Vitamin D Deficiency and Its Correlation with Coronary Artery Ectasia

D Vitamini Eksikliği ve Koroner Arter Ektazi Arasındaki İlişki

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ABSTRACT

Objectives: Vitamin D plays a pivotal role in cardiovascular system and its deficiency is related to various of cardiovascular disorders. We investigated the association between serum vitamin D level and coronary artery ectasia formation.

Methods: Our study included 45 patients with coronary artery ectasia and 55 patients with normal coronary artery. Vitamin D and parathyroid hormone levels were obtained before coronary angiography.

Results: Baseline characteristic features were similar between groups. The Vitamin D levels and serum calcium levels were significantly lower in the coronary artery ectasia group compare to control group (respectively; 15.6 ng/ml vs. 12.0 ng/ml; p=0.002 and 9,52 vs. 9.0 ; p< 0.001). PTH level of CEA patients were higher than the control group (44.0 pg/ml vs. 29.5 pg/ml; p=0.018).

Conclusion: Our results showed a significant inverse correlation between Vitamin D deficiency and coronary artery ectasia.

Key Words: Coronary artery ectasia; Inflammation; Vitamin D; Vitamin D deficiency.

ÖZET

Amaç: D vitamini kardiyovasküler sistemin düzenlenmesinde çeşitli aşamalarda önemli rol oynayan ve eksikliği çeşitli kardiyovasküler bozukluklara yol açan steroid yapılı bir moleküldür. Biz bu çalışmamızda; D vitamini düzeyi ile koroner arter ektazi (KAE) oluşumu arasındaki ilişkiyi araştırdık.

Yöntem: Çalışmamıza KAE olan 45 hasta ve normal koroner arterli 55 hasta dahil edildi. D vitamini ve parathormon (PTH) seviyesi için kan örnekleri koroner anjiografi planlanan hastalarda işlem öncesinde alındı. Normal koroner arter olan hastalar ile KAE saptanan hastalar arasında d vitamini ve parathormon seviyeleri arasında fark olup olmadığı analiz edildi.

Bulgular: Başlangıç karakteristik özellikleri gruplar arasında benzerdi. D vitamini ve serum kalsiyum düzeyleri koroner arter ektazi grubunda kontrol grubuna göre anlamlı olarak düşüktü. (sırasıyla; 15.6 ng/ml vs. 12.0 ng/ml; p=0.002 and 9,52 vs. 9.0 ; p< 0.001). PTH düzeyi ise KAE olan hastalarda normal koroner arter hastalarına kıyasla daha yüksek saptanmıştır. group (44.0 pg/ml vs. 29.5 pg/ml; p=0.018).

Sonuç: Çalışmamız koroner arter ektazisi olan hastalarda normal koroner arter saptanan hastalara kıyasla D vitamini düzeyinin istatistiki olarak anlamlı düzeyde düşük, parathormon seviyesinin ise yüksek olduğunu saptadık.

Anahtar Sözcükler: Koroner arter ektazisi; İnflamasyon; D Vitamini eksikliği; D Vitamini.

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INTRODUCTION

Coronary artery ectasia (CAE) is defined as a localised or diffuse dilatation of the epicardial coronary arteries exceeding 1.5 fold than the normal coronary artery segment(1). It can be detected in up to 8% of routine angiographic evaluation(2). There are several causes attributed to ectasia and atherosclerosis is the most common among them(3).

Vitamin-D plays an important role in blood pressure regulation, modulation of cell growth and vascular smooth muscle proliferation through renin-angiotensin-aldosterone system (RAAS). These effects of vitamin D are accepted to be related with vitamin D receptors (VDR) which found in different cells. These receptors were shown to be found particularly in artery surfaces, cardiomyocytes, endocrin organs, immune system cells, endothelial cells, smooth muscle cell surfaces, platelets, inflammatory cells that can be effective in proliferation and differentiation(4-6) Moreover,vitamin D defiency adversly affects cardiovascular system by activating RAAS(7). The arterial remodelling the key mechanism and fundamental to coronary artery disease progression moreover leading to ectasia formation.

There are increasing evidence with conducted studies that RAAS activation leads to aneurysm formation in both abdominal and thoracic aorta. Studies demonstrated a correlation and a increased prevelence of coronary ectasia in patients with abdominal and ascending aortic aneurysm. (8,9). In the light of these studies, there can be a reverse relation between low Vitamin D levels and coronary ectasia.

In this study; we aim to investigate the association of vitamin D deficiency and coronary artery ectasia.

MATERIAL and METHODS

We included 45 patients (28 male, mean age: 58±10 years) in this study with isolated coronary artery ectasia without any significant stenosis. 55 subjects (35 male, mean age:55±11 years) with normal angiograms are included in the control group. The indication for coronary angiogram was determined according to patients' symptoms such as presence of tyical angina or atypical angina with positive or equivocal non-invasive test (positive cardiac stress test, ischemia in myocardial perfusion scintigraphy, patients with recently detected left ventricular wall motion abnormalities or coronary computed tomography angiography) results. Vitamin D samples were taken after the coronary angiogram if the patients were suitable for our study.

Every patient in each group were evaluated in terms of medical history, physical examination, blood biochemistry, electrocardiography and transthoracic echocardiography. Patients with obstructive coronary artery disease (who had coronary artery stenosis >%20), chronic renal failure, chronic liver disorders, chronic heart failure, pregnancy, anemia, intestinal malabsorption syndrome, previous gastrectomy, ongoing vitamin D therapy, diabetes mellitus, known or suspected malignancy, heamatological disorders, obesity, obstructive sleep apnea syndrome and patients that receiving replacement of thyroid hormones, immunosupressive treatments were excluded from the study.

The study was conducted according to the recommendations of the Declaration of Helsinki on Biomedical Research Involving Human Subjects. The Institutional Ethics Committee approved the study protocol and each participant provided written informed consent.

Coronary Angiography

Standard Judkins technique with femoral approach was used for coronary artery visualization. All patients were electively underwent coronary artery angiography using Toshiba Digital Radiography System DFP-8000D model device. Stenotic coronary artery disease (CAD) was defined as >20% stenosis in any main coronary artery (i.e., left anterior descending, circumflex, or right coronary artery). Coronary artery ectasia was defined as dilatation of the coronary artery > 1.5 fold than the adjacent segment diameter of normal coronary artery. The results of coronary angiographies were evaluated by at least two interventional cardiologists who blinded to the patients.

Laboratory testing

Blood was obtained for routine hematologic and biochemical tests following 12 hours of fasting period. Siemens ADVIA Centaur® and ADVIA Centaur XP Automated Chemiluminescence® Systems were used to eveluate plasma or serum 25-OH-D and PTH levels. The test materials used were highly specific for 25-OH-vitamin D2 and 25-OH-vitamin D3. 25-OH-vit D levels between 4,2-150 ng/ml(10,5-375 nmol/L) can be measured according to manufacturer. The accepted reference range for intact parathormone (PTH) is 14 to 72 pg/mL (1.48-7.63 pmol/L) within normal blood calcium levels in this laboratory measurement. The blood samples for vitamin D and PTH were taken after the coronary angiography from 6 Fr femoral sheath, patients who were eligible to study.

Statistical Analyses

Statistical Package for the Social Sciences Program (SPSS) version 20.0 (SPSS, Chicago, IL, USA) was used for the statistical analyses. Results were presented as mean, standart deviation, maximum and minimum for continuous variables; as count and percent for categorical variables. Student's T test was performed to compare means of the continuous variables. Logistic regression model was used to determine the independent risk factors for CAE. A p value below than 0.05 was considered significant.

RESULTS

The baseline characteristics of the patients for each group are shown in Table 1. The patient group and the control group did not differ by means of age, sex, gender distribution, smoking status body mass index.

The vitamin D levels and serum calcium levels were significantly lower in the CEA group compare to control group (respectively; 15.6 ng/ml vs. 12.0 ng/ml; p=0.002 and 9,52 vs. 9.0; p < 0.001) (Figure 1). On the other hand PTH level of CEA patients were higher than the control group (44.0 pg/ml vs. 29.5 pg/ml; p=0.018).

Forward stepwise logistic regression analysis showed that vitamin D and serum calcium levels are independent predictors of CEA (Table 2).

Table 1. Baseline characteristics of the study patients

	Overall (100)	Control Group (n=55)	CAE (n=45)	P Value
Age, y	57±11	55±11	58±10	0.44
Sex, Male, n(%)	63(63)	35(63.6)	28(62.2)	0.88
Hypertension, n(%)	59(59)	31(56.4)	28(62.2)	0.55
Smoking, n(%)	43(43)	23(41.8)	20(44.4)	0.79
Diabetes Mellitus, n(%)	23(23)	11(20.0)	12(26.7)	0.43
Hyperlipidemia, n(%)	24(24)	9(16.4)	15(33.3)	0.048
Family history, n(%)	10(10)	4(7.3)	6(13.3)	0.31
Fasting blood glucose, mg/dl	94.5(86-108)	94(85-109)	96(91-107)	0.53
Creatinine, mg/dl	0.84(0.70-0.97)	0.80(0.65-0.96)	0.91(0.76-1.00)	0.091
Total cholesterol, mg/dl	191±40	186±40	196±41	0.24
HDL, mg/dl	40(37-45)	41(37-46)	39(34-44)	0.14
LDL, mg/dl	120±34	118±34	124±34	0.38
Triglyceride, mg/dl	132.5(96-195)	125(95-185)	161(103-205)	0.17
Hemoglobin, gr/dl	13.8±1.8	13.9±1.7	13.8±1.8	0.23
Platelet count, x10.e3/ul	239(189-282)	243(191-290)	224(179-259)	0.086
Vitamin D level, µg/L	13,5(11.0-16.9)	15.6(11.6-18.1)	12.0(10.0-15.0)	0.002
Parathormone level,	36.9(21.6-56.9)	29.5(19.4-47.4)	44.0(26.0-71.0)	0.018
Calcium, mg/dl	9.29(9.00-9.78)	9.52(9.27-9.86)	9.00(9.00-9.20)	<0.001
Number of ectatic coronary	arteries			
1		-	21	
2		-	17	-
3		-	7	

CAE: coronary artery disease, HDL: high density lipoprotein, LDL: Low density lipoprotein

Table 2. Univariate and multivariate regression analysis showing independent predictors of isolated Coronary Artery Ectasia

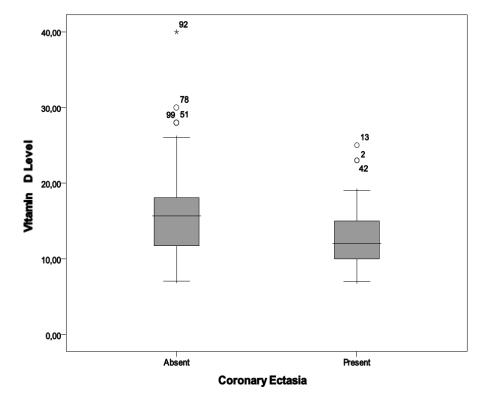|	OR	CI	p	OR	CI 95%	p
Hyperlipidemia	2.556	0.993-6.580	0.052			
Creatinine	0.956	0.812-1.126	0.593			
Platelet count	0.995	0.989-1.001	0.10			
Vitamin D	0.871	0.790-0.960	0.005	0.880	0.795-0.974	0.014
Parathormone	1.020	1.003-1.037	0.022			
Calcium	0.169	0.062-0.456	<0.001	0.179	0.064-0.505	0.001

Figure 1. The relationship between vitamin D level (µg/L) and coronary artery ectasia

DISCUSSION

Our study showed that Vitamin D and PTH levels are significantly different between CEA patients and the control group with normal coronary artery.

There are several pathophysiological mechanisms proposed for identifying the underlying process of CAE formation such as endothelial dysfunction, atherothrombosis and vascular remodelling (10). Recently studies defined the cardioprotective effect of vitamin D through receptors detected on cardiomyocytes, vascular smooth muscle cells, endothelium. These findings urge clinicians to conduct new studies in order to understand the vitamin D effect on cardiovascular system and its role on cardiovascular diseases (CVD) (11).

There are accumulating evidence about potential role of vitamin D on blood pressure regulation, besides inhibiting the uptake of cholesterol by macrophages thus foam cell formation and atherosclerosis. Low levels of vitamin D also inversely related to blood levels of inflammatory markers such as C-reactive protein and interleukin-6, along with elevated matrix metalloproteinase (MMP)-9 levels where each of them have been reported as a predisposant to CAD formation. Vitamin D replacement in patients with Type 2 diabetes mellitus was shown to improve endothelial function (12-15). Coronary artery ectasia is considered to be as a result of vascular remodelling. Unprojected plaque into the vessel lumen may buldge outwards thus intialise ectasia formation.

Any disturbance in the system maintaining cardiovascular integrity such as renin angiotensin system activation or increased inflammatory response or activation of MMPs may lead to ectasia and aneurysm development. Vitamin D more or less has an initialize ectasia formation. Any disturbance in the system maintaining cardiovascular integrity such as renin angiotensin system activation or increased inflammatory response or activation of MMPs may lead to ectasia and aneurysm development. Vitamin D more or less has an impact on each system considering its receptors on related cell surfaces. In the lights of these data vitamin D can be related to ectasia formation through miscalleneous pathway, most important of all renin angiotensin system.

Demir et al. revealed similar results in patients with coronary ectasia compare to control group supporting our findings(16). In our study we found significantly lower levels of vitamin D and serum calcium in patients with ectatic coronary artery compare to normal coronary artery and the PTH levels were significantly higher in ectasia group. High parathormone levels are associated with insulin ressistance and hypertension. Shekarkhar et al. reported that higher serum PTH levels are associated with the number of stenotic coronary arteries and Van Ballegooijen et al. also pointed out increased risk of CVDs with higher PTH concentration. (17,18) Vitamin D deficiency causes secondary hyperparatiroidsm and may mediate the detrimental effects of inaduquate vitamin D levels.

CONCLUSION

Coronary artery ectasia is common in practice and vitamin D deficiency may be an important contributor to pathopshysiology in these patients.

Conflict of interest
No conflict of interest was declared by the authors.

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