Short Communication

Correlation between vitamin D level and coronary artery calcification

Hamidreza Sajjadieh[1], Amirreza Sajjadieh[1], Zahra Kasaei Koopaei[2], Shahram Oveisgharan[3]

[1]Department of Internal Medicine, Isfahan University of Medical Science, Isfahan, Iran, [2]Department of Pathology, Isfahan University of Medical Science, Isfahan, Iran, [3]Rush Alzheimer's Disease Center, Rush University Medical Center, Chicago, IL, USA

Background: Considering the role of Vitamin D in cardiovascular disease (CVD) and the relationship between coronary artery calcification (CAC) and CVD, we aimed to investigate the association between the serum level of Vitamin D and CAC. **Materials and Methods**: This was a cross-sectional study on 67 consecutive patients who were referred for performing computed tomography angiography. We used Spearman correlation to evaluate the relationship between Vitamin D and CAC and then linear regressions to control for demographics and vascular risk factors. **Results:** There was no association between CAC and Vitamin D levels (Spearman coefficient = −0.03, P = 0.805). After controlling for age, sex, hypertension, hyperlipidemia, diabetes mellitus, and smoking, there was still no association between Vitamin D and CAC score (estimate = 0.001, S. E. = 0.020, P = 0.942). **Conclusion:** We did not find the association between the serum level of Vitamin D and coronary artery calcification.

Key words: Atherosclerosis, computed tomography angiography, coronary artery diseases, vascular calcification, Vitamin D

How to cite this article: Sajjadieh H, Sajjadieh A, Koopaei ZK, Oveisgharan S. Correlation between vitamin D level and coronary artery calcification. J Res Med Sci 2020;25:51.

INTRODUCTION

Nowadays, cardiovascular disease (CVD) is considered one of the most common and important noncommunicable diseases.[1] Several studies have shown that there is a strong association between Vitamin D deficiency and an increased risk of CVD.[2,3]

Coronary artery calcification (CAC) is considered as a risk factor in addition to traditional risk factors such as diabetes mellitus (DM), hypertension (HTN), smoking, and hypercholesterolemia that will improve the prediction of CVD risk categorization. Computed tomography angiography (CTA) can measure the calcium score of coronary arteries which is an established marker of CAC and atherosclerosis.[4]

Most of the studies which evaluate the relationship between Vitamin D and CAC were published based on the United States population.[5] In addition, the results regarding this issue are still inconclusive. The aim of the present study is to gain more insight on the association between the serum level of Vitamin D and CAC in the Iranian population.

MATERIALS AND METHODS

In our cross sectional study, cardiologists referred 67 consecutive patients based on the indications of cardiac CTA between April 2016 and October 2018. The indication of cardiac CTA was according to the American Heart Association guideline.[6]

Vitamin D measurement

Based on Vitamin D levels, we classified patients into three groups: Vitamin D sufficient (Vitamin D ≥20 ng/mL), insuficient (12–20 ng/mL), or deicient (<12 ng/mL).[7]

Access this article online

Quick Response Code:

Website: www.jmsjournal.net

DOI: 10.4103/jrms.JRMS_1080_18

Address for correspondence: Dr. Amirreza Sajjadieh, Department of Internal Medicine, Isfahan University of Medical Science, Isfahan, Iran.
E-mail: amirsajjadieh@yahoo.com

Submitted: 19-Jan-2019; **Revised:** 15-Jul-2019; **Accepted:** 17-Feb-2020; **Published:** 22-May-2020

Coronary artery calcification assessment

CAC was assessed by CTA. The coronary artery calcium score (CACS) was calculated by the Agastone scoring method (Smart Score software). The CACS equal to zero was assumed as the absence of CAC and CACS greater than zero as the presence of CAC. In this study, we examined the association of Vitamin D with the presence of CAC and with its severity.

Assessment of other variables

Age, gender, past medical history of HTN, hyperlipidemia, DM, and smoking were obtained using the questionnaire administrated by a trained nurse.

Statistical analysis

We used *t*-test and Mann–Whitney for bivariate comparison of quantitative variables, and Chi-square for the comparison of categorical variables between patients with and without CAC. Then, we used logistic regression to examine the association between Vitamin D levels and CAC and linear regressions to examine the association between Vitamin D levels and CACS. The models were controlled for the demographics. The analyses were performed using the Statistical Package for Social Sciences software (SPSS, version 22).

RESULTS

The characteristics of the recruited patients are shown in Table 1. They were on average 57 years and 60% were men. Patients with and without CAC were not different in HTN, smoking, creatinine, and C-reactive protein levels. However, patients with CAC were older and reported hypercholesterolemia and DM more compared to patients without CAC [Table 1].

Vitamin D level and coronary artery calcifications

Vitamin D level was not different between patients with (median = 31.5 ng/ml and interquartile range [IQR] = 24.4 ng/ml) and without (median = 31.1 ng/ml and IQR = 30.2 ng/ml) CAC ($P = 0.779$). In a logistic regression model, Vitamin D level was not related to the odds of CAC (odds ratio = 1.00 (95% confidence interval: 0.97–1.03; $P = 0.995$).

In a sensitivity analysis, we examined Vitamin D as a categorical variable following the recent clinical guideline.[7] CAC was not different in the Vitamin D categories (Chi-square = 1.72, $P = 0.423$).

Vitamin D levels and coronary artery calcium scores

The association between Vitamin D level and CACS was weak and insignificant (Spearman correlation coefficient = 0.03; $P = 0.805$). After excluding patients with CACS = 0, there was still no association between Vitamin D levels and CACS (Spearman correlation coefficient = −0.01, $P = 0.975$) [Figure 1].

Table 1: Baseline clinical characteristics of patients according to coronary artery calcification status

Characteristics	Total (*n*=67), *n* (%)	Without CAC (*n*=30), *n* (%)	With CAC (*n*=37), *n* (%)	*P*
Age (year)	56.6±10.9	53.2±12.1	59.0±9.4	0.036
Sex				
Female	27 (40)	11 (37)	16 (43)	0.625
Male	40 (60)	19 (63)	21 (57)	
Hyperlipidemia	35 (52)	12 (60)	23 (62)	0.048
Hypertension	30 (45)	11 (37)	19 (51)	0.325
Smoking	10 (15)	3 (10)	7 (19)	0.304
Diabetes	16 (24)	4 (13)	12 (32)	0.045
Creatinine (mg/dl)	1.0±0.1	1.0±0.2	1.0±0.1	0.373

CAC=Coronary artery calcification

Table 2: The association between the serum levels of Vitamin D and coronary artery calcification score*

	Association of Vitamin D with CAC score	
	Estimate (SE)	*P*
Model 1	0.007 (0.018)	0.704
Model 2	−0.005 (0.019)	0.807
Model 3	0.001 (0.020)	0.942

*All the models are linear regressions with the Vitamin D as the predictor and CAC score as the outcome, Model 1 was not controlled for any other covariate, Model 2 was controlled for age and sex, Model 3 was controlled for age, sex, hypertension, diabetes mellitus, smoking, and hyperlipidemia. SE=Standard error, CAC=Coronary artery calcification

As clinical and demographic characteristics of patients might have resulted in insignificant association between serum Vitamin D levels and CACS, we leveraged linear regressions to examine the simultaneous association of covariates with the CACS in the presence of Vitamin D. As CACS did not have a normal distribution, we transformed the CACS by a natural logarithmic function and used this transformation values as the outcome of the succeeding regression models. Then, we examined the association between Vitamin D with CACS in linear regression models controlled for the demographics and clinical characteristics. The addition of terms for vascular risk factors did not change the conclusion that Vitamin D was not related to CACS [Table 2].

In a sensitivity analysis, we examined the association of the CACS with the categories of Vitamin D. Medians of CACS were not different in different categories of Vitamin D (<12: median = 0.0, IQR = 8.5; 12–20: median = 0.0, IQR = 169.0; ≥20: Median = 7.0, IQR = 159; Kruskal-Wallis Chi-square = 2.272, $P = 0.321$).

DISCUSSION

According to the study of Framingham,[8] we can predict the 10-year risk of CAD, though the prediction does not have high accuracy, and better CAD prediction models are needed. Recently, some studies showed interest in the

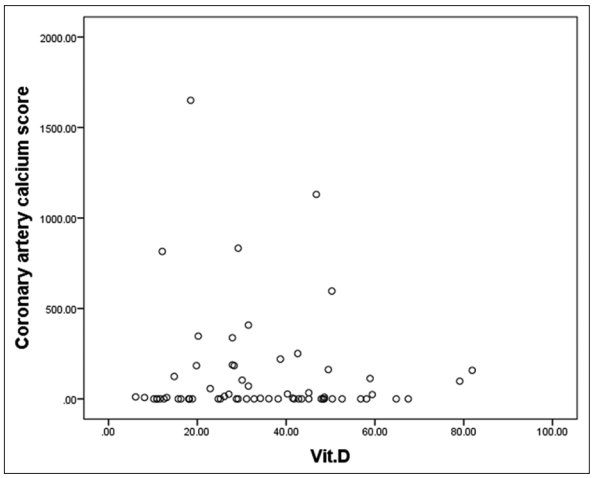

Figure 1: Spearman correlation between Vitamin D and coronary artery calcium score

relationship between the serum Vitamin D level and CAC because the CAC considered a strong marker for CAD.[5,9] However, studies investigating the association between serum level of Vitamin D and CAC had mixed and very contrasting results.[5,10-12]

Leveraging data from near to 70 adults, we found that Vitamin D was not associated with CAC. Controlling for demographics and vascular risk factors did not change this conclusion.

In our opinion, the main reason that can explain contrasting results about the association between Vitamin D level and CAC is that many studies did not adjust their results with the confounding variables. All of the traditional cardiovascular risk factors in the Framingham study[8] such as smoking, DM, HTN, hyperlipidemia, age, and sex can interfere with the association of Vitamin D level and CAC. For instance, Lee *et al.*'s study[11] was based on middle-aged men, whereas the study of Lim[12] was a cohort limited to elderly people. Therefore, all of the possible cardiovascular confounding variables must be considered in future investigations.

Our study has some limitations, including small sample size and lack of information about patients' calcium and parathyroid hormone levels and their drugs use. In addition, its design was a cross-sectional one which precludes causality conclusion. This study has also several strengths. It was the first research investigating an association between Vitamin D level and CAC in Isfahan, Iran attempting adjustment for different confounders. We used standardized methods to obtain patients CACs and Vitamin D levels.

CONCLUSION

In conclusion, we did not find any association between serum vitamin D level and coronary artery calcification. Other mechanisms may be involved in the association between vitamin D level and cardiovascular outcomes.

Acknowledgment

The authors would like to thank the Isfahan University of Medical Sciences (Research Project number: 396601) for their financial support.

Financial support and sponsorship

This study was financially supported by the Isfahan University of Medical Sciences.

Conflicts of interest

There are no conflicts of interest.

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