

Association between 25-hydroxy vitamin D deficiency and severity of coronary artery involvement

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Introduction

The crucial role of vitamin D deficiency on coronary calcification has been recently suggested [1]. In this regard, some mediating mechanisms explained in the role of vitamin D deficiency include an increased risk for hypertension and insulin resistance, thickening of the arterial walls, increased risk for respiratory disorder, activation of inflammatory markers, as well as an increased risk for arterial calcification or hardening. It has been shown that a reduction of vitamin D levels lower than 30 ng/ml may increase the risk for coronary artery disease [2, 3]. With regard to association between vitamin D deficiency and coronary artery disease, it has been shown a negative association between serum 1,25-vitamin D levels and amounts of vascular calcification [4]. This data suggests a potential role for endogenous 1,25-vitamin D in an inhibition of vascular calcification and thus increasing serum level of vitamin D can effectively reduce coronary calcification, leading to a reduced risk of calcified coronary atherosclerotic lesions [5].

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ABSTRACT

Objective: The evident data is insufficient in explaining association between the serum level of vitamin D and an occurrence of severe coronary artery disease. Vitamin D deficiency has been linked to an increased risk of coronary artery disease (CAD) and cardiovascular (CV) death. We aimed to investigate whether serum 25-hydroxy vitamin D was associated with severity of coronary artery involvement.

Methods: 341 patients fulfilled the criteria of the Rose questionnaire and Minnesota codes on coronary artery disease were consecutively included into this cross-sectional survey. The number of involved coronary vessels were assessed by reviewing the coronary angiography reports. 25-hydroxy vitamin D was measured by radioimmunoassay.

Results: Lower 25-hydroxy vitamin D was found in those with more severe coronary disease (normal coronary condition 26.78 ± 17.07 , one-vessel 17.70 ± 14.31 ng/ml, two-vessel 17.49 ± 16.10 ng/ml, and three-vessel 16.04 ± 12.17 ng/dl, $p=0.029$). The prevalence rate of vitamin D deficiency in a normal coronary state, single-vessel disease, two-vessel disease, and three-vessel disease were 31.2%, 72.9%, 73.9%, 78.7% respectively ($p=0.001$). The level of vitamin was adversely associated only with serum triglyceride level ($r = -0.156$, $p = 0.005$), but not with other lipid profiles or FBS. Also, the serum level of 25-hydroxy vitamin D was directly correlated with patients' age ($r = 0.203$, $p < 0.001$).

Conclusions: Vitamin D deficiency can predispose to develop coronary artery involvement and progress coronary atherosclerosis.

KEY WORDS:

Coronary artery
25-hydroxy vitamin D
deficiency

Histological investigations have discovered some mechanisms for vitamin D deficiency for progressing vascular wall changes. In fact, 1,25-Vitamin D is known to regulate the deposition of calcium in the axial skeleton, and the current data suggest it may regulate the deposition of calcium in the vascular wall as well [6]. Also, low serum levels of 25-hydroxyvitamin are associated with insulin

resistance and metabolic syndrome, two important risk factor for development of coronary atherosclerosis [7]. In total, lower vitamin D levels have been associated with CVD, hypertension, diabetes, high-density lipoprotein cholesterol and low-density lipoprotein (LDL) cholesterol, and surrogate measurements of cardiovascular risk such as coronary artery calcification [8,9]. However, the evident data is insufficient in explaining association between the serum level of vitamin D and an occurrence of severe coronary artery disease. We aimed to investigate whether serum 25-hydroxyvitamin D was associated with severity of coronary artery involvement.

Materials and methods

All patients fulfilled the criteria of the Rose questionnaire and Minnesota codes on coronary artery disease were consecutively included into this cross-sectional survey. The exclusion criteria were a history of surgery within 6 months ago or having hematologic disease or any haemoglobinopathy or coagulopathy, a history of chronic clinical conditions such as liver, kidney disease or malignancies, or a history of cerebrovascular disease or other simultaneous cardiovascular disorders. All baseline information including demographic characteristics, cardiovascular risk factors, medications, or laboratory parameters, were collected from the hospital recorded files. The numbers of involved coronary vessels were assessed by reviewing the coronary angiography reports, the presence and severity of coronary disease was determined using the number of coronary artery involvement and left main lesion. Also, 25-hydroxy vitamin D was measured by radioimmunoassay and using proper kit. Vitamin D deficiency was defined as levels <20 ng/ml.

Statistical analysis

Results were presented as mean \pm standard deviation (SD) for quantitative variables and were summarized by absolute frequencies and percentages for categorical variables. Categorical variables were compared using chi-square test or Fisher's exact test when more than 20% of cells with an expected count of less than 5 were observed. Quantitative variables were also compared with the Mann-Whitney U

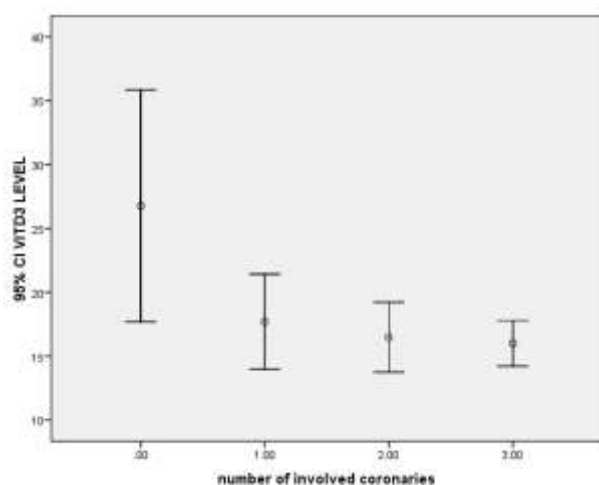
test. To determine the association between the level of 25-hydroxy vitamin D and other quantitative variables, the Pearson or Spearman correlation test was applied. Statistical significance was determined as a p value of ≤ 0.05 . All statistical analysis was performed using SPSS software (version 19.0, SPSS Inc., Chicago, Illinois).

Results

Totally, 341 patients (mean age 61.08 ± 9.71 years, ranged 32 to 85 years, 74.5% male) were assessed. The mean body mass index was 26.30 ± 3.42 kg/m². Regarding cardiovascular risk factors, 36.4% were diabetics, 28.4% were hypertensive, and 44% were smokers. The mean serum level of triglyceride was 147.48 ± 69.44 mg/dl, the mean HDL level was 37.17 ± 7.60 mg/dl, the mean LDL level was 99.04 ± 33.85 mg/dl, and the mean serum FBS was 136.41 ± 59.52 mg/dl. On admission, 42.8% were admitted with NSTEMI pattern, 22.3% with STEMI pattern, 29.0% as unstable angina, and 5.9% as stable angina. Overall, 94.1% were initially diagnosed with acute coronary syndrome. Among those with STEMI pattern, 63.2% had anterior wall infarction, 30.3% had inferior wall infarction, and others had lateral wall involvement. Regarding severity of coronary artery disease, 17.3% had single-vessel disease, 25.5% had two-vessel disease, 0.3% had two vessels involvement with left main lesion, 49.9% had three-vessel disease, and 2.3% had three vessels involvement with left main lesions. Mean serum level of vitamin D was 17.21 ± 14.00 ng/ml. In this regard, 74.2% had vitamin D deficiency.

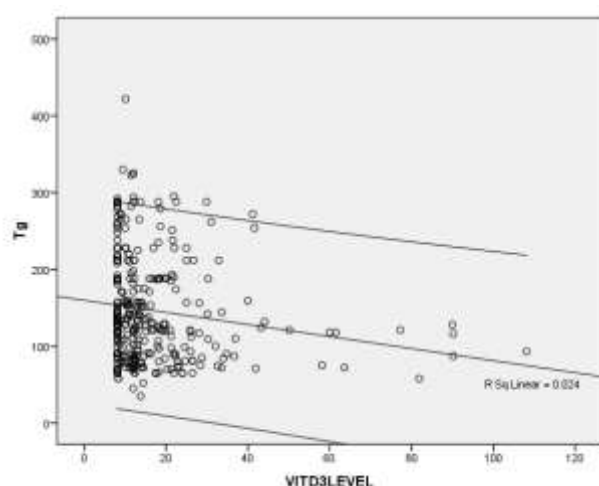
Regarding the association between coronary disease severity and the serum level of vitamin D, lower 25-hydroxy vitamin D was found in those with more severe coronary disease (normal coronary condition 26.78 ± 17.07 , one-vessel 17.70 ± 14.31 ng/ml, two-vessel 17.49 ± 16.10 ng/ml, and three-vessel 16.04 ± 12.17 ng/dl, $p = 0.029$) (Figure 1). The prevalence rate of vitamin D deficiency in a normal coronary state was 31.2%, in single-vessel disease was 72.9%, in two-vessel disease was 73.9%, and in three-vessel disease was 78.7% ($p = 0.001$).

Figure 1. Mean serum 25-hydroxy vitamin D according to the number of coronary diseases.



With respect to the association between serum level of 25-hydroxy vitamin D and laboratory markers, the level of vitamin D was adversely associated only with serum triglyceride level ($r = 0.156$, $p = 0.005$), but not with other lipid profiles or FBS (Figure 2). Also, the serum level of 25-hydroxy vitamin D was directly correlated with the patients' age ($r = 0.203$, $p < 0.001$).

Figure 2. Association between serum 25-hydroxy vitamin D and serum triglyceride level.



Discussion

Our study could confirm recent suggestions on association between vitamin D deficiency and the progression of both coronary atherosclerosis. In fact, vitamin D deficiency may lead to development of coronary artery disease. Re-

garding the association between the role of vitamin D and an inhibition of pathways involved in atherosclerosis especially inflammatory pathways, it has been demonstrated that vitamin D suppresses inflammation via several pathways, such as an inhibition of prostaglandin and cyclooxygenase pathways, upregulation of anti-inflammatory cytokines, decrease of cytokine induced expression of adhesion molecules, reduction of matrix metalloproteinase 9, and down-regulation of the renin-angiotensin-aldosterone system [10,11]. Vitamin D deficiency stimulates systemic and vascular inflammation, enabling atherogenesis [4]. The proinflammatory nuclear factor κ B mediates partly the association between endothelial dysfunction and low vitamin D status [10]. Thus, it seems that vitamin D deficiency can be considered as a major risk factor for coronary atherosclerosis. Large epidemiological studies have highlighted vitamin D deficiency as a marker of cardiovascular risk [12], promoting accelerated atherosclerosis [13,14] and subsequent cardiovascular events [10]. Chronic vitamin D deficiency causes increasing insulin resistance, and enables the development of metabolic syndrome and diabetes mellitus [4]. Vitamin D has also some antiatherogenic functions, inhibiting the formation of foam cells, cholesterol uptake by the macrophages, and enabling HDL transport [15]. Lower serum 25-hydroxyvitamin D was associated with the metabolic syndrome and its components, especially HDL cholesterol concentration [16]. Vitamin D deficiency was associated with vascular stiffness, which is a known predictor of cardiovascular morbidity and mortality [10] and a marker of subclinical atherosclerosis.

It can finally conclude that vitamin D deficiency can predispose to develop coronary artery involvement and progress coronary atherosclerosis. In this regard, it seems that consuming vitamin D supplements can reduce the risk of cardiovascular disease. Also, food-based strategies for the enhancement of vitamin D status in the population can lower cardiovascular risk because of confirming a causal link between low vitamin status and cardiovascular pathology.

Conflict of Interest

We declare that we have no conflict of interest.

References

- 1 Anagnostis P, Athyros V. G, Adamidou F, Florentin M, Karagiannis A. Vitamin D and cardiovascular disease: a novel agent for reducing cardiovascular risk?. *Curr Vasc Pharmacol* 2010; 8 (5): 720-30.
- 2 Anderson JL, May HT, Horne BD, Bair TL, Hall NL, Carlquist J F, et al. Relation of vitamin D deficiency to cardiovascular risk factors, disease status, and incident events in a general healthcare population. *Am J Cardiol* 2010;106 (7): 963-8.
- 3 Arad Y, Spadaro L. A, Roth M, Scordo J, Goodman K, Sherman S, et al. Serum concentration of calcium, 1,25 vitamin D and parathyroid hormone are not correlated with coronary calcifications. An electron beam computed tomography study. *Coron Artery Dis* 1998; 9 (8): 513-8.
- 4 Lee JH, O'Keefe JH, Bell D, Hensrud DD, Holick MF. Vitamin D deficiency. An important, common, and easily treatable cardiovascular risk factor? *J Am Coll Cardiol* 2008; 52 (24):1949–1956,
- 5 Al Mheid I, Patel RS, Tangpricha V, Quyyumi AA. Vitamin D and cardiovascular disease: is the evidence solid? *Eur Heart J* 2013; 34(48):3691–3698.
- 6 Kunadian V, Ford GA, Bawamia B, Qiu W, Manson JE. Vitamin D deficiency and coronary artery disease: A review of the evidence. *Am Heart J* 2014; 167(3):283-291.
- 7 Wang TJ, Pencina MJ, Booth SL, Jacques PF, Ingelsson E, Lanier K, et al. Vitamin D deficiency and risk of cardiovascular disease. *Circulation* 2008; 117(4):503–511.
- 8 Choi AI, Lo JC, Mulligan K, Schnell A, Kalapus SC, Li Y, et al. Association of vitamin D insufficiency with carotid intima-media thickness in HIV-infected persons. *Clin Infect Dis* 2011;52(7):941-4.
- 9 Ross AC, Judd S, Kumari M, Hileman C, Storer N, Labbato D, et al. Vitamin D is linked to carotid intima media thickness and immune reconstitution in HIV-positive individuals. *Antivir Ther* 2011;16(4):555-63.
- 10 Kunadian V, Ford GA, Bawamia B, Qiu W, Manson JE., Vitamin D deficiency and coronary artery disease: A review of the evidence. *Am Heart J* 2014; 167(3) 283–291.
- 11 Ferder M, Inserra F, Manucha W, Ferder L. The world pandemic of vitamin D deficiency could possibly be explained by cellular inflammatory response activity induced by the renin-angiotensin system. *Am J Physiol* 2013; 304(11):1027–1039.
- 12 Pilz S, Gaksch M, O'Hartaigh B, Tomaschitz A, März W. The role of vitamin D deficiency in cardiovascular disease: where do we stand in 2013? *Arch Toxicol* 2013; 87(12); 2083-2103.
- 13 Wang T. J, Pencina M. J, Booth S. L, et al. Vitamin D deficiency and risk of cardiovascular disease. *Circulation* 2008; 117(4): 503–511, 2008.
- 14 Norman PE. Powell JT. Vitamin D, shedding light on the development of disease in peripheral arteries. *Arterioscler Thromb Vasc Biol* 2005; 25(1) 39-46.
- 15 Oh J, Weng S, Felton S. K, et al. 1,25(OH)₂ vitamin D inhibits foam cell formation and suppresses macrophage cholesterol uptake in patients with type 2 diabetes mellitus. *Circulation* 2009; 120(8) 687-698.
- 16 Maki K C, Rubin M R, Wong L G, et al. Serum 25-hydroxyvitamin D is independently associated with high-density lipoprotein cholesterol and the metabolic syndrome in men and women. *J Clin Lipidol* 2009; 9(4) 289-296.