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The Association Between the Serum Level of 25-Hydroxy Vitamin D and the Echocardiographic Indices of Left Ventricular Function in Patients With no Significant Coronary Artery Disease

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Abstract

Objectives: Multiple studies have shown that vitamin D deficiency can increase the risk of cardiovascular disorders. However, the role of vitamin D in increasing the risk of coronary atherosclerotic disorders and cardiac dysfunction is yet unknown. Accordingly, the present study aimed to assess the relationship between the serum level of vitamin D and the echocardiographic indices of the left ventricular (LV) function or valvular defects.

Materials and Methods: This cross-sectional study was performed on 80 consecutive patients who were the candidate for diagnostic coronary angiography and demonstrated a sign of slow coronary flow (SCF) or minimal coronary artery disease (CAD) while without any evidence of CAD. The serum level of 25-hydroxy vitamin D was measured by ELISA (enzyme-linked immunosorbent assay) method. Finally, patients were evaluated by transthoracic 2D, Doppler echocardiography, and tissue Doppler imaging in order to investigate the systolic and diastolic function of the left ventricle.

Results: Based on angiography reports, 36.2% of patients had normal coronaries while 50.0%, 7.6%, and 6.2% of them were diagnosed with isolated minimal CAD, isolated SCF, and a combination of minimal CAD and SCF, respectively. In addition, the mean serum level of 25-hydroxy vitamin D in our patients was 30.33 ± 19.27. Further, the mean level of this parameter was 29.37 ± 22.16, 30.39 ± 16.22, 18.24 ± 4.32, and 44.65 ± 25.52 in the normal coronary group, as well as patients with isolated minimal CAD, concurrent minimal CAD and SCF, and those with isolated SCF, respectively, indicating no significant difference among the groups regarding 25-hydroxy vitamin D concentration ($P=0.147$). Furthermore, the level of 25-hydroxy vitamin D had no relationship with the echocardiography indices of the LV function or valvular defects.

Conclusions: In general, the serum level of 25-hydroxy vitamin D may not be a predictive factor for the LV function or valvular defects.

Keywords: 25-Hydroxy vitamin, LV diastolic function, LV systolic function slow coronary flow, Coronary artery disease

Introduction

The role of vitamin D is fundamentally well-known in bone metabolism. In other words, it plays a role as the most important metabolic component in maintaining calcium homeostasis through the digestive intake of calcium (1). Discovering the presence of vitamin D receptors on many body cells such as immune, vascular, and cardiovascular cells demonstrates the possibility of the involvement and participation of this vitamin in other vital organs (2). Based on this evidence, extensive research has highlighted vitamin D as a major contributor to the pathogenesis of many non-musculoskeletal disorders such as infectious or inflammatory disease, cancers, or cardiovascular diseases (2).

The relationship between vitamin D and various risk factors of heart disease has been very noticeable in recent years. Various observational studies and some clinical intervention studies have investigated the likelihood of a relationship between vitamin D deficiency, as well as coronary heart disease progression and its risk factors (3, 4). Some studies indicated increased mortality and cardiac morbidity with vitamin D deficiency (5). In addition, a decrease in the serum levels of vitamin D was associated with inflammation, an increase in coronary artery calcium score, endothelial dysfunction, and vascular stiffness (6, 7). Previous evidence suggests that vitamin D and calcium supplements can not only control the risk factors of cardiovascular diseases such as hypertension, metabolic syndrome, and diabetes but also can reduce various cancers (8,9). According to a previous study, one year of high-dose vitamin D_3 supplementation had significant and clinically relevant improvements in the secondary outcomes of left ventricular ejection fraction (LVEF) and left ventricular (LV) dimensions and volumes (10), representing that vitamin D has a beneficial effect in reverse remodeling (11). Further, a significant increase

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in the serum B-type natriuretic peptide levels and the impairment of cardiac systolic and diastolic function was observed in vitamin D deficient patients using tissue Doppler imaging measures (12). However, another study demonstrated that vitamin D deficiency was not related to LV diastolic dysfunction (13).

Overall, the role of vitamin D_3 in coronary heart disease remains unclear and controversial results require more precise studies to determine the role of vitamin D_3 in the development of coronary artery disease (CAD). Moreover, few studies are available about the role of vitamin D deficiency in the occurrence of a slow coronary flow (SCF) phenomenon. Therefore, the present study sought to evaluate the critical role of vitamin D deficiency in increasing the likelihood of SCF and minimal CAD.

Materials and Methods

The current cross-sectional study was conducted on a total of 80 consecutive patients who were the candidate for diagnostic coronary angiography. These patients showed no sign of CAD except for some evidence of SCF or minimal CAD. In this regard, SCF was defined as late opacification in the epicardial coronary arteries without significant stenosis which was manifested by corrected thrombolysis in myocardial infarction frame count >27 with a correction factor of 1.7 for the left anterior descending coronary artery based upon images acquired at 30 frames/seconds. Minimal CAD was also defined as less than 50% narrowing of any coronary artery. In our study, the exclusion criteria were a history of using calcium or vitamin D supplementations, some evidence of liver or kidney dysfunction, pregnancy, a history of myocardial infarction, breastfeeding, and a history of taking antiepileptic drugs.

Prior to performing angiography, a questionnaire was administered to collect data related to demographic characteristics, the history of hypertension, diabetes and dyslipidemia, smoking and drug use. A day after angiography, venous blood samples were taken to measure the serum levels of 25-hydroxy vitamin D, fasting blood sugar, and lipid profiles before receiving any medications. Furthermore, the serum lipids including triglyceride, total cholesterol, and high-density lipoprotein were estimated by enzymatic method Pars Azmoon kit (Pars Azmoon Inc., Iran). Additionally, 25-hydroxy vitamin D level was measured by the ELISA (enzyme-linked immunosorbent assay) technique. In this study, 25-hydroxy vitamin D level less than or equal to 21 ng/mL and was considered as deficiency and values higher than this amount was considered normal. Eventually, the systolic and diastolic functions of the left ventricle were evaluated using transthoracic 2D, Doppler echocardiography, and tissue Doppler imaging.

The obtained data were presented as mean ± standard deviation. Categorical variables were compared by chi-square or Fisher exact test. Mann- Whitney U test or *t* test was used to compare the quantitative variables as well. Similarly, the relationship between quantitative variables was assessed using Pearson's or Spearman's correlation. All analyses were conducted in SPSS, version 16 (SPSS Inc., Chicago, IL). *P* values of 0.05 or less were considered statistically significant.

Results

In total, 80 patients (including 38.8% males) were included in the study, with a mean age of 54.02 ± 11.52 years and a mean body mass index (BMI) of 28.84 ± 5.09 years. Regarding cardiovascular risk factors, 56.2%, 21.2%, and 5.0% were hypertensive, diabetic, and hyperlipidemic, respectively. A family history of cardiovascular disorders was revealed in 1.2% as well. With regard to oral medications, the use of diuretics, calcium channel blockers, anti-diabetic drugs, beta channel blockers, angiotensin-converting enzyme inhibitors, statins, and aspirin was found in 17.5%, 6.2%, 21.2%, 35.0%, 33.8%, 27.5%, and 33.8%, respectively (Table 1). Based on angiography reports, 36.2% had normal coronaries while 50.0%, 7.6%, and 6.2% of the patients were diagnosed with isolated minimal CAD, isolated SCF, and a combination of minimal CAD and SCF, respectively. In the echocardiography assessment of LV functional state, the mean LV ejection fraction, the LV ventricular end-systolic diameter, the mean LV end-diastolic diameter, and the mean e/e' were 50.14 ± 9.94%, 3.56 ± 0.73 mm, 5.08 ± 0.72 mm, and 10.46 ± 5.64, respectively. Likewise, the mean e' velocity, the mean Tei index, the mean declaration time, and the mean tricuspid annular plane systolic excursion were 7.63 ± 2.71, 0.50 ± 0.19, 343.76 ± 110.68, and 2.01 ± 0.88 as well. In addition, as regards valvular disorders, 51.2%, 20.0%, and 17.5% of the patients suffered from

Table 1. Basic Characteristics of Patients

Characteristics	
Sex, No.(%)	
Male	31 (38.8)
Female	49 (61.2)
Mean age	54.02±11.52
Mean BMI (kg/m^2)	28.84±5.09
Risk factors, No.(%)	
Hypertension	45 (56.2)
Hyperlipidemia	4 (5)
Diabetes mellitus	17 (21.2)
Smoking	9 (11.2)
Positive family history	1 (1.2)
Drug history, No.(%)	
Diuretic use	14 (17.5)
CCB use	5 (6.2)

BMI: body mass index; CCB: calcium channel blockers.

Table 2. Cardiac Indices

Angiography results	
Normal	29 (36.2%)
Minimal CAD	40 (50%)
Slow flow	6 (7.5%)
Minimal CAD + slow flow	5 (6.2%)
Echocardiographic data	
Mean LVEF	50.14±9.94
Mean LVEDD	5.08±0.72
Mean LVESD	3.56±0.73
Mean e/e'	10.46±5.46
Mean e' velocity	7.63±2.71
Mean Tei index	0.50±0.19
Mean declaration time	110.68± 343.76
Mean TAPSE	2.01±0.88
Valvular involvement	
MR	41 (51.2%)
TR	16 (20%)
AI	14 (17.5%)

CAD: Coronary artery disease; LVEF: Left ventricular ejection fraction; LVEDD: Left ventricular end-diastolic diameter; TAPSE: Tricuspid annular plane systolic excursion; MR: Mitral regurgitation; TR: Tricuspid regurgitation; AI: Aortic insufficiency.

Table 3. The Serum Level of 25-Hydroxy Vitamin D Based on the Presence or Absence of Cardiovascular Risk Factors or the Use of Medications

Factor	Group With Condition	Group Without Condition	*P* Value
Male gender	29.83±16.68	30.63±20.90	0.858
Age > 60 year	30.34±20.80	30.30±15.76	0.992
Hypertension	30.36±20.49	30.29±17.87	0.988
Hyperlipidemia	41.48±18.44	29.74±17.04	0.238
Diabetes mellitus	33.42±27.04	29.49±16.77	0.459
Smoking	32.01±21.78	30.11±19.09	0.783
Diuretic use	27.26±16.06	30.97±19.93	0.516
Calcium blocker use	34.74±13.42	30.03±19.63	0.600
Anti-diabetic use	27.77±17.44	31.02±19.81	0.541
Beta-blocker use	30.12±17.71	30.43±20.22	0.946
ACE inhibitor use	31.83±21.99	29.56±17.90	0.622
Statin use	29.65±24.50	30.58±17.12	0.848
Aspirin use	26.24±12.15	32.41±21.85	0.178

ACE, Angiotensin-converting enzyme.

mitral regurgitation, tricuspid regurgitation, and aortic insufficiency, respectively (Table 2).

The mean serum level of 25-hydroxy vitamin D in our patients was 30.33 ± 19.27. As shown in Table 3, the level of 25-hydroxy vitamin D relied on no baseline variables including gender, age, BMI, the presence of traditional cardiovascular risk factors, or cardiovascular-related medications. Further, Table 4 summarizes the data related to the serum level of 25-hydroxy vitamin D based on the coronary artery condition and valvular heart disease. As presented, the mean level of 25-hydroxy vitamin D was 29.37 ± 22.16, 30.39 ± 16.22, 18.24 ± 4.32, and 44.65 ± 25.52 in the normal coronary group, as well as in patients with isolated minimal CAD, concurrent minimal CAD and SCF, and those with isolated SCF. Accordingly, no difference was observed regarding 25-hydroxy vitamin D concentration among the groups (*P*=0.147). Furthermore, no relationship was found between serum vitamin D level and coronary artery condition (Figure 1). As indicated in Tables 4 and 5, the level of 25-hydroxy vitamin D was not related to the echocardiography indices of the LV function or valvular defects.

Table 4. The Serum Level of 25-Hydroxy Vitamin D Based on the Coronary Artery Condition and Valvular Heart Disease

Coronary Artery Condition	Level of Vitamin D
Normal	29.37±22.16
Minimal CAD	30.39±16.22
Minimal CAD+ slow flow	18.24 ±4.32
Isolated slow flow	44.65±25.52
Valvular pathology	
MR	17.17±29.52
TR	27.01±15.48
AI	35.42±23.48

CAD: Coronary artery disease; MR: Mitral regurgitation; TR: Tricuspid regurgitation; AI: Aortic insufficiency.

Table 5. The Association Between the Serum Level of 25-Hydroxy Vitamin D and Cardiac Functional Parameters

Factor	R Coefficient	*P* Value
LVEF	-0.051	0.653
LVEDD	0.172	0.126
LVESD	0.023	0.841
e/e'	-0.022	0.847
e' velocity	-0.095	0.452
Tei index	-0.155	0.171
Declaration time	0.050	0.663
TAPSE	0.038	0.738

LVEF: Left ventricular ejection fraction; LVEDD: Left ventricular end-diastolic diameter; LVESD: Left ventricular end-systolic diameter; TAPSE: Tricuspid annular plane systolic excursion.

Discussion

Various studies investigated vitamin D deficiencies and the increased risk of cardiovascular disorders, especially in relation to coronary atherosclerotic disorders and cardiac dysfunction. Based on the findings, the administration of vitamin D supplements through the inhibitory effect on inflammatory and oxidative processes can prevent the development of coronary artery atherosclerosis. However, what has so far been questioned, also mentioned in the present study, is the difference in the serum levels of this vitamin between normal individuals and the groups of

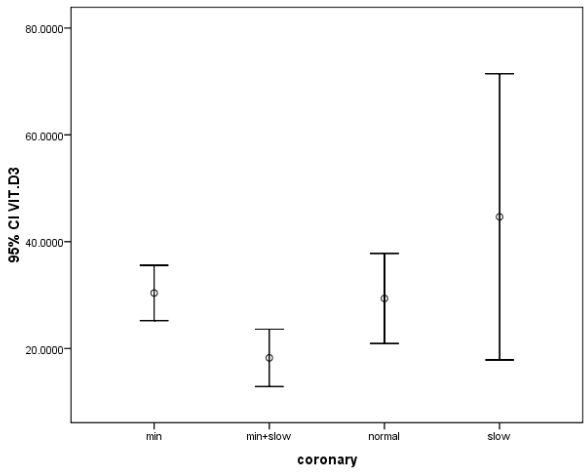

Figure 1. The Mean Serum Level of 25-hydroxy Vitamin D According to Coronary Artery Condition.

people with minimal CAD and SCF. Based on angiographic findings of this study, there was no difference in the level of vitamin D between the patient groups and healthy controls. Moreover, no relationship was observed between the serum level of vitamin D and the severity of cardiac systolic and diastolic dysfunction.

First, it seems that the magnitude of vascular pathology in the minimal CAD was less than that involving the reabsorption or the metabolism processes of vitamin D. In other words, in the stages prior to significant coronary atherosclerosis, vitamin D levels were not disturbed and vitamin D deficiency was related to the onset of relevant coronary heart disease. However, knowing whether vitamin D supplements prevent the progression of both coronary artery phenomena (i.e., minimal CAD and SCF) is a matter of importance.

In the present study, there was no relationship between vitamin D levels and SCF or minimal CAD. Furthermore, the LV systolic and diastolic function evaluated by conventional 2D, and Doppler method and tissue Doppler imaging showed no significant differences between the groups.

Contrarily, some studies have strongly confirmed this relationship. For example, Oz et al (14) found a strong correlation between vitamin D deficiency with SCF and endothelial dysfunction in subclinical atherosclerosis. It is noteworthy that we failed to find a similar study in this regard thus the relationship between cardiac dysfunction and vitamin D levels would require further evaluation.

Conclusions

Based on the findings, no pathogenic relationship was observed between vitamin D deficiency and SCF or minimal CAD. It seems that vitamin D deficiency plays no role in the early stages of coronary atherosclerosis as minimal CAD. Studies in this regard are very limited and thus further evaluation is reasonable, especially at the pathologic level.

This study was limited by a small number of patients, therefore, multicenter studies with an adequate number of patients are required to for further delineate the relationship between the serum vitamin D level and myocardial function. Additionally, tissue Doppler imaging is angle-dependent thus using newer echocardiographic modalities for the assessment of systolic and diastolic function including strain rate imaging can be more accurate.

Conflict of Interests

Authors have no conflict of interests.

Ethical Issues

Ethical issues have been completely observed by the authors.

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