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Original Article

Association Between 25-Hydroxyvitamin D Levels and the Carotid Intima-Media Thickness

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ABSTRACT

Background: There are insufficient data on the association between the serum level of vitamin D and the carotid intima-media thickness (CIMT). The aim of this study was to investigate the association between the level of serum 25-hydroxyvitamin D and the CIMT.

Methods: This cross-sectional study recruited 341 patients. The level of 25-hydroxyvitamin D was measured with radioimmunoassay, and the CIMT was measured with color Doppler ultrasound.

Results: The mean serum level of 25-hydroxyvitamin D was 14.88±14.63 ng/mL in the patients with a significant carotid artery involvement and 17.02±13.56 ng/mL in those without a carotid involvement, with the difference between the 2 groups constituting statistical significance (*P*=0.034). The prevalence rate of vitamin D deficiency in those with and without a carotid involvement was 88.6% and 74.4%; the rate was significantly higher in the former group (*P*=0.039).

Conclusions: Our study confirmed recent suggestions regarding the association between vitamin D deficiency and the progress of atherosclerosis in carotid arteries as CIMT. ***(Iranian Heart Journal 2019; 20(1):15-19)***

KEYWORDS: Vitamin D deficiency, Carotid plaque, Intima-media thickness, Atherosclerosis

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Atherosclerosis is a progressive disease and plays an essential role in the pathophysiology of cardiovascular disease. Multiple risk factors have been considered for atherosclerosis, including vitamin D deficiency, the role of which has been under investigation in recent years. Vitamin D deficiency may lead to metabolic disorders and the development of atherosclerosis. [1,2] One of the predictors of

future vascular events may be carotid plaque thickness. [3,4] Recent studies have shown that 25-hydroxyvitamin D deficiency is a predisposing factor for cardiovascular events. [5, 6,7] The crucial effects of vitamin D deficiency on changes in the carotid intima-media thickness (CIMT) have been recently suggested. [8] Vitamin D has protective effects on metabolic diseases, and the proposed mechanisms by which vitamin D may confer protection against cardiovascular diseases include effects on the renin-angiotensin system, inflammatory cytokines, and calcium deposition in vascular smooth muscles. [9,10] Previous research has also revealed an association between low vitamin D serum levels and the carotid subclinical markers of atherosclerosis, even independent of the other indices of mineral factors and traditional cardiovascular risk factors. [11,12] However, there is a dearth of information on the association between the serum level of vitamin D and the CIMT. The aim of the present study was, therefore, to investigate the association between the level of serum 25-hydroxyvitamin D and the CIMT.

METHODS

Patients referred to Rajaie Cardiovascular, Medical, and Research Center, affiliated with Iran University of Medical Sciences, Tehran, Iran, between June 2014 and September 2015 without carotid artery plaques or a history of cardiovascular diseases were consecutively included into this cross-sectional survey. The exclusion criteria were comprised of a history of surgery within the preceding 6 months, having hematologic diseases or coagulopathy, a history of chronic kidney diseases, a history of liver diseases, malignancies, and a history of cardiac or cerebrovascular disorders. All the demographic characteristics and laboratory parameters were collected from recorded files. The measurement of the blood serum 25-hydroxyvitamin D3 concentration was made via radioimmunoassay and proper laboratory kits. Vitamin D deficiency was defined as a serum level of less than 20 ng/mL. The CIMT was measured with color Doppler ultrasound. A single trained radiologist, who was blinded to the clinical characteristics of the participants, performed the scan using a high-resolution Philips ultrasonography machine with a 7-MHz probe. Both common carotid arteries were scanned proximally to the bifurcation and then distally to the bifurcation. The CIMT was measured off-line from the media-adventitia interface to the intima-lumen interface at the left and right common carotid arteries. The results were presented as means ± standard deviations (SDs) for the quantitative variables with a normal distribution. The association between the level of 25-hydroxyvitamin D and the other quantitative variables was determined using the Pearson test. Statistical significance was defined as a *P* value of equal to or less than 0.05. All the statistical analyses were conducted using the SPSS software, version 19.0 (SPSS Inc, Chicago, Illinois).

RESULTS

Totally, 341 patients at a mean age of 61.08±9.71 years (range: 32–85 y) were assessed. Males accounted for 74.5% of the whole study population. The mean body mass index was 26.30±3.42 kg/m^2. Regarding cardiovascular risk factors, 36.4% of the patients 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, and the mean low-density lipoprotein level was 99.04±33.85 mg/dL. With respect to carotid involvement, 1.2% of the study population had a significant unilateral (left) common carotid involvement, 1.5% had a significant unilateral (right) common carotid involvement, 5.3% had a significant unilateral left internal or external carotid artery disease, 4.4% had a significant unilateral right internal

or external carotid artery disease, and 0.6% had a bilateral internal and external carotid artery involvement.

The mean serum level of 25-hydroxyvitamin D was 14.88±14.63 ng/mL in the patients with a significant carotid artery involvement and 17.02±13.56 ng/mL in those without a carotid involvement; the difference between the 2 groups constituted statistical significance (*P*=0.034). The prevalence rate of vitamin D deficiency in those with and without a carotid involvement was 88.6% and 74.4%; the rate was significantly higher in the former group (*P*=0.039). As is depicted in Figure 2, a higher serum level of 25-hydroxyvitamin D was found in the normal carotid artery status.

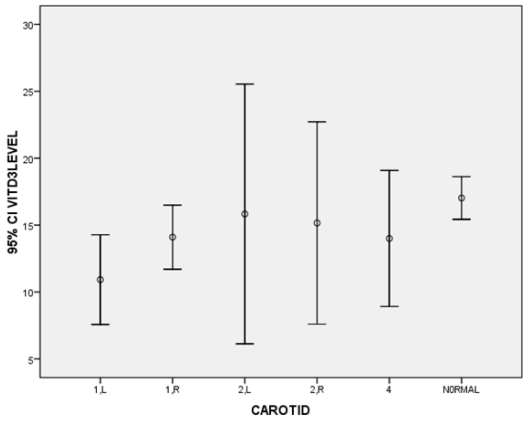

Figure 1. Association between the 25-hydroxyvitamin D level and the triglyceride level

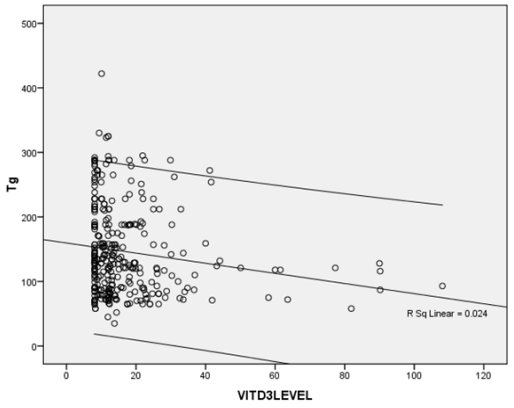

Figure 2. Association between the 25-hydroxyvitamin D level and carotid artery stenosis

DISCUSSION

The association between the CIMT and cardiovascular diseases has been evaluated in several studies. In a study by Kablak-Ziembicka et al [13] on patients with a mean CIMT over 1.15 mm, the likelihood of coronary artery disease was 94%.

With respect to the association between vitamin D deficiency and the CIMT, previous studies have revealed an inverse association between 25-(OH)D levels and subclinical atherosclerosis, measured via the CIMT. [13,14] Carelli et al [15] demonstrated that the 25-hydroxyvitamin D level was inversely associated with the CIMT and the maximal carotid plaque thickness. Prior research has shown that a high calcium-phosphorus product is an independent risk factor for coronary artery diseases and an increased CIMT in adults with chronic kidney diseases. [16,17] Grimes et al [18] also recognized that mortality from ischemic heart diseases was inversely associated with the number of hours of sunlight in the United Kingdom. It is reasonable to screen individuals with the highest risk for vitamin D insufficiency, especially those with cardiovascular diseases, and treat them with vitamin D to a 25(OH)D level of 30 ng/mL. [19] Wang et al [6] showed that vitamin D ingestion in diabetic patients led to a significant improvement in the endothelial function. Targher et al [14] reported an inverse relationship between serum 25-hydroxyvitamin D3 concentrations and theCIMT in patients with type 2 diabetes.

The cross-sectional design of the present study can be deemed its salient limitation. A cohort study can establish causality. Most of our patients had vitamin D deficiency; the etiology

may be multifactorial and due to malnutrition and reduced sun exposure. We would recommend population studies with a wider range of serum vitamin D levels. The majority of our patients were male, and we would suggest that gender-specific population studies be undertaken to shed sufficient light on the issue. It would also be desirable to conduct another study with a view to determining a cutoff point for the vitamin D level which may predispose to atherosclerosis.

Our study results confirmed the recent suggestions as regards the association between vitamin D deficiency and the progression of the CIMT. Vitamin D deficiency may lead to an increased CIMT.

It can finally be concluded that vitamin D deficiency can predispose to atherosclerosis. The progression of atherosclerosis in carotid arteries as the CIMT can be another manifestation of vitamin D deficiency. In this regard, it appears that vitamin D supplements might reduce the risk of cardiovascular diseases. Additionally, food-based strategies for the enhancement of the vitamin D status in the population might lower the atherosclerosis risk because of the causal link.

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