Research Article
Volume 8:3,2020
DOI: 10.37421/jcdd.2020.8.406

Journal of Cardiovascular Diseases & Diagnosis

ISSN: 2329-9517 **Open Access**

The Relationship between Plasma Vitamin D Level and Heart Valves Calcification

Feldman Viktor K[1*], Laish-Farkash A[2], Litvak S[3], Gefel D[4], Cohen O[5] and Yosefy C[1]

[1]*Department of Orthopedics, Meir Medical center, Kfar-Saba and Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel*

[2]*Department of Cardiology, Assuta Ashdod University Medical center, The Faculty of Health Sciences, Ben-Gurion University of the Negev, Israel*

[3]*School of Nutritional Sciences, The Robert H. Smith Faculty of Agriculture, Food and Environment, the Hebrew University of Jerusalem, Rehovot, Israel*

[4]*Department of Medicine, Barzilai University Medical center, Ashkelon and The Faculty of Health Sciences, Ben-Gurion University of the Negev, Israel*

[5]*Department of Cardiology, Barzilai University Medical Center, Ashkelon and The Faculty of Health Sciences, Ben-Gurion University of the Negev, Israel*

Abstract

Background: There is conflicting data regarding the association between low levels of plasma vitamin D and ischemic heart disease (IHD). We aimed to investigate the relationship between plasma vitamin D levels and heart valve calcification in hospitalized patients with IHD versus non-IHD controls.

Methods: A prospective case control study comprising two age and gender-matched groups. The study group included consecutive patients hospitalized due to acute coronary syndrome (ACS); the control group included consecutive non- IHD patients hospitalized for non-cardiac causes. Blood samples for 25-hydroxyvitamin D level (25(OH)D) were drawn. An echocardiogram was performed during the first 3 days of hospitalization and reviewed for presence and degree of valvular calcification (VC).

Results: Forty patients with ACS and 40 controls (age 58 ± 11 years, 64% male in both groups) were included. Mean plasma 25(OH)D vitamin level in the entire cohort was 24.5 ± 8 ng/ml. Valve calcification rates were similar in ACS versus non-ACS group (28 vs. 21 had VC; 18 vs. 12 had aortic valve calcification (AVC); 21 vs. 14 had mitral valve calcification (MVC), respectively; p=NS for all). We found no significant relationship between vitamin D level and VC, AVC, or MVC rate or degree in the entire cohort and in each group alone (p=NS for all). There was a negative correlation between 25(OH)D levels and age in the ACS group (r=-0.399, p=0.012).

Conclusions: We did not find a significant relationship between plasma vitamin D levels and the rate or degree of calcification of either aortic/mitral/both valves in hospitalized patients with/without IHD.

Keywords: Vitamin D; Acute coronary syndrome; Heart valves; Aortic valve stenosis; Mitral valve stenosis

Abbreviations: IVS-D: Interventricular Septal Thickness at end Diastole; LPW-D: Left Posterior Ventricular Wall Diameter; LVEF: Left Ventricular Ejection Fraction; LVEDD: Left Ventricular End Diastolic Diameter; LVESD: Left Ventricular End Systolic Diameter; RVEDD: Right Ventricular End Diastolic Diameter; AVC: Aortic Valve Calcification; MVC: Mitral Valve Calcification; SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; CVA: Cerebrovascular Accident; NYHA: New York Heart Association; BMI: Body Mass Index; BSA: Body Surface Area; WHR: Waist Hip Ratio; ACE-I/ARB: Angiotensin-Converting Enzyme Inhibitor/Angiotensin Receptor Blocker; eGFR: estimated Glomerular Filtration Rate; SGPT: Serum Glutamic-Pyruvic Transaminase; SGOT: Serum Glutamic Oxaloacetic Transaminase; LDL: Low-Density Lipoprotein; HDL: High-Density Lipoprotein; VC: Valvular Calcification.

Introduction

Low level of plasma vitamin D [25-hydroxyvitamin D (25(OH)D)] is a worldwide pandemic. It is estimated that about a third of the world's population suffers from vitamin D deficiency [1]. There is mounting evidence stemming from epidemiological and clinical studies supporting an association between low 25(OH)D levels and ischemic heart disease (IHD) or an association with known risk factors for IHD, such as diabetes, hypertension, and obesity [2]. High vitamin D level was found to be protective against heart diseases in some studies [3], while others showed neutral effect [4,5] or even a correlation with greater risk for IHD [4]. The mechanisms by which 25(OH)D might affect the development and progression of CVD have not been fully elucidated [6]. Among the potentially relevant mechanisms are antiproliferative effect on myocardial cells, involvement in the regulation of gene expression, regulation of blood pressure, effects on glycemic control, and inflammatory cytokines [6]. Valvular calcification (VC) such as mitral valve calcification (MVC) and aortic valve calcification (AVC) are also known risk factors for IHD [7]. Valve calcification leads to a slow and progressive destruction of the valve leaflets, damaging their free mobility and function [4]. The process of valve calcification shares common mediators that also participate in the formation of atherosclerotic plaques in the coronary vessels [8]. In previous reports, our group has found an association between MVC and presence of calcium in the right coronary tree and between AVC and the presence of calcium in the left coronary tree. Thus, AVC and MVC may serve as a "window" that implies the presence of calcium in the coronary arteries as

***Address for Correspondence:** Feldman Viktor, Department of Orthopedics, Meir Medical center, Kfar-Saba and Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel, Tel: +972545401797; E-mail: viktor.feldman@clalit.org.il*

***Received:** 24 May, 2020; **Accepted:** 29 May, 2020; **Published:** 06 June, 2020*

well [9]. Moreover, previous studies have shown that lack of heart valves calcification is a much stronger predictor for the absence of IHD than gender, hypertension, or family history of coronary artery disease (CAD) [10].

We hypothesized that there is an association between the plasma 25(OH)D level and valve calcification (VC) rate or degree. We investigated whether the results are different among IHD and non-IHD patients. Since hypovitaminosis D is prevalent and easily correctable [1], establishing the relationship between plasma vitamin D level and VC may have a profound public health implication.

Methods

Study design and population

This prospective case-control study was conducted at Brazilian Medical Center in Ashkelon, southern Israel, between August 2016 and February 2017. The study protocol was approved by the hospital's Ethics Committee, and all participants signed a written informed consent form.

The study cohort comprised patients that were admitted to the internal medicine or cardiology departments. The patients were assigned to two groups. Study population group, comprising consecutive patients hospitalized due to acute coronary syndrome (ACS) [(unstable angina (UA), non-ST elevation myocardial infarction (NSTEMI), and ST elevation myocardial infarction (STEMI)], according to the ACC/AHA guidelines [11,12]. Patients were included if coronary angiography during the same hospitalization revealed at least one significant (>70%) stenosis in at least one coronary artery. The control group comprised age and gender matched participants with no history of IHD who were hospitalized in the internal medicine department due to other diseases (eg: asthma, pneumonia).

Exclusion criteria were: pregnancy and breast-feeding, rheumatic heart disease, congenital heart disease, bicuspid aortic valve, bone disease, celiac disease, cystic fibrosis, inflammatory bowel disease, liver disease, pancreatitis, adrenal disease, renal disease, thyroid disease, Whipple's disease, patients on glucocorticoids, anticonvulsants, or anti-rejection drugs treatment, consumption of vitamin D preparations, calcium or multivitamin supplements, creatinine blood levels >1.5 mg/dL, or estimated glomerular filtration rate (eGFR) <60 ml/min, missing data, refusal or difficulty to sign an informed consent.

Data collection

Demographic and medical information were collected via medical records and structured questionnaires. The following details were recorded: age, gender, background illnesses, smoking history, regular medication, and dietary supplement intake of vitamin D, calcium, or multivitamins during a one-month period prior to the hospitalization. Physical examination data included blood pressure measurement on admission, measurements of height, weight, and thigh and waist circumferences. Blood samples for complete blood count, electrolytes, and a single blood sample for 25(OH)D and parathyroid hormone (PTH) levels were drawn from each patient within three days of admission, following an overnight fast. Serum 25(OH)D level was measured using the Liaison 25(OH)D Total Assay (DiaSorin, Stillwater, MN), a direct competitive chemiluminescent immunoassay that detects vitamins D2 and D3 with a detection limit of 4.0 ng/ml. Vitamin D deficiency was defined as a 25(OH)D level of ≤ 20 ng/ml and vitamin D insufficiency as 21-29 ng/ml [3]. Plasma PTH was measured by chemiluminescent immunoassay, with the use of the Immulite 2000 Analyzer (Siemens Medical Solutions Diagnostics, LA, CA), which consists of a solid-phase, two-site enzyme-labeled immunometric assay.

Echocardiographic technique

Echocardiographic data were obtained during the first 3 days of hospitalization. 2D transthoracic echocardiography (TTE) was performed using a commercially available iE33 echo machine (Philips Medical Systems, Andover, MA). S5-1-MHz transducer was used. Standard M-mode, 2D images, and color Doppler data were acquired from the parasternal and apical views (4-, 2-, and 3-chamber) and digitally stored in cine-loop format. Echocardiography studies were reviewed for different echocardiographic parameters (including the presence of MVC or AVC, and their degrees) by two senior cardiologists that were blinded to the echocardiographic and angiography results. AVC was defined as focal areas of increased echogenicity and thickening of the leaflets without restriction of motion MVC was defined as a dense, localized, highly reflective area at the base of the posterior mitral leaflets without restriction of motion VC was defined as the presence of the criteria for MVC, AVC, or both. The degrees of calcification were scored as following:

0: No calcification;

1: Mildly calcified (small isolated spots);

2: Moderately calcified (multiple larger spots); and

3: Heavily calcified (extensive thickening and calcification of all cusps) [13].

Statistical Analysis

Data were analyzed using SPSS statistical software (SPSS, version 25.0, IBM, NY, USA). Data are presented as average ± standard deviation for continuous variables and as n (%) for non-metric parameters. Baseline patient characteristics and echocardiographic data were compared for the ACS versus the control group. For comparison between two groups in continuous parameters, we used T-test or Mann-Whitney non-parametric test, each when appropriate (according to Shapiro-Wilk test). The $\chi 2$ test was used for qualitative variables. Pearson's or Spearman correlation was used for association between continuous variables, each according to its distribution. $p<0.05$ was considered statistically significant.

Results

Patient population

Baseline characteristics of the population are shown in Table 1. Ninety-eight patients were screened for the study, 18 met one or more of the exclusion criteria and were excluded.

Table 1. Study population characteristics.

Characteristics	ACS patients (n=40)	Non-ACS patients (n=40)	p-value
Age (years)	58 ± 11	58.7 ± 11	0.86
Male sex	32 (64)	32 (64)	1
SBP (mmHg)	137.4 ± 24.7	131.7 ± 22.4	0.3
DBP (mmHg)	81.2 ± 15.0	76.9 ± 11.0	0.2
Diagnosis at admission			
UA	9 (22.5)		
STEMI	14 (35)		0.1

NSTEMI	17 (42.5)		
Medical history			
Diabetes mellitus	20 (52.6)	11 (28.2)	0.029*
NYHA Class ≥ II	1 (2.6)	2 (5.1)	1
Prior CVA	4 (10.5)	0	0.055
Chronic lung disease	1 (2.6)	1 (2.6)	1
Dyslipidemia	25 (64)	12 (31)	0.003*
Hypertension	19 (50)	11 (28)	0.05
Current smoker	15 (38.5)	11 (28)	0.33
Anthropometric Parameters			
Weight (kg)	79.2 ± 9.5	78.2 ± 15.6	0.74
Height (m)	1.7 ± 0.1	1.7 ± 0.1	0.56
BMI (kg/m^2)	27.2 ± 3.0	26.5 ± 5.6	0.51
BSA (m^2)	1.9 ± 0.1	1.9 ± 0.2	0.84
Waist circumference mean (cm)	99.4 ± 10.9	98.3 ± 11.4	0.66
Thigh circumference (cm)	94 ± 8.6	86.2 ± 17.3	0.01*
WHR	1.1 ± 0.1	1.2 ± 0.3	0.02*
Medications on admission			
Diuretics	3 (7.7)	3 (7.7)	1
ACE-I/ARB	12 (31)	2 (5.1)	0.003*
Beta blockers	11 (29)	7 (17.9)	0.25
Aspirin	18 (46.2)	7 (18)	0.008*
Coumadin	2 (5.3)	0 (0)	0.14
Laboratory studies			
Vitamin D (ng/ml)	23.0 ± 6	26 ± 9	0.12
PTH (pg/ml)	58.0 ± 31.1	60.1 ± 45.7	0.8
Glucose (mg/dL)	128.4 ± 48.5	120.7 ± 39.0	0.49
Creatinine (mg/dL)	1.0 ± 0.2	1.0 ± 0.1	0.66
Urea (mg/dL)	33 ± 9.2	30.6 ± 8.8	0.25
eGFR	83.7 ± 12.3	0.2 ± 12.6	0.25
SGPT (IU/L)	26.6 ± 11.8	29.6 ± 24.7	0.59
SGOT (IU/L)	26.8 ± 15.1	28.6 ± 17.8	0.96
Albumin (g/dL)	3.9 ± 0.4	3.9 ± 0.5	0.74
Hemoglobin (g/dL)	13.8 ± 1.3	13.9 ± 1.4	0.87
Phosphorus (mg/dL)	3.5 ± 0.5	3.5 ± 0.6	0.87
Calcium (mg/dL)	9.0 ± 0.4	8.9 ± 0.4	0. 45
Triglycerides (mg/dL)	153.7 ± 56.7	144.1 ± 67.2	0.5
Total cholesterol (mg/dL)	172.5 ± 47.6	185.2 ± 39.2	0.2
LDL (mg/dL)	106.1 ± .5	116.4 ± 31.1	0.21
HDL (mg/dL)	35.7 ± 8.4	39.8 ± 12.4	0.09
Vitamin D status			
Hypovitaminosis	33 (84.6)	27 (69.2)	0.14
Insufficiency	16 (41)	17 (43.6)	0.9
Deficiency	17 (43.6)	10 (25.6)	0.09

Note: Data are presented as n (%) or as mean ± SD. Calcification Degree: 1=No Calcification, 1=Mild Calcification, 2=Moderate Calcification; NS=Not Significant. *p<0.05

The study cohort comprised 80 patients, 40 patients with ACS and 40 age and gender matched controls. Mean age was 58 ± 11 in the ACS group and 58.7 ± 11 in the control group (p=0.86). Thirty-two (64%) of the patients were male in both groups. Among the ACS patients, 9 (22.5%) were diagnosed with UA, 17 (42%) NSTEMI, and 14 (35%) STEMI (p=0.1). In the ACS group, there were significantly more patients with diabetes mellitus, dyslipidemia, larger thigh circumference and waist-hip ratio (WHR), and tendency towards hypertension, history of CVA, and larger waist circumference. There was a significantly higher use of aspirin and ACE inhibitors in the ACS group. The mean 25(OH)D level in the entire cohort was 24.5 ± 8 ng/ml. Mean 25(OH)D level was similar in the ACS and non-ACS groups: 23 ± 6 ng/ml vs. 26 ± 9, respectively; p=0.12). Hypovitaminosis D was found in 60 patients (77%) [33 (84.6%) in ACS group and 27 (69.2%) in controls; p=0.14]. Deficiency levels were found in 17 cases (43.6%) versus 10 (25.6%) in controls (p=0.09). Insufficiency levels were found in 33 cases (42.3%) versus 16 (41%) in controls (p=0.9).

Relationship between 25(OH)D plasma level and valve calcifications

Echocardiographic characteristics are shown in Table 2. The rates of VC, AVC, and MVC were similar in ACS and non-ACS patients: 28 (72%) vs. 21 (54%) had VC (p=0.1), 18 (46%) vs. 12 (31%) had AVC (p=0.16), and 21 (54%) vs. 14 (41%) had MVC (p=0.19) (Figure 1). No significant correlation was found between mean plasma 25(OH)D level and VC rate in the entire cohort (r=-0.048, p=0.46), in the ACS group (r=-0.044, p=0.19), and in control group (r=-0.047, p=0.86). No significant correlation was found between mean plasma 25(OH)D level and AVC rate in the entire cohort (r=-0.111, p=0.06), ACS group (r=-0.1, p=0.2), and controls (r=-0.12, p=0.19). There was no significant correlation between mean plasma 25(OH)D level and MVC rate in the entire cohort (r=-0.109, p=0.16), the ACS group (r=-0.107, p=0.3), and controls (r=-0.055, p=0.6) (Figure 2).

There was no association between mean 25(OH)D level and AVC or MVC degree in the ACS or control groups [(p=0.1, p=0.19), (p=0.6, p=0.16), respectively]. No significant correlation was found between low plasma 25(OH)D level (Deficiency levels) and VC, AVC, and MVC in the entire cohort [(r=-0.044, p=0.48), (r=-0.126, p=0.68), (r=-0.055, p=0.63), respectively], in the ACS group [(r=-0.128, p=0.38), (r=-0.107, p=0.2), (r=-0.66, p=0.16), respectively], and in the controls [(r=-0.044, p=0.48), (r=-0.106, p=0.3),

(r=-0.255, p=0.12), respectively]. 25(OH)D level had negative correlation with age in the ACS group (r=-0.399; p=0.012) but not in the control group (r=-0.205; p=0.21).

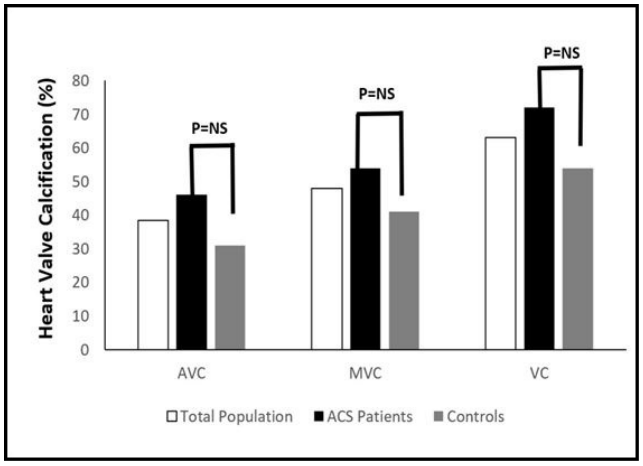

Figure 1. Distribution of VC, AVC and MVC among the entire cohort, ACS and control groups.

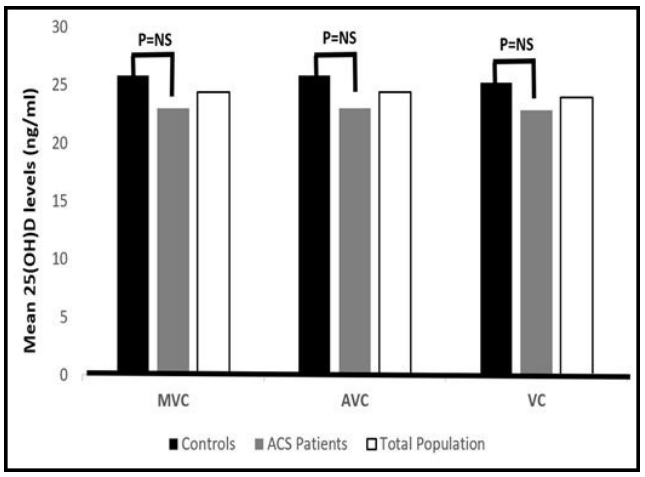

Figure 2. Mean plasma 25(OH)D level in relation to valvular calcification among the study groups.

Table 2. Echocardiographic characteristics of study population.

Characteristics	ACS patients (n=40)	Non-ACS patients (n=40)	p-value
LVEF (%)	51.1 ± 16	56.9 ± 13.7	0.1
LPW-D (mm)	9.62 ± 1.6	9.77 ± 1.4	0.64
IVS-D (mm)	10.7 ± 1.8	10.62 ± 1.8	0.9
LVEDD (mm)	51.6 ± 7.2	49.9 ± 5.5	0.2
LVESD (mm)	37 ± 10.8	33.3 ± 8.3	0.1
RVEDD (mm)	30.5 ± 4.6	31.8 ± 5.2	0.26
LVEF (mm)	51 ± 16	57 ± 14	0.09
Pulmonary pressure (mmHg)	26 ± 6	27 ± 8.9	0.58
LVEDDi	27 ± 3.7	25.9 ± 3.8	0.22
LVESDi	19.8 ± 6	17.5 ± 4.4	0.052*
VC	28 (72)	21 (54)	0.1
AVC	18 (46)	12 (31)	0.16
0	21 (54)	27 (69)	0.1
1	11 (28)	10 (26)	1
2	7 (18)	2 (5)	0.14
MVC	21 (54)	14 (41)	0.19
0	18 (46)	23 (59)	0.2
1	16 (41)	15 (38)	0.9
2	5 (13)	1 (3)	NS
Mitral insufficiency	14 (36)	13 (33)	0.76
Tricuspid insufficiency	26 (66.7)	25 (64)	0.8

Note: Data are presented as n (%) or as mean ± SD. Hypovitaminosis D (≤ 30 ng/ml), vitamin D insufficiency (21-29 ng/ml), Vitamin D deficiency (≤ 20 ng/ ml). *p<0.05

Discussion

To the best of our knowledge, this is the first study that tested the association between plasma vitamin D levels and calcification of the cardiac valves in the sunny climate of the Middle East. We found no significant relationship between plasma vitamin D levels and the rate or degree of calcification of heart valves in either patients with IHD or in patients without IHD.

Previous studies showed an association between valve and coronary calcification, suggesting that AVC and MVC might be predictive for the presence of calcium in the coronary arterial tree [9]. Moreover, studies have shown that the lack of valvular calcification is a much stronger predictor for the absence of IHD than gender, hypertension, or family history of CAD [14]. Scragg et al. found significantly lower 25(OH)D levels in patients with myocardial infarction compared to controls [15]. Giovannucci et al. showed that during a 10-year follow up, men with vitamin D deficiency were at significantly higher risk of developing myocardial infarction compared to those with sufficient levels of vitamin D [3]. Schmidt-Gayk et al. noted that serum levels of 25(OH)D were not elevated in patients with myocardial infarction [4].

Contrary to other studies that showed the opposite, Linden et al. reported that patients with myocardial infarction appear to have a higher intake of vitamin D than controls [5] and Rajasree et al. found that elevated 25(OH)D levels (above 89 ng/ml) are a multivariate-adjusted risk factor for IHD [16].

This discrepancy may be explained by experimental animal models, in which both excessive and insufficient vitamin D concentrations were associated with atherosclerosis formation. Alternatively, this could be due to the different cut-off levels used to define vitamin D deficiency in the previous studies [14].

We found no significant relationship between plasma 25(OH)D level and VC, AVC, and MVC rate or degree in hospitalized patients with established IHD and in patients without IHD. Moreover, 25(OH)D levels were similar in ACS and non-ACS patients in the population of this study. Our findings may be limited due to the relatively small population size, which limited the statistical power.

Inpatients are more likely to have medical conditions associated with vitamin D deficiency. Therefore, in this study, we used strict inclusion and exclusion criteria to exclude any medical state known to affect the vitamin D status. Acute illness could suppress endogenous vitamin D synthesis, but the half-life of serum 25(OH)D is approximately 3 weeks [17], and thus its level could not have been influenced by a short period of illness prior to obtaining the blood samples in the present study. A single serum 25(OH)D measurement is considered by some to understate the predictive power of 25(OH)D, as it cannot fully capture cumulative vitamin D exposure [18], failing to consider the intra-individual seasonal variation in plasma 25(OH)D levels. Vitamin D levels are largely affected by the season of the year, even in countries with subtropical climates such as Israel: at the end of the summer and beginning of fall, vitamin D levels are at their peak, and at the end of winter and the beginning of spring, they are at their lowest point [11,12]. This is due to the angle of the sun, which is altered such that the UVB light reaching the skin is below the necessary range for vitamin D synthesis. Cloud cover and more layers of clothing during the winter further decrease skin exposure to UVB [11]. On the other hand, Platz et al. found the correlation coefficient between two measurements of vitamin D taken 3 years apart to be moderately high, which may indicate that a single serum measurement of this compound can still be a useful tool in epidemiological studies [19].

We used structured questionnaires and strict inclusion and exclusion criteria to minimize the factors affecting 25(OH)D status and its relation to valvular calcification. However, we cannot absolutely rule out the possibility of residual confounding factors. A combination of a baseline blood 25(OH)D concentration with data about lifetime diet, and sunlight exposure could likely be the best way to estimate vitamin D status throughout a person's lifetime [19], which could allow us to draw a more precise conclusion about the individual's real 25(OH)D status.

The gold standard for determination of valvular calcification degree is an ECG-gated multi-detector CT (MDCT). Very high correlation between MDCT and TEE was established by recent studies; therefore, we believe that the echocardiographic data in this study was accurate [9]. We could not rule out the possibility that some controls may have had an asymptomatic IHD.

Even though Israel is close to the geographic equator and has abundant sunshine throughout the year, we found a high prevalence of hypovitaminosis D. This has been previously described in sub-populations at risk, such as the elderly, institution residents [20], and immigrants from sunny countries [21]. The present study focused on hospitalized patients, which represents a more general and diverse population [8]. A previous study conducted by Hochwald et al. [6] found a high rate of hypovitaminosis D among inpatients in Israel. Our data shows that hypovitaminosis D is common in the sunny climate of Israel not only among at-risk populations and supports the findings of previous studies conducted in other sunny countries [12].

Although a consensus regarding the optimal level of blood 25(OH)D has yet to be established, most experts agree that it should be at least 30 ng/ml [14]. We found no differences between 25(OH)D levels per category (deficiency and insufficiency) among the study and control populations (Table 1). There was no correlation between low (deficiency) 25(OH)D levels and valvular calcification of any type. We believe that the criteria we used to categorize vitamin D levels as sufficiency, deficiency, and insufficiency could partially account for the results. As different cut-off levels are used in the literature, it is difficult to compare our findings with those of previous publications.

Statistical analysis revealed an inverse correlation between age and plasma vitamin D levels that was significant in the ACS patients' group. The elderly are at particular risk for vitamin D deficiency or insufficiency due to a combination of decreased skin 7-DHC (the precursor for cutaneous synthesis of vitamin D), decreased mobility or institutionalization that discourage sun exposure, decreased renal production of 25(OH)D, and decreased intake of fortified foods. According to the literature, NSTEMI patients tend to be older and have more prior cardiac morbidity and non-cardiac diseases than STEMI patients [22]. In this study, the population size was not large enough for statistical testing, thus a possible link needs to be tested in larger studies.

Conclusion

Factor Xa inhibitors are approved for the prevention of clot formation in non-valvular atrial fibrillation and for treating deep venous thromboembolism and pulmonary embolism. These classes of medications are known CYP3A4 and CYP2J2 inhibitors vulnerable to drug-drug interactions and are known to be risk factors for GI bleeding. Although not a common finding, these medications are possible risk factors for acute liver injury, as seen in our patient. Our case serves to raise awareness of the potential risk of acute liver injury in Factor Xa Inhibitors and to open the door for further studies on whether there is an increased risk of liver injury in Eastern Asian people. Hypovitaminosis D is prevalent in hospitalized patients, despite the sunny climate in our country. Plasma 25(OH)D levels are similar in patients with IHD and patients without IHD. Plasma 25(OH)D level is not associated with the rate or with the degree of VC, AVC, or MVC in patients with or without IHD. Moreover, no correlation exists between low 25(OH)D and valve calcification in patients with or without IHD. Patient age is a risk factor for hypovitaminosis D in IHD patients. Larger, further investigations are warranted to test the link between vitamin D status and valvular calcification.

Highlights

1) There is no correlation between plasma vitamin D level and the rate of Aortic and Mitral valve calcification.

2) Vitamin D levels are similar in hospitalized patients with established ischemic heart disease and non-cardiac hospitalized patients.

3) Inverse correlation exists between age and plasma vitamin D levels in patients with ischemic heart disease but not in the non-cardiac patients.

Key Messages

There is conflicting data regarding the association between low levels of plasma vitamin D and ischemic heart disease.

1) Vitamin D levels are similar in hospitalized patients with established ischemic heart disease and non-cardiac hospitalized patients.

2) There is no significant relationship between plasma vitamin D levels and the rate or degree of calcification of either aortic/mitral/both valves in hospitalized patients with/without IHD

3) Patient age is a risk factor for hypovitaminosis D in patients with ischemic heart disease but not in non-cardiac patients.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflicts of Interest

Authors have no conflict of interest to declare.

References

1. Michael F. Holick, "Vitamin D Deficiency Medical Progress Michael F. Holick." *N Engl J Med* 357 (2007): 266-281.

2. Kendrick, Jessica, Giovanni Targher, Gerard Smits, and Michel Chonchol. "25-Hydroxyvitamin D deficiency is independently associated with

cardiovascular disease in the Third National Health and Nutrition Examination Survey." *Atherosclerosis* 205 (2009): 255-260.

3. Giovannucci, Edward, Yan Liu, Bruce W. Hollis, and Eric B. Rimm. "25-hydroxyvitamin D and risk of myocardial infarction in men: A prospective study." *Arch Intern Med* 168 (2008): 1174-1180.
4. Schmidt-Gayk, H., J. Goossen, F. Lendle, and D. Seidel. "Serum 25-hydroxycalciferol in myocardial infarction." *Atherosclerosis* 26 (1977): 55-58.
5. Lindén, Victor. "Vitamin D and myocardial infarction." *Br Med J* 3 (1974): 647-650.
6. Li, Yan Chun, Juan Kong, Minjie Wei, and Zhou-Feng Chen, et al. "1,25-Dihydroxyvitamin D 3 is a negative endocrine regulator of the renin-angiotensin system." *J Clin Invest* 110 (2002): 229-238.
7. Hochwald, Ori, Ilana Harman-Boehm, and Hana Castel. "Hypovitaminosis D among inpatients in a sunny country." *Isr Med Assoc J* 6 (2004): 82-87.
8. Bostick, Roberd M., Lawrence H. Kushi, Ying Wu, and Katie A. Meyer, et al. "Relation of calcium, vitamin D, and dairy food intake to ischemic heart disease mortality among postmenopausal women." *Am J Epidemiol* 149 (1999): 151-161.
9. Yosefy, Chaim, Ariela Malushitsky, Jafary Jamal, and Gideon Sahar, et al. "Association between mitral and aortic valve calcification and preferential left or right coronary artery disease." *J Heart Valve Dis* 18 (2009): 627-633.
10. Thomas, Melissa K., Donald M. Lloyd-Jones, Ravi I. Thadhani, and Albert C. Shaw, et al. "Hypovitaminosis D in medical inpatients." *N Engl J Med* 338 (1998): 777-783.
11. Bolland, Mark J., Andrew B. Grey, Ruth W. Ames, and Barbara H. Mason, et al. "The effects of seasonal variation of 25-hydroxyvitamin D and fat mass on a diagnosis of vitamin D sufficiency." *Am J Clin Nutr* 86 (2007): 959-964.
12. Unger, Marianna D., Lilian Cuppari, Silvia M. Titan, and Maria Cláudia T. Magalhães, et al. "Vitamin D status in a sunny country: Where has the sun gone?." *Clin Nutr* 29 (2010): 784-788.
13. Kizer, J. R., Warren B. Gefter, Andrew S. DeLemos, and Benjamin J. Scoll, et al. "Electron beam computed tomography for the quantification of aortic valvular calcification." *J Heart Valve Dis* 10 (2001): 361-366.
14. Bischoff-Ferrari, Heike A., Edward Giovannucci, Walter C. Willett, and Thomas Dietrich, et al. "Estimation of optimal serum concentrations of 25-hydroxyvitamin D for multiple health outcomes." *Am J Clin Nutr* 84 (2006): 18-28.
15. Scragg, Robert, Rodney Jackson, Ian M. Holdaway, and Thomas Lim, et al. "Myocardial infarction is inversely associated with plasma 25-hydroxyvitamin D3 levels: a community-based study." *Int J Epidemiol* 19 (1990): 559-563.
16. Rajasree, S., K. Rajpal, C. C. Kartha, and P. S. Sarma, et al. "Serum 25-hydroxyvitamin D 3 levels are elevated in South Indian patients with ischemic heart disease." *Eur J Epidemiol* 17 (2001): 567-571.
17. Millen, Amy E., and Lisa M. Bodnar. "Vitamin D assessment in population-based studies: a review of the issues." *Am J Clin Nutr* 87 (2008): 1102S-1105S.
18. Rosenhek, Raphael, Thomas Binder, Gerold Porenta, and Irene Lang, et al. "Predictors of outcome in severe, asymptomatic aortic stenosis." *N Engl J Med* 343 (2000): 611-617.
19. Platz, Elizabeth A., Michael F. Leitzmann, Bruce W. Hollis, and Walter C. Willett, et al. "Plasma 1, 25-dihydroxy-and 25-hydroxyvitamin D and subsequent risk of prostate cancer." *Cancer Causes Control* 15 (2004): 255-265.
20. Zamboni, Mauro, Elena Zoico, Paolo Tosoni, and Alessandra Zivelonghi, et al. "Relation between vitamin D, physical performance, and disability in elderly persons." *J Gerontol A Biol Sci Med Sci* 57, (2002): M7-M11.
21. Ginat-Israeli, Talia, Zvi Dranitzki, and Uri Straus. "Nutritional rickets in infants immigrating to Israel from Ethiopia." *Isr Med Assoc J* 5 (2003): 291-292.
22. Bode, Christoph, and Andreas Zirlik. "STEMI and NSTEMI: The dangerous brothers." *Eur Heart J* (2007): 1403-1404.

How to cite this article: Feldman Viktor K., Laish-Farkash A, Litvak S, and Gefel D, et al.. "The Relationship between Plasma Vitamin D Level and Heart Valves Calcification". J Cardiovasc Dis Diagn 8 (2020) doi: 10.37421/jcdd.2020.8.406