Association of vitamin D deficiency with coronary artery disease in Mexican population: Genetics of atherosclerotic disease study

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Abstract

Objective: *To investigate the independent association between vitamin D deficiency (VDD) and coronary artery disease (CAD) in Mexican adult population.* **Method:** *Matched case-control study. Data cardiovascular on risk factors, medication use, physical activity, alcohol use, smoking and vitamin D consumption were obtained. Biochemical variables, anthropometric and blood pressure were measured. 25(OH)D was quantified by chemiluminescence.* **Results:** *We studied 250 patients with established CAD and 250 age-gender-body mass index (BMI) matched control subjects, with a mean age of 53 ± 6.1 years and BMI of 28 ± 3.5 kg/m^2. Deficiency of 25(OH)D was significantly higher in the control group (21.2 vs. 16%). Multiple logistic regression analysis did not show association between VDD and CAD (OR: 1.37 [0.08-23.2]). Multiple linear regression analysis also showed that statin use (b = 2.2; p = 0.004) and no alcohol use (b = −1.8; p = 0.03) significantly increased 25(OH)D levels.* **Conclusions:** *No independent association between VDD and the presence of coronary artery disease was found in Mexican adult population. The results suggest that treatment with statins and absence of alcohol consumption, might be the explanation for the higher concentrations of 25(OH)D observed in patients with CAD.*

KEY WORDS: *Vitamin D deficiency. Coronary artery disease. Genetics of atherosclerotic disease study.*

Introduction

Coronary artery disease (CAD) is the first cause of death in the world[1]. In Mexico, for a long time it was considered to be an uncommon disease but, in the past few years, its prevalence has had a considerable increase, and it has become the first cause of mortality[2]. Projections for the year 2030 indicate that this trend is going to continue[3].

In recent years, the interest the study of vitamin D (VD) metabolism has increased. Dietary consumption provides only 10% of previtamin D, and the main source to obtain it is therefore endogenous synthesis, which results from the transformation of 7-dehydrocholesterol that is present in the skin by the effect of exposure to solar ultraviolet B rays. Epidemiological studies conducted in apparently healthy subjects have reported deficiency prevalences ranging from 2 to 90%, depending on the cutoff point used and the study population[4]. Approximately three decades ago, Robert Scragg postulated that the increase in 25(OH)D concentrations is a protecting factor against cardiovascular disease[5]. Since that date, a large number of studies have reported that adequate 25(OH)D concentrations are associated with lower prevalence of diabetes, hypertension, dyslipidemia and metabolic syndrome[6-9]. On the other

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hand, an association has been reported of 25(OH)D deficiency with higher prevalence of asymptomatic CAD[10] and cardiovascular events such as myocardial infarction[11] and mortality of cardiovascular and non-vascular causes[12]. However, there are several studies that have not found an association between deficiency of this vitamin and cardiovascular disease[13,14].

Considering the controversy existing about the association of VD with cardiovascular disease, and taking into account that VD deficiency (< 30 ng/mL) in Mexico has a high prevalence (30%)[15] and that cardiovascular disease is the first cause of death, the purpose of the present study was to investigate the independence of the association between 25(OH)D deficiency and CAD in a Mexican adult population.

Methods

A matched case-control study was designed, nested within the Genetics of Atherosclerotic Disease (GEA – *Genética de la Enfermedad Aterosclerosa*) study, which was designed to investigate the genomic bases of CAD and assess relationships between traditional and emerging risk factors with clinical and subclinical atherosclerotic disease in the Mexican adult population. Project GEA cross-sectional phase took place from June 2008 to February 2013, with special care in a broad characterization of participants with and without CAD. Sampling was by convenience and 1000 patients with CAD and 1500 control subjects were included, with ages ranging from 35 to 75 years; all subjects were Mexico City residents. The CAD group was selected from the outpatient clinic and the hemodynamics department of the National Institute of Cardiology Ignacio Chávez, with premature CAD defined as a personal history of myocardial infarction, angioplasty, revascularization surgery or angiography with coronary stenosis ≥ 50%, diagnosed in men prior to 55 years and in women prior to 65 years of age. Patients with an acute cardiovascular event within 3 months prior to the study or with congestive heart failure were excluded. The control group was comprised by open-population volunteers who had no clinical manifestations of CAD or a family history of premature CAD, and who attended upon invitation through printed media. Of both groups, patients with renal, hepatic or thyroid conditions, malignant diseases or on treatment with corticosteroids were excluded[16]. The project was approved by the Ethics Committee of the National Institute of Cardiology Ignacio Chávez, and was carried out according to the guidelines of the Declaration of Helsinki. All patients signed an informed consent form.

Of the total sample, 250 patients with CAD and 250 control subjects, older than 40 years, matched by age ± 1 year, gender, and BMI ± 1 kg/m^2, were selected. The group of cases was defined by the presence of well-established CAD, and the control group, by the absence of subclinical atherosclerosis, which was established by measuring the coronary artery calcium (CAC = 0 A.U.) by multidetector computed axial tomography. For this study, individuals with diabetes mellitus, history or evidence of renal, hepatic, thyroid or oncologic disease, and those on corticosteroid treatment or use of VD supplements were excluded. All participants were applied standardized questionnaires to obtain demographic information, family and personal history of cardiovascular risk factors, alimentary patterns[17], physical activity[18], use of medications and consumption of tobacco and alcohol.

The sample size, estimated using the Freeman formula[18], was 250 subjects per group, with a control: case ratio of 1:1.

Clinical and anthropometric measurements

Weight was measured with a calibrated scale and height was measured using a wall stadiometer (SECA 222, Hamburg, Germany). BMI was calculated by dividing the weight in kilograms by the squared height in meters. Overweight was considered when BMI was 25-29.9 kg/m^2, and obesity when it was ≥ 30 kg/m^2. Waist circumference was measured with a fiberglass measuring tape, at a level midway between the lower rib margin and iliac crest. Blood pressure was measured in the sitting position, after a 10-minute rest period, using a digital sphygmomanometer (Welch Allyn, series 52000), and the average of the latter two of three consecutive measurements was recorded for analysis.

Venous blood samples were obtained after a 12-hour fasting. Glucose, total cholesterol (TC), triglycerides (Tg) and high-density lipoprotein cholesterol (HDL-C) concentrations were measured in fresh samples using enzymatic-colorimetric standardized procedures (Roche/Hitachi, Germany) in a Hitachi 902 automatic analyzer (Hitachi LTD, Tokyo, Japan). Low-density lipoprotein cholesterol (LDL-C) was calculated with the Friedewald equation modified by De Long et al.[20]. In the endocrinology laboratory, lipid determinations' precision and accuracy are periodically evaluated by the Atlanta Center for the Control and Prevention of

Diseases. Total high-sensitivity C-reactive protein (hs-CRP) and apolipoprotein B were quantified by immunonephelometry (BN Pro Spec Nephelometer, Dade Behring Marburg GmbH, Germany). The coefficient of variation was < 6% for all assays. Serum insulin was determined by radioimmunoassay (Millipore Cat. No. HI-14K, MO, USA), with intra-assay and inter-assay coefficients of variation of 2.1 and 6.8%, respectively. Hyperinsulinemia was defined as a value ≥ 16.97 µU/mL in women and ≥ 15.20 µU/mL in men. Insulin resistance was estimated by means of the insulin resistance homeostatic model (IR-HOMA)[21], and was deemed to be present when values were above percentile 75 (3.66 in women and 3.38 in men). Adiponectin concentration was determined by immunoassay (Quantikine ELISA, R&D Minneapolis, USA). For low adiponectin, values below percentile 25 were taken as reference (8.67 µg/mL in females and 5.3 µg/mL in males). These IR-HOMA and adiponectin values were obtained from a sub-sample of the GEA study that included 131 men and 185 women without obesity and with blood pressure, glucose and lipid normal values. Diabetes mellitus was defined according to the American Diabetes Association criteria[22], or when participants referred using medications for glucose control and in those with a previous diabetes diagnosis established by a physician. Dyslipidemias were defined according to the following cutoff points: hypercholesterolemia, TC > 200 mg/dL or LDL-C > 130 mg/dL; hypertriglyceridemia, Tg > 150 mg/dL; low HDL-C, < 40 mg/dL in men and < 50 mg/dL in women; and atherogenic index, TC/HDL-C ratio > 4.5. Concentration of 25(OH)D was quantified by chemiluminiscence (Architect plus CI8200), which has good correlation (r = 0.90)[23] with liquid chromatography-mass spectrometry, which is considered to be the reference method. Low, mid and high controls were used, which showed variation coefficients of 3.6, 3.1 and 4.05%, respectively. Inter-assay coefficient of variation was 2.1%. VD deficiency was considered when 25(OH)D concentrations were < 20 ng/mL[24]. The seasons of the year were classified according to the dates established for the northern hemisphere. VD consumption was obtained using a semi- quantitative food frequency questionnaire (FFQ)[17] designed and validated by the National Institute of Public Health. The amounts consumed per day were calculated by means of the System of nutritional habits and nutriment consumption evaluation (SNUT – *Sistema de evaluación de hábitos nutricionales y consumo de nutrimentos*) program[25]. Physical activity was quantified using a questionnaire that provides information on frequency, intensity and duration[18].

Computed tomography is a validated method to quantify CAC[26]. Measurements were made using a 64-slice (Somatom Sensation, Siemens, Malvern, PA, USA) or 256-slice multidetector scanner (Somatom Definition Flash, Siemens, Erlangen, Germany), before and after February 2009, respectively. The study was obtained with cardiac synchronization using a prospective protocol with the following parameters: 120 kV, 120 mA and 3-mm slice thickness. CAC was quantified according to the method of Agatston[27]. The images were interpreted by an expert radiologist, in a workstation (Leonardo Workstation, Siemens, Forcheim, Germany) supplied with a specific program for calcium index analysis (CaScoring, Siemens, Forcheim, Germany). The Agatston score test-retest, used to assess intra-observer reliability showed a very high intra-class correlation coefficient (0.99).

Data are presented as the mean ± standard deviation, median (interquartile range) or percentage. Between-group comparisons were made with Student's t, Mann-Whitney U and chi-square statistical rests, as appropriate. Simple and multiple conditioned logistic regression analysis was used to assess the independent relation between 25(OH)D deficiency and CAD with adjustments according to 5 models that were constructed with variables that were significantly different in the bivariate analysis and had no colinearity. Linear and multiple regression analyses were also carried out in order to find out 25(OH)D concentration-modifying variables. Additionally, 25(OH)D concentration was estimated eliminating the effect of statin treatment, with values being obtained for the difference of receiving or not treatment between each group (CAD group, –1.4 ng/mL; control group, 0.33 ng/mL). A p-value < 0.05 was considered to be significant. Statistical analysis was performed with the STATA/MP 13 software (StataCorp, Inc., College Station, Texas, USA).

Results

Two hundred and fifty patients with CAD and 250 age-, gender- and BMI-matched control subjects were studied, the characteristics of which are shown in table 1. In the total population, 82% were of the male gender, mean age was 53 years and BMI was 28 kg/m^2. In CAD patients, TC, HDL-C, LDL-C and apolipoprotein B concentrations, atherogenic index and VD intake were significantly lower in comparison with the control group (p < 0.05). Conversely, insulin concentration and

Table 1. Clinical and biochemical characteristics of the study population according to the presence of coronary artery disease

	CAD group (n = 250)	Control group (n = 250)	p
Gender (M), %*	82.4	82.4	0.99
Age, years*	53.3 ± 6.0	53.5 ± 6.2	0.61
BMI, kg/m2*	28.0 ± 3.5	27.9 ± 3.5	0.78
SBP, mmHg	114.5 [106-123.5]	113.2 [105.5-122]	0.47
DBP, mmHg	72 [65.5-77.5]	71 [66.5-76.5]	0.83
TC, mg/dL	163.7 [139.8-195.0]	187.0 [164.5-209.0]	< 0.001
Tg, mg/dL	159.5 [116.0-208.0]	160.6 [113-233.7]	0.77
HDL-C, mg/dL	38.1 [32.0-45.2]	40.3 [34.0-49.0]	0.01
LDL-C, mg/dL	97.8 [76.0-118.2]	114.2 [93.2-135.4]	< 0.001
Atherogenic index	4.2 [3.4-5.1]	4.5 [3.6-5.5]	0.02
Glucose, mg/dL	89.5 [84-95]	90 [85-95]	0.95
Insulin, μIU/mL	18.2 [14.5-26.4]	16.6 [12.3-23.1]	0.002
IR-HOMA	4.0 [3.1-6.0]	3.6 [2.6-5.2]	0.003
ApoB, mg/L	80 [65-103]	96.5 [77-116]	<0.001
Adiponectin, μg/mL	5.1 [3.3-8.2]	6.1 [3.8-10.1]	0.007
CRP, mg/L	1.1 [0.6-2.2]	1.2 [0.6-2.4]	0.37
Smoking, %	12	22.8	0.001
Alcohol use, %	72.1	82.6	0.006
Physical activity index	7.9 ± 1.2	7.9 ± 1.2	0.70
Vitamin D			
25(OH) D, ng/mL	28 ± 8.2	25 ± 6.8	< 0.001
25(OH) D status, %			
Optimal (≥ 30 ng/mL)	34.8	21.2	0.001
Insufficient (20-29.9 ng/mL)	49.2	57.6	0.13
Deficient (< 20 ng/mL)	16	21.2	0.001
Vitamin D intake, IU/day	129.6 [88.1-219.0]	158.9 [102.3-249.1]	0.01
Season of sampling, %			
Spring	22.4	20	
Summer	29.6	29.6	
Autumn	28.4	36	0.20
Winter	19.6	14.4	
Statins use, %	91.2	6.8	<0.001

Data are expressed as mean ± standard deviation and median (interquartile range).
*Matching variables. p < 0.05 significant.
ApoB: apolipoprotein B; BMI: body mass index; CAD: coronary artery disease; CRP: C-reactive protein; DBP: diastolic blood pressure; HDL-C: high-density lipoprotein cholesterol; IR-HOMA; insulin resistance homeostatic model; LDL-C: low-density lipoprotein cholesterol; SBP: systolic blood pressure; TC: total cholesterol; Tg: triglycerides.

IR-HOMA value were significantly higher (p > 0.005). Among the inflammation profile-related parameters, CRP values were not different between both groups, but adiponectin concentration was observed to be statistically significantly higher in the control group (p = 0.007). The proportion of statin-treated participants was significantly larger in patients with CAD (91.2 vs. 6.8%; p < 0.001). Smoking and frequency of alcoholic beverages consumption were 10 percentage points higher in the control group (p < 0.01).

25(OH)D concentration in the CAD group was significantly higher in comparison with the control group (28 ng/mL vs. 25 ng/mL; p < 0.001), although VD consumption was significantly lower in the CAD group

(129.6 vs. 158.9 IU; p = 0.001). The prevalence of 25(OH)D insufficiency (20-29.9 ng/mL) was higher in control subjects (57.6 vs. 49.2%; p = 0.13), as well as the prevalence of deficiency (< 20 ng/mL; 21.2 vs. 16%; p = 0.001). Blood sampling were proportionally in both study groups at each season of the year (p = 0.20), which allowed controlling the effect produced by solar exposure at different seasons on circulating 25(OH)D concentrations. The remaining variables were similar in both groups.

Cardiovascular risk factors prevalence by study group is shown in figure 1. Arterial hypertension showed a significantly higher prevalence in patients (63.2 vs. 13.2%; p < 0.0001) and, similarly, both resistance to elevated insulin (66.4 vs. 54.4%; p = 0.006) and low adiponectin values (57.6 vs. 45.3%; p = 0.007) were observed with significantly higher frequency in the CAD group, whereas elevated LDL-C was more prevalent among controls (30.4 vs. 19.2%; p = 0.004). Other abnormalities showed similar frequencies in both groups, but it should be noted that prevalences were high: low HDL-C had a prevalence of 62.4 vs. 55.6%, hypertriglyceridemia, of 54.4 vs. 56%, and altered fasting glucose, 15.2 vs. 14% in the CAD group and the control group, respectively.

To investigate the independence of the relationship between 25(OH)D deficiency and CAD, a conditioned logistic regression analysis was carried out adjusting for variables that showed to be significantly different in the bivariate analysis. Table 2 shows that no association was found even in the unadjusted model.

In order to find out factors that might have influenced on 25(OH)D concentrations, simple and multiple linear regression analyses were also used, adjusted by variables that have been described as VD modifiers in the literature (Table 3). Simple and multiple analysis results show that, in total population, the use of statins increases 25(OH)D concentration by

Table 2. Association of 25(OH) D deficiency and coronary artery disease

	OR (95% CI)	p
25(OH) D deficiency (< 20 ng/mL)	0.68 (0.42-1.10)	0.12
Model 1	0.85 (0.28-2.55)	0.78
Model 2	0.83 (0.27-2.51)	0.74
Model 3	0.97 (.29-3.2)	0.97
Model 4	1.48 (0.33-6.5)	0.60
Model 5	1.37 (0.08-23.2)	0.80

Values expressed as odds ratio (OR) and 95% confidence interval (CI).
Conditioned multivariate logistic regression analysis.
Model 1: vitamin D deficiency + statins.
Model 2: model 1 + atherogenic index > 4.5.
Model 3: model 2 + IR-HOMA and adiponectin.
Model 4: model 3 + smoking and alcohol use.
Model 5: model 4 + vitamin D intake.

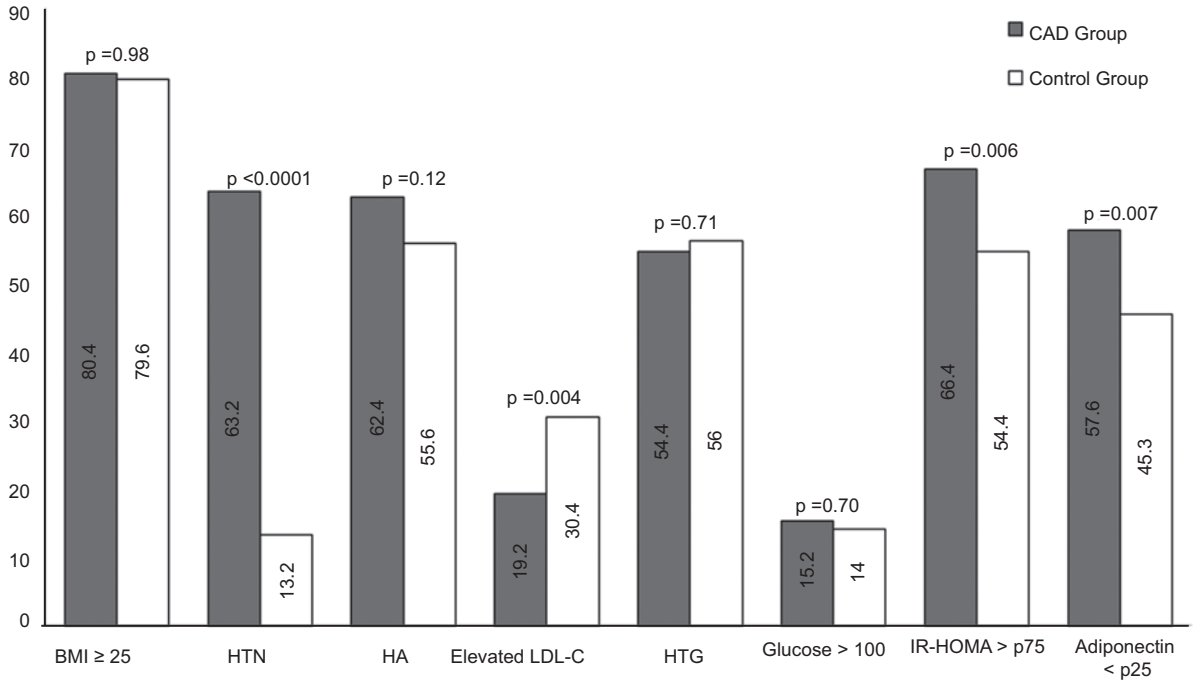

Figure 1. *Prevalence of metabolic abnormalities in patients with coronary artery disease (CAD) and in the control group. HTN: hypertension; BMI: body mass index; HA: hypoalphalipoproteinemia; HTG: hypertriglyceridemia; IR-HOMA: insulin resistance homeostatic model; LDL-C: low-density lipoprotein cholesterol.*

2.2 ng/mL, and accounts for 14% of variation (p = 0.004); in contrast, the use of alcohol decreases it by 1.8 ng/mL and accounts for 10% of 25(OH)D low concentrations (p = 0.03). Pravastatin was the most commonly used statin by study participants, followed by atorvastatin, simvastatin and rosuvastatin (Table 4). In addition, 25(OH)D concentration was estimated eliminating the effect of statin treatment in the CAD group (–1.4 ng/mL) and the control group (0.33 ng/mL). The estimated 25(OH)D concentration maintained significantly higher values in the CAD group in comparison with the control group (26.7 vs. 25.04 ng/mL; p = 0.01), but the prevalence of VD deficiency increased by 5.2 percentage points and became equal to that of the control group (21.2 vs. 20.8%; p = 0.50). However, contrary to expectations, 25(OH)D concentration by statin type and dose not show a dose-response increase.

Discussion

In the present study, after adjusting for statin treatment, atherogenic index > 4.5, IR-HOMA, adiponectin, smoking, alcohol use and VD intake, the multivariate regression analysis did not show an association of 25(OH)D deficiency with the presence of CAD or cardiovascular risk factors. These results are in contrast with studies that have shown that low VD values are associated with a systemic inflammatory state, favor insulin resistance and activate the renin-angiotensin-aldosterone system, with a subsequent elevation of blood pressure and cardiac muscle and smooth muscle cell hypertrophy[28-30]. Consistent with these findings, several observational studies have reported an association between 25(OH)D deficiency and the presence of clinical[13,13-33] and subclinical CAD[34-38]. In a case-control study where both patients with coronary disease and patients with stroke were included, 25(OH)D deficiency, defined by concentrations lower than 15 ng/mL, showed a high prevalence in patients (68%) and controls (54%), and was found to be associated with the presence of cardiovascular disease (OR: 2.9 [1.67-5.12]; p < 0.001)[33]. Similarly, in 1370 subjects aged from 45 to 84 years, out of which 394 had chronic renal failure, De Boer et al.[14] reported 25(OH)D deficiency (<15 ng/mL) in 73.2% of the population, as well as its modest, but independent relationship with CAD prevalence (RR: 1.06 [1.00-1.13]; p = 0.06). In another study, Lim et al.[38] reported, in 921 subjects older than 65 years, that 25(OH)D deficiency (< 30 ng/mL), observed in 94% of the study population, was associated with coronary stenosis ≥ 50% (OR: 2.08 [1.16-4.68]). However, other investigations have not observed this association. In a study performed in 387 survivors of a first myocardial infarction, with their respective 387 age- and gender-matched controls, 25(OH)D deficiency (< 30 ng/mL), which was found in 80% of patients and 75% of the control group, showed no association with coronary heart disease (OR: 1.01 [0.82-1.25][13]. However, the most important support to the results obtained in our study is lent by two recent systematic reviews and meta-analyses[39,40]. In one, 82 prospective cohort studies, 84 randomized controlled interventions, 20 meta-analyses of 208 prospective studies and 8 meta-analyses of 88 randomized controlled interventional trials were included[39]. In the other one, the authors analyzed 76 systematic reviews of observational studies, 48 meta-analyses of observational studies and 57 meta-analyses of randomized controlled interventional trials[40]. Both these reviews of the extensive literature on the subject identified a discrepancy between observational-type studies and randomized controlled trials, since most supplementation studies failed to show an effect of VD on cardiovascular disease. Therefore, the authors concluded that VD deficiency is most probably a poor health status marker rather than the cause of the disease.

Among the factors that influence on circulating 25(OH)D concentrations[41], no influence of gender,

Table 3. Linear regression analysis of factors associated with 25(OH)D concentration

	Simple			Multivariate*		
	b	β	p	b	β	p
Statins use	2.73	0.17	< 0.001	2.2	0.14	0.004
Alcohol use	–2.10	–0.11	0.01	–1.8	–0.10	0.03

Values are expressed as coefficients b and β. Simple and multivariate linear regression analysis (adjusted for sex, age, positive smoking, BMI, total physical activity, season of the year and vitamin D intake).
*R^2=4%.

Table 4. Statins use by study group

	CAD group (n = 228)	Control group (n = 16)	p
Pravastatin, n (%)	83 (36.4)	7 (43.7)	0.59
Atorvastatin, n (%)	50 (21.9)	5 (31.2)	0.36
Simvastatin, n (%)	50 (21.9)	2 (12.5)	0.53
Rosuvastatin, n (%)	43 (18.8)	2 (12.5)	0.74
Simvastatin + ezetimibe, n (%)	2 (0.88)	0	0.99

Fisher´s exact test: p < 0.05 significant.
CAD: coronary artery disease.

age, tobacco consumption, BMI, physical activity, season of the year when the sampling was made or VD intake was observed in the population of our study. However, alcohol non-consumption and treatment with statins were associated with 25(OH)D higher values.

Both in total population and in the CAD group, alcohol non-consumption was associated with significantly higher 25(OH)D concentrations, which is consistent with the observation that subjects with higher consumption than 20 grams of alcohol per day have lower 25(OH)D concentrations[42].

Statin therapy is another factor that modifies serum 25(OH)D values. The association of statin use with 25(OH)D concentrations was observed in a study of 208 women with VD supplementation for 3 years[43]. The values of this form of VD were higher in all 51 women who were statin users, both at baseline and during treatment, regardless of whether they received placebo or VD. In another study that investigated the effect of atorvastatin at daily doses of 10-80 mg on VD concentrations in patients with ischemic heart disease, Pérez-Castrillón et al.[44] found a 25(OH)D increase of 17.08 ± 7 to 19.6 ± 7.9 ng/mL (p = 0.003), and a 75 to 57% decrease in the proportion of patients with VD deficiency after 1 year of statin therapy. These results are notably similar to those of the present study, where 25(OH)D values in 91.2% of patients treated with any statin (28 ± 8.1 ng/mL) were significantly higher than those observed in 8.8% of statin non-users (26.6 ± 9.5 ng/mL) and in the control group (25.03 ± 6.7 ng/mL). Although currently there is no certainty about the mechanism by means of which statins increase circulating concentrations of this vitamin, it has been speculated that, since 7-dehydrocholesterol is precursor of both cholesterol and 25(OH)D, hydroxy-methyl-glutaryl-coenzyme A reductase inhibition by the action of statins would increase the substrate for 25(OH)D synthesis[44].

Strengths of our study include that participants with no clinical data of vascular disease, with and without CAC, and those with well-defined coronary artery disease, have been broadly characterized from the clinical, biochemical and radiologic points of view. The broad characterization of the study groups enabled adjusting for a large number of confounders and, in addition, subjects with diabetes were excluded, thus eliminating a highly confounding factor for CAD and a modifier of 25(OH)D concentrations; furthermore, unlike previous studies, there was certainty that the control group had no subclinical atherosclerosis.

The limitations of this work include, first, due to its cross-sectional desing, a causal relationship between VD deficiency and CAD cannot be established. Second, 25(OH)D measurement was measured only once, but 25(OH)D concentrations have been shown to apparently to be constant along time[45]. Third, most of the patients had treatment with statins, and could therefore not be excluded; however, when correction was made for the statin effect, 25(OH)D concentrations and the prevalence of VD deficiency were similar between the group of patients and the control group.

In conclusion, the results of this study in Mexican Mestizo population were not found association between 25(OH)D deficiency and the presence of CAD. Treatment with statins and lower alcohol consumption are important factors that influence on circulating 25(OH)D concentrations. In patients with CAD, 25(OH)D concentration was higher, and the prevalence of a state of deficiency of this vitamin was lower than in their gender-, age- and BMI-matched controls. The results suggest that treatment with statins and lower alcohol consumption might be the explanation for the higher 25(OH)D concentrations found in patients with CAD.

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