Arterial Stiffness and Vitamin D Levels: the Baltimore Longitudinal Study of Aging

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Context: The importance of vitamin D for bone health has long been acknowledged. Recent evidence suggests that vitamin D can also play a role in reducing the risk of several other diseases, including cardiovascular disease.

Objective: The aim of this study is to test the hypothesis that 25-hydroxyvitamin D (25-OH D) is an independent cross-sectional correlate of central arterial stiffness in a normative aging study population.

Design and Settings: We conducted a cross-sectional analysis.

Subjects: We studied 1228 healthy volunteers (50% males; age, 70 ± 12 yr) of the Baltimore Longitudinal Study of Aging.

Main Outcome Measures: We measured carotid-femoral pulse wave velocity (PWV) and 25-OH D levels.

Results: We found a significant inverse association between PWV and 25-OH D levels (adjusted $r^2 = 0.27$; $\beta = -0.43$; $P = 0.001$). After adjusting for age, gender, ethnicity, season of blood draw, estimated glomerular filtration rate, physical activity level, cardiovascular risk factors score (smoking, visceral obesity, hypercholesterolemia, hypertension, and diabetes), calcium/vitamin D supplementation, serum calcium, and PTH levels, the association between PWV and 25-OH D levels was only slightly reduced and remained statistically significant (adjusted $r^2 = 0.34$; $\beta = -0.34$; $P = 0.04$).

Conclusions: Vitamin D levels are inversely associated with increased arterial stiffness in a normative aging population, irrespective of traditional risk factor burden. Further research is needed to understand the mechanism of this association and to test the hypothesis that vitamin D supplementation can reduce arterial stiffness. (***J Clin Endocrinol Metab*** **97: 3717–3723, 2012)**

The importance of vitamin D for bone health has long been acknowledged. Recent evidence suggests that vitamin D can also play a role in reducing the risk of several other diseases, including cardiovascular disease (1, 2). Vitamin D deficiency is a highly prevalent condition affecting up to 50% of the U.S. population and is associated with hypertension, insulin resistance, congestive heart failure, and blood levels of inflammatory markers (1, 2).

Mechanisms underlying vitamin D deficiency-mediated increased risk of cardiovascular disease still remain

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Abbreviations: BMI, Body mass index; Cac, corrected calcium; eGFR, estimated glomerular filtration rate; iPTH, intact PTH; MET, metabolic equivalents; 25-OH D, 25-hydroxyvitamin D; PWV, pulse wave velocity; RAAS, renin-angiotensin-aldosterone system; VDR, vitamin D receptor.

unclear. The evidence that endothelial cells express a vitamin D receptor and possess the enzymatic system to convert the primary circulating form of vitamin D, 25-hydroxyvitamin D (25-OH D), to the active form, 1,25-dihydroxyvitamin D, has provided new working hypotheses into the function of this vitamin (3, 4). Vitamin D influences endothelial and smooth muscle cell function by exerting antiproliferative effects on vascular smooth muscle (5), mediates inflammation by regulating lymphocyte and monocytes/macrophage differentiation and release of inflammatory cytokines (6), and modulates the renin-angiotensin-aldosterone system (RAAS) (7). This in turn might determine monocyte infiltration and cholesterol retention in the vascular wall contributing to the atherosclerotic process (8, 9).

The aim of this project was to investigate the relationship between 25-OH D plasma levels and arterial stiffness, with the hypothesis that arterial stiffness [measured by carotid-femoral pulse wave velocity (PWV)] is associated with vitamin D levels independent of age. We also explored the putative role of factors that may confound this relationship.

Subjects and Methods

Study population

The Baltimore Longitudinal Study of Aging (BLSA) is a prospective study of normative aging conducted by the National Institute on Aging, Intramural Research Program since 1958. BLSA participants are healthy volunteers 31–97 yr of age who undergo standardized testing across multiple body systems over 2 to 3 d at regular intervals (10). The study cohort for this cross-sectional analysis included all participants with 25-OH D levels and PWV data obtained during their regularly scheduled BLSA study visit.

Anthropometrics, smoking status assessment, and physical activity level

Height (in meters) and weight (in kilograms) were measured for all participants. Body mass index (BMI) was calculated as body weight (in kilograms) divided by height (in meters) squared. Obesity was defined as a BMI of 30 kg/m^2 and above. Visceral obesity was defined as waist circumference greater than 102 cm in men and 88 cm in women. Systolic and diastolic blood pressure, mean arterial pressure, and heart rate determinations were performed at the time of PWV analysis with an oscillometric device (Dash 4000 Monitor; General Electric, Milwaukee, WI), after a 5-min quiet resting period. Hypertension, hypercholesterolemia, and diabetes mellitus were defined according to the Seventh Report of the Joint National Committee on the Prevention, Detection, Evaluation and Treatment of High Blood Pressure; Adult Treatment Panel III; and American Diabetes Association criteria, respectively (11–13). Smoking status was ascertained by a questionnaire that classified each subject as an ever or never smoker. Medication use (antihypertensives and hypoglycemic agents), and calcium and/or vitamin D supplementation were also verified at the time of the BLSA visit. Participants were classified with respect to their levels of weekly physical activity and exercise program [metabolic equivalents (MET) per week] using validated standard questionnaires (14). Alcohol intake data were ascertained by a questionnaire. We defined a standard serving of alcohol as 13.7 g of ethanol and categorized average alcohol consumption as none or less than one, one to less than three, or at least three servings per week (15).

Laboratory testing

Blood samples were drawn at rest from the antecubital vein after an overnight fast between 0700 and 0800 h. Serum albumin was measured with a commercial enzymatic test (Roche Diagnostics GmbH, Mannheim, Germany). Automated chemical analysis was used for analysis of calcium and creatinine. Corrected calcium (Cac) was computed as Cac = (4.0 g/dl − (plasma albumin)) × 0.8 + (serum calcium) as previously reported (16). Estimated glomerular filtration rate (eGFR) was computed according the Modification of Diet in Renal Disease Study (MDRD) equation (17). Concentrations of plasma triglycerides and total cholesterol were determined by enzymatic method (ABA-200 ATC Biochromatic Analyzer; Abbott Laboratories, Irving, TX). The concentration of high-density lipoprotein cholesterol was determined by a dextran sulfate-magnesium precipitation procedure. Low-density lipoprotein cholesterol concentrations were estimated by using the Friedewald formula. The fasting plasma glucose concentration was measured by the glucose oxidase method (Beckman Instruments, Inc., Fullerton, CA). Serum intact PTH (iPTH) was determined using a chemiluminometric immunoassay (ADVIA Centaur iPTH; Siemens Medical Solutions Diagnostics, New York, NY), with an interassay variation coefficient of approximately 8%. Serum 25-OH D levels were assayed in duplicate and measured by liquid chromatography-mass spectrometry at Mayo Clinic laboratories (Rochester, MN) within 1 wk from data collection. Serum was obtained within 3 h from blood collection and stored at −80 C. Serum was collected and maintained in iced water until processed. Lower detection limit was 4 ng/ml, and the interassay coefficient of variation was 10%.

Arterial stiffness testing

Evaluation was performed in the supine position in a dark, quiet room. After simultaneous acquisition of pressure waveforms in the right common carotid artery and right femoral artery, pulse transit times between these two sites were automatically measured by the Complior SP device (Artech Medical, Paris, France), as previously described and validated (18). The distance traveled by the pulse wave was measured to the nearest centimeter with an external tape measure over the body surface. This distance was measured by subtracting the distance between the manubrium and the carotid sampling site from the sum of the distances between the manubrium and the umbilicus and the umbilicus and the femoral sampling site. PWV was calculated by dividing the distance traveled by the pulse wave by the pulse transit time. Measurements of PWV were made in triplicate and averaged for the analyses.

Statistical analysis

Study variables are described as the mean ± SD (unless otherwise specified) for continuous variables or as counts or proportions for categorical variables. Age, BMI, 25-OH D levels,

lipid profile, and PWV values were treated as continuous variables. Diagnosed hypertension, hypercholesterolemia, diabetes mellitus, smoking, gender, medication use (antihypertensive drugs or glucose-lowering agents), and vitamin D/calcium supplementation were categorical variables. Continuous variables were tested for normality with the Kolmogorov-Smirnov criterion. Skewed variables were log-transformed and tested again for normality before any parametric analysis. Univariate correlations between 25-OH D concentrations and measured parameters were performed with Pearson's correlation. Differences in age-adjusted means of PWV across 25-OH D tertiles were tested by general linear models. Multiple linear regression analysis was used to test the association between PWV and 25-OH D levels. Models adjusted for potential confounding factors based upon a review of the relevant literature, including age, gender, race, season of blood draw, eGFR, physical activity level, cardiovascular risk score (visceral obesity, smoking, hypercholesterolemia, hypertension, and diabetes), calcium and vitamin D supplements, serum calcium, and iPTH levels. Multicollinearity among the covariates was tested using the variance inflation factor. Statistical significance was based on two-tailed tests, and P values ≤ 0.05 were considered significant. All analyses were performed using SAS (version 9.1; SAS Institute, Inc., Cary, NC) with significance set at $P < 0.05$.

Results

Baseline characteristics of the 1288 subjects are shown in Table 1. Mean 25-OH D level was 34 ng/ml (range, 7 to 89 ng/ml) and mean PWV was 8.6 ± 2.0 m/sec.

Relationship between vitamin D levels and subject characteristics

Serum 25-OH D was significantly lower in men and in both African-Americans men and women, and in subjects with the highest cardiovascular risk scores (Table 2). African-Americans were more likely to have hypertension (64 *vs.* 46%; $P < 0.001$) and obesity (33 *vs.* 22%; $P < 0.001$) compared with Caucasians, whereas there was no difference for diabetes and hypercholesterolemia. Thirty-seven percent of participants had 25-OH D levels below 30 ng/ml, and 10% of participants had 25-OH D levels below 20 ng/ml. Across participant subgroups with 25-OH D below 20 ng/ml, between 20 and 30 ng/ml, and above 30 ng/ml, there was a significant difference in systolic blood pressure [systolic blood pressure = 129 ± 16, 126 ± 16, and 124 ± 17 mm Hg, respectively ($P = 0.0001$)]; in diastolic blood pressure [diastolic blood pressure = 69 ± 8, 67 ± 10, and 66 ± 10 mm Hg, respectively ($P = 0.003$)]; in BMI [BMI = 29.5 ± 0.4, 28 ± 0.2, and 26 ± 0.2 kg/m^2, respectively ($P < 0.0001$)]; and in PWV [PWV = 9.0 ± 0.2, 8.7 ± 0.9, and 8.5 ± 0.6 m/sec, respectively ($P = 0.02$)]. Twenty-nine percent of African-Americans had 25-OH D levels below 30 ng/ml, and 24% had 25-OH D levels below 20 ng/ml; whereas 25% of Caucasians had 25-OH D levels below 30 ng/ml, and 4% had 25-OH D levels below 20 ng/ml ($P < 0.0001$ between groups). Twenty-three percent of the study cohort was obese. Among obese participants, 36% had 25-OH D levels below 30 ng/ml, and 17% had 25-OH D levels below 20 ng/ml.

Participants taking regular vitamin D supplementation had higher 25-OH D levels (40.9 ± 12.1 *vs.* 35.5 ± 11.2 ng/ml; $P < 0.0001$) and were significantly older (73.6 ± 10.5 *vs.* 71.6 ± 11.7 yr; $P = 0.02$). African-Americans were less likely to be taking vitamin D supplementation compared with Caucasians (34 *vs.* 46%; $P = 0.0001$).

Relationship between PWV and subject characteristics

No differences in mean PWV were observed between Caucasian and African-American cohorts (8.8 ± 2.0 *vs.*

TABLE 1. Descriptive and clinical characteristics of the study cohort (n = 1228)

Demographics	
Age (yr)	70 ± 12
Male, n (%)	648 (50)
BMI (kg/m^2)	27 ± 4
Waist circumference (cm)	91 ± 12
Caucasian, n (%)	799 (65)
African-American, n (%)	335 (27)
Smoking, n (%)	573 (48)
Physical activity level (MET/wk)	95 ± 66
Alcohol intake (drinks/wk)[a]	
None or <1, n (%)	285 (28)
1 to 3, n (%)	287 (29)
> 3, n (%)	419 (13)
Hypertension, n (%)	628 (50)
Hypercholesterolemia, n (%)	479 (37)
Obesity, n (%)	281 (23)
Diabetes, n (%)	273 (22)
Cardiovascular parameters	
Systolic blood pressure (mm Hg)	125 ± 17
Diastolic blood pressure (mm Hg)	66 ± 9
Mean arterial pressure (mm Hg)	98 ± 12
Heart rate (beats/min)	64 ± 10
PWV (m/sec)	8.6 ± 2.0
Medications	
Antihypertensive drugs, n (%)	562/628 (89.5)
Hypoglycemic agents, n (%)	114 (14.6)
Calcium and Vitamin D supplements, n (%)	549 (42.6)
Hormone replacement therapy, n (%) [women]	70 (5.4)
Laboratory	
Fasting glucose (mg/dl)	90 ± 17
Creatinine (mg/dl)	1.0 ± 0.3
Albumin (g/dl)	4.2 ± 0.3
eGFR (ml/min/1.73 m^2)	77 ± 18
Cac (mg/dl)	9.2 ± 0.4
Total cholesterol (mg/dl)	189 ± 38
LDL-cholesterol (mg/dl)	110 ± 33
HDL-cholesterol (mg/dl)	59 ± 16
Triglycerides (mg/dl)	101 ± 56
PTH (pg/ml)	38 ± 18
25-OH D (ng/ml)	34 ± 12

Data are expressed as mean ± SD or proportions. HDL, High-density lipoprotein; LDL, low-density lipoprotein.

[a] Missing = 297.

TABLE 2. Relationship between vitamin D status and subject characteristics

	ng/ml	*P* value
Gender		
Men	33.0 ± 10.8	0.0001
Women	35.6 ± 12.9	
Race		
Caucasian	36.0 ± 10.8	<0.0001
African-American	30.2 ± 13.4	
Vitamin D supplement		
Yes	40.9 ± 12.1	<0.0001
No	35.3 ± 11.2	
Cardiovascular risk score[b]		
0–1	34.4 ± 0.5	0.05[a]
2–3	34.6 ± 0.4	
4–5	31.5 ± 0.2	

[a] *P* for trend.

[b] Cardiovascular risk score = visceral obesity (yes/no), smoking (yes/no), hypertension (yes/no), hypercholesterolemia (yes/no), and diabetes (yes/no).

8.7 ± 2.1 m/sec, respectively; $P = 0.27$). PWV was significantly higher among subjects with hypertension (9.1 ± 1.9 *vs.* 8.0 ± 2.1 m/sec, respectively; $P < 0.001$) and diabetes (9.3 ± 2.0 *vs.* 8.4 ± 2.1 m/sec, respectively; $P < 0.001$); whereas no differences were observed in mean PWV according to obesity (8.7 ± 1.9 *vs.* 8.6 ± 2.1 m/sec, respectively; $P = 0.30$) and smoking (8.7 ± 1.9 *vs.* 8.5 ± 2.1 m/sec, respectively; $P = 0.19$). Highest PWV tertiles (11.0 ± 1.5 m/sec) were associated with lower physical activity levels (93.4 MET/wk) ($P < 0.0001$); whereas lower PWV tertiles (mean PWV = 6.6 ± 0.6 m/sec) were associated with the highest physical activity level tertiles (99.3 MET/wk) ($P < 0.0001$).

Relationship between vitamin D levels and arterial stiffness

After adjusting for age, we found a significant inverse correlation between PWV and 25-OH D levels ($\beta = -0.43$; $P = 0.001$). Subjects in the lowest 25-OH D tertiles (<20 ng/ml) showed the highest PWV (8.8 m/sec), compared with second to third tertiles (8.6 m/sec, 8.5 m/sec, respectively; p for trend = 0.04).

To verify whether the association between 25-OH D and PWV was not attributable to confounding variables known to be associated with PWV and 25-OH D levels were added as covariates in the age- and sex-adjusted linear model relating PWV to 25-OH D levels (Table 3). After adjusting for age, gender, race, and season of blood draw, the association between PWV and 25-OH D levels remained highly statistically significant (Table 3, model 1). The association between PWV and 25-OH D levels remained unchanged after eGFR was added to the model (Table 3, model 2). Similarly, this association remained significant after adjusting for physical activity level and a cardiovascular risk score (visceral obesity, smoking, hypercholesterolemia, hypertension, and diabetes; Table 3, model 3). Finally, the association between PWV and 25-OH D levels still remained significant after adjusting for calcium and vitamin D supplements, serum calcium (Cac), and iPTH levels (Table 3, model 4). A 25-OH D by-sex and -race interaction term was also included in the fully adjusted model. The interaction term was not statistically significant, suggesting that the nature of association between PWV and 25-OH D levels is substantially similar among the sex group. Separate analysis in the nonsmoker cohort showed that after adjusting for age, gender, race, season of blood draw, physical activity level, calcium and vitamin D supplements, serum calcium, and iPTH levels, the association between PWV and 25-OH D levels remained significant [$\beta = -0.46$; Stb (standardized beta) = −0.09; $P = 0.04$].

Discussion

In the present study, we found an inverse association between arterial stiffness and 25-OH D levels, independent

TABLE 3. Hierarchical multivariate models examining the relationship between PWV and 25-OH D levels

	Model 1		Model 2		Model 3		Model 4		
Covariates	Std B	*P*	Std B	*P*	Std B	*P*	B	Std B	*P*
Age (yr)	0.50	<0.0001	0.52	<0.0001	0.47	<0.0001	0.07	0.47	<0.0001
Gender (men)	0.14	<0.0001	0.14	<0.0001	0.16	<0.0001	0.66	0.16	<0.0001
Race (Caucasian)	−0.02	0.24	−0.03	0.18	−0.03	0.17	−0.07	−0.05	0.07
Season of blood draw (autumn/winter)	−0.12	<0.0001	−0.12	<0.0001	−0.11	<0.0001	−0.61	−0.14	<0.0001
eGFR (ml/min/1.73 m^2)			0.05	0.02	0.05	0.03	0.008	0.07	0.02
Physical activity level (MET/wk)					−0.05	0.07	−0.001	−0.05	0.11
Cardiovascular risk score[a]					0.07	0.003	0.15	0.09	0.005
Calcium/vitamin D supplements							0.14	0.03	0.28
Serum Cac (mg/dl)							−0.04	−0.06	0.03
iPTH (pg/ml)							0.03	0.008	0.78
25-OH D (ng/dl)	−0.07	0.005	−0.06	0.006	−0.05	0.03	−0.34	−0.07	0.04

For each model, standardized β-coefficient (Std B) and *P* values are given. For model 4, unstandardized β-coefficient (B), Std B, and *P* values are given. In parentheses, reference values or units are given where appropriate.

[a] Cardiovascular risk score = visceral obesity (yes/no), smoking (yes/no), hypertension (yes/no), hypercholesterolemia (yes/no), and diabetes (yes/no).

of age and several confounders. We studied a large multiethnic population over a wide age range and with a relatively low risk factors burden, and we used state-of-the art methods to assess arterial stiffness. These findings are in line with the well-established associations between vitamin D deficiency and a broad range of cardiovascular disorders and risk factors (1), providing a possible explanation of how lower vitamin D levels, by precipitating vascular stiffening, might predispose individuals to a higher risk for development of cardiovascular disease and adverse events.

Arterial stiffness increases with advancing age (19) and is a powerful predictor of mortality and morbidity (20, 21), hypertension (22), and decline in cognitive function (23). Accumulating evidence suggests that cardiovascular disease is associated with vitamin D deficiency. Various epidemiological studies have reported reduced 25-OH D concentrations in patients with previous and prevalent cardiovascular or cerebrovascular diseases (24, 25). Population-based studies have partially, but not consistently, documented that poor vitamin D status is associated with an increased risk of cardiovascular events and cardiovascular mortality (26–28). Meta-analyses performed so far on this topic support the finding that low 25-OH D concentrations are associated with incident cardiovascular disease (29). In this context, Grandi *et al.* (25) found that the risk of cardiovascular mortality was increased by 83% (hazard ratio, 1.83; 95% confidence interval, 1.19–2.80) in individuals with low 25-OH D levels. Data from randomized controlled trials are sparse and have partially, but not consistently, shown some beneficial effects of vitamin D supplementation on cardiovascular risk factors (30, 31). Of note, Al Mheid *et al.* (32) recently reported that vitamin D insufficiency is associated with increased arterial stiffness and endothelial dysfunction in healthy subjects. Interestingly, these authors found that in 42 subjects with vitamin D insufficiency, normalization of 25-OH D at 6 months was associated with increases in reactive hyperemia index and subendocardial viability ratio, and a decrease in mean arterial pressure (32). In a random sample of 560 subjects selected from the general population, Mayer *et al.* (33) reported a negative trend in PWV among 25-OH D quartiles. These authors found that subjects in the lowest 25-OH D quartile (<20 ng/ml) showed the highest aortic PWV (9.04 m/sec), compared with second to fourth quartiles (8.07, 7.93, and 7.70 m/sec, respectively; P for trend <0.0001) (33). The association between 25-OH D and PWV remained significant after adjustment for age, gender, and other potential confounders including hypertension, obesity, lipid profile, kidney function, drug treatment (statin, antihypertensives), and history of cardiovascular disease (33). More recently, Lee *et al.* (34) reported that low 25-OH D levels independently predicted PWV ($P < 0.001$) in individuals with type 2 diabetes (n = 305) after adjustment for other risk factors such as age, smoking, hypertension, C-reactive protein, diabetes duration, hypertension duration, glycated hemoglobin, and BMI.

Evidence is accumulating that vitamin D may also exert various direct effects on the cardiovascular system (1). Heart and blood vessels are target tissues for vitamin D and express both vitamin D receptor (VDR) and 1α-hydroxylase. VDR-knockout and 1α-hydroxylase-knockout mice develop heart failure despite normalized calcium levels (35). Increased activation of the RAAS seems to be the mediating pathway because RAAS blockade with, for example, the angiotensin-converting enzyme inhibitor captopril reverses cardiac abnormalities in these mouse models (35, 36). The crucial role of vitamin D for myocardial health is further supported by increased VDR expression in myocardial hypertrophy (37). VDR expression increased in cardiac myocytes and fibroblasts after treatment with the prohypertrophic vasoactive peptide endothelin. Experimental studies documented antihypertrophic and antiproliferative actions of vitamin D metabolites, which down-regulate several genes involved in the development of myocardial hypertrophy. VDR activation modulates cardiac calcium flux and thereby induces an accelerated relaxation of cardiomyocytes, which may improve diastolic function of the heart. Vitamin D-mediated regulation of cardiac extracellular matrix turnover may also be important to maintain cardiac health (38). Vitamin D may also protect against atherosclerosis, vascular calcification, and endothelial dysfunction. Antiatherosclerotic vitamin D effects may include inhibition of macrophage cholesterol uptake and foam cell formation, down-regulation of vascular smooth muscle cell proliferation and migration, and suppression of inflammation-triggered endothelial activation and expression of endothelial adhesion molecules (8, 27, 39). Vitamin D effects may also protect against endothelial dysfunction, for example, by antioxidative actions and by inhibiting lipid peroxidation (27). Finally, vitamin D may reduce vascular calcification, for example, by inhibiting bone morphogenic proteins, but data on this topic are somewhat controversial (27). Conversely, vitamin D overload is used as a model of vascular stiffening (39). Therefore, poor vitamin D status as well as vitamin D intoxication may contribute to vascular calcification (8, 27, 40). Observational and interventional studies showed inconsistent results regarding the association of vitamin D with subclinical atherosclerosis markers such as carotid intima-media thickness (27, 41). Several, but not all, interventional studies showed that vitamin D supplementation im-

proves endothelial function (8, 36, 42). Therefore, large trials assessing the effect of vitamin D supplementation on vascular structure and endothelial function in individuals with vitamin D deficiency are encouraged.

Study limitations

The cross-sectional, observational design of the present study precludes definitive conclusions regarding the causal relationship between arterial stiffness and vitamin D levels. It should be also highlighted that the magnitude of contribution of low 25-OH D status to arterial stiffness might be variable and modest. The BLSA population is a series of volunteers who are healthy at the time of enrollment and tend to be highly educated and to have a high socio-economic status. Thus, not surprisingly, the prevalence of vitamin D deficiency in the BLSA is lower than in other published studies. A limitation of this study is that information on important determinants of serum 25-OH D concentration, such as sun exposure and vitamin D intake from food sources, were not collected. In addition, we did not explore the putative mediating effect of alcohol consumption. Moderate, regular alcohol consumption by apparently healthy people is associated with lower cardiovascular morbidity and mortality than in abstainers (15). Mechanisms supporting this include beneficial regulation of lipids and fibrinolysis, decreased platelet aggregation and coagulation factors, beneficial effects on endothelial function, and inflammation and insulin resistance. Of note, 43% of participants reported more than three servings per week. However, because such information is missing for about 25% of the study population (297 participants), alcohol consumption data were not included in the regression model as covariate. Finally, in this study we did not explore the putative mediating effect of inflammatory status. Despite the aforementioned limitations, this study has several unique strengths. First, this study measured carotid-femoral PWV, which is the "gold standard" for the noninvasive assessment of arterial stiffness. Second, this study was performed in the context of a normative aging study that included both sexes with careful assessment of several potential confounders of the arterial stiffness/vitamin D status relationship.

Conclusions

Vitamin D levels are associated with increased arterial stiffness in a normative aging population, irrespective of traditional risk factors burden. Further research is needed to further clarify the mechanisms by which vitamin D affects arterial stiffness and to test the hypothesis that vitamin D supplementation may prevent cardiovascular disease.

Acknowledgments

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