0.9 - 1.2)	0.05
Sex		0.7 (0.3 - 1.4)	0.3
Smoking		1.8 (0.8 - 3.6)	0.1
Diabetes		2 (1.4 - 2.4)	0.03
Hypertension		2.6 (1.1 - 8.1)	0.01
Dyslipidemia		3.3 (1.2 - 10.2)	0.02
Vitamin D level	< 20	3.4 (1.7 - 6.7)	0.001
	> 20 (REF)		
PTH level	< 40	1.8 (0.8 - 4.1)	0.12
	≥ 40 (REF)		

Abbreviations: OR; odds ratio, CI; confidence interval, PTH; parathyroid hormone

Our findings showed that vitamin D levels did not significantly impact LVSF in different groups. However, Cubbon et al. demonstrated increased mortality in chronic HF patients due to left ventricular systolic dysfunction caused by 25 (OH) D deficiency (26). Our work agrees with Arto et al. findings, where 25 (OH) D levels were not correlated with EF in children with Grave's disease (18). We found that PTH levels were not related to variations in LVSF. Consistent with this, based on Altay et al.'s findings, serum PTH levels correlated with LVEF (27). Akin et al. found that vitamin D serum levels were related to CADs (28). However, the difference with our study is that instead of the SYNTAX score, they used the Gensini score.

5.1. ***Conclusion***

This study indicates that the risk of CAD in patients with vitamin D deficiency differs from other groups, with an inverse relationship existing between CAD and vitamin D. Moreover, CAD risks did not vary according to different levels of PTH.

5.2. Ethical Approval

This study was approved by the institutional ethics committee under the ethical approval code IR.GUMS.REC.1395.230.

5.3. Informed Consent

Informed consent was obtained from all participants.

Acknowledgements

There is no acknowledgement.

Authors' Contribution

Conception and design: AM, AS, FM; data analysis and interpretation: JK, MG, AS; manuscript drafting: FM, AM, YB, MG; critical revision of the manuscript: YB, AS, FM; final approval of the manuscript: all authors.

Funding/Support

The authors have no funding/support related to the material in the manuscript.

Financial Disclosure

The authors have no financial interests related to the material in the manuscript.

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