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ORIGINAL RESEARCH

Vitamin D deficiency is associated with coronary artery calcification in cardiovascularly asymptomatic African Americans with HIV infection

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Objective: Patients with HIV infection are at increased risk for coronary artery disease (CAD), and growing evidence suggests a possible link between vitamin D deficiency and clinical/subclinical CAD. However, the relationship between vitamin D deficiency and coronary artery calcification (CAC), a sensitive marker for subclinical CAD, in those with HIV infection is not well investigated.

Methods: CAC was quantified using a Siemens Cardiac 64 scanner, and vitamin D levels and the presence of traditional and novel risk factors for CAD were obtained in 846 HIV-infected African American (AA) participants aged 25 years or older in Baltimore, MD, USA without symptoms or clinical evidence of CAD.

Results: The prevalence of vitamin D deficiency (25-hydroxy vitamin D $<$10 ng/mL) was 18.7%. CAC was present in 238 (28.1%) of the 846 participants. Logistic regression analysis revealed that the following factors were independently associated with CAC: age (adjusted odds ratio [OR]: 1.11; 95% confidence interval [CI]: 1.08–1.14); male sex (adjusted OR: 1.71; 95% CI: 1.18–2.49); family history of CAD (adjusted OR: 1.53; 95% CI: 1.05–2.23); total cholesterol (adjusted OR: 1.006; 95% CI: 1.002–1.010); high-density lipoprotein cholesterol (adjusted OR: 0.989; 95% CI: 0.979–0.999); years of cocaine use (adjusted OR: 1.02; 95% CI: 1.001–1.04); duration of exposure to protease inhibitors (adjusted OR: 1.004; 95% CI: 1.001–1.007); and vitamin D deficiency (adjusted OR: 1.98; 95% CI: 1.31–3.00).

Conclusion: Both vitamin D deficiency and CAC are prevalent in AAs with HIV infection. In order to reduce the risk for CAD in HIV-infected AAs, vitamin D levels should be closely monitored. These data also suggest that clinical trials should be conducted to examine whether vitamin D supplementations reduce the risk of CAD in this AA population.

Keywords: African Americans, HIV infection, antiretroviral therapy, coronary artery calcification, vitamin D deficiency

Introduction

A large body of literature indicates that patients with HIV infection are at increased risk for coronary artery disease (CAD).[1–8] This may be related, in part, to the metabolic effects associated with the long-term use of antiretroviral therapies (ARTs), particularly as HIV infection is increasingly a chronic, manageable disease. As a racial/ethnic group in the United States, African Americans (AAs) have the highest overall CAD mortality.[9] Although many traditional risk factors are more prevalent in AAs, traditional risk factors alone do not entirely explain the increased CAD risk.

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It is well known that vitamin D deficiency is highly prevalent in AAs.[10] Recent evidence suggests that vitamin D deficiency is associated with an increased risk for clinical CAD,[11–13] and we previously reported that vitamin D deficiency is associated with subclinical CAD in AA chronic cocaine users and in AAs with HIV infection.[14–16] Coronary artery calcification (CAC) is a sensitive measure of subclinical coronary atherosclerosis and a strong risk factor for future cardiovascular events.[17] We therefore investigated the prevalence of vitamin D deficiency in AAs with HIV infection and without known CAD or CAD symptoms, and whether vitamin D deficiency was an independent predictor of the presence of CAC. The objective of this study, therefore, was to test the hypothesis that vitamin D deficiency is independently associated with increased prevalence of subclinical CAD in AAs with HIV infection, using baseline cross-sectional data from a cohort of participants aged 25 years or older in Baltimore, MD, USA.

Methods

Study participants

Between August 2003 and December 2012, 848 HIV-infected AA study participants from Baltimore, MD were enrolled in an observational study investigating the effects of cocaine use and antiretroviral regimens on subclinical atherosclerosis. The goal of the overall study was to investigate the association of HIV infection, cocaine abuse, ART, and other factors that might explain the increased risk for subclinical atherosclerosis in AA men and women with HIV infection.

Inclusion criteria were age 25 years or older, AA race, and HIV infection. Exclusion criteria were: (1) any evidence of clinical CAD; (2) any symptoms believed to be related to CAD; (3) glomerular filtration rate <60 mL/minute/1.73 m^2; (4) known allergy to the contrast used for computed tomography (CT); (5) pregnancy; and (6) infrequent cocaine use (defined as using cocaine fewer than four times a month or for less than 6 consecutive months). Chronic cocaine users (defined as use of cocaine by any route for at least 6 months, administered at least four times a month), and non-cocaine users (those who had never used cocaine) were enrolled however.

A medical chart review was used to confirm the information on medical history and medications that was provided by the study participants. Interviews regarding sociodemographic information and drug-use behaviors were conducted; clinical examinations, blood pressure (BP) measurement, echocardiography, and 64-slice multidetector CT coronary angiography (contrast-enhanced) were performed; and lipid profiles, vitamin D, and high-sensitivity C-reactive protein (hsCRP) levels obtained.

The Johns Hopkins Medicine Institutional Review Board approved the study protocol and consent form, and all study participants provided written informed consent. All procedures used in this study were in accordance with institutional guidelines.

Main procedures

Vitamin D measurement

Sera were collected, centrifuged, and stored at −70°C until analyzed. Serum 25-hydroxy (OH) vitamin D was determined by a direct, competitive chemiluminescence immunoassay (DiaSorin, Saluggia, Italy).[18] The level of detection for 25-OH vitamin D was 4 ng/mL. This method accurately measures vitamins D2 and D3 and is reported as a total 25-OH vitamin D. The reference range is 32–100 ng/mL. This study identifies vitamin D deficiency according to the Framingham Offspring Study[13] as serum 25-OH vitamin D <10 ng/mL.

Coronary artery calcium

A noncontrast modified discrete cosine transform scan was performed on a Sensation Cardiac 64 scanner (Siemens Healthcare, Erlangen, Germany) to determine the coronary artery calcium score with a sequential scan of 3 mm slices with prospective electrocardiogram triggering, 30×0.6 mm detector collimation, and tube current 135 mAs at 120 kV. At each CAC measurement, each study participant underwent two scans. A radiologist (EKF), blinded to the participants' clinical data and risk factor profiles, independently evaluated all CT scans with the use of an interactive scoring system to calculate Agatston score.

Statistical analysis

Statistical analysis was performed with SAS software (v 9.3; SAS Institute, Cary, NC, USA). All continuous parameters were summarized by medians and interquartile ranges (IQRs), and all categorical parameters were summarized as proportions. To compare between-group differences in demographic and clinical characteristics, lipid profiles, drug-use behaviors, and other factors, the nonparametric Wilcoxon two-sample test was used for continuous variables and the chi-square test was employed for categorical variables.

The presence of CAC was defined as any Agatston score >0 at baseline. Univariate logistic regression models were first fitted to evaluate the crude association between the presence of CAC and each of the factors –

including age, sex, family history of CAD, cigarette smoking, alcohol use, cocaine use, total serum cholesterol, high-density lipoprotein (HDL)-cholesterol, low-density lipoprotein (LDL)-cholesterol, serum triglycerides, vitamin D, hsCRP, glucose level, BP, body mass index, baseline CD4 cell count, baseline HIV RNA quantification, and ARTs, individually. Variables on cocaine and other illegal drug use included frequency, forms, administration mode (injection, smoking, etc), and duration of drug use. ARTs were categorized on the basis of exposure to three classes – nucleoside reverse transcriptase inhibitors (NRTIs), non-NRTIs (NNRTIs), and protease inhibitors (PIs). Serum 25-OH vitamin D levels were classified into 4 groups: <10.0 ng/mL, 10.0–19.9 ng/mL, 20.0–29.9 ng/mL, and ≥30 ng/mL. Those factors that were significant at the $P < 0.15$ level in the univariate models were put into the multiple logistic regression models to identify the ones independently associated with the presence of CAC. Those variables that ceased to make significant contributions to the models were deleted in a stagewise manner and a new model was refitted. This process of eliminating, refitting, and verifying continued until all of the variables included were statistically significant, yielding a final model.[19] The Framingham Risk Score was calculated to estimate the CAD risk.[20] The *P*-values reported are two-sided. A *P*-value < 0.05 indicated statistical significance.

Results

General characteristics

The general and clinical characteristics of the study participants by the presence of CAC are presented in Table 1. The median age (with IQR) was 46 (41–51) years. Of the 846 participants in this study, 534 (63.1%) were male, 83.2% were cigarette smokers, and 76.2% were chronic cocaine users.

The median vitamin D level was 18.0 ng/dL (IQR: 11.0–27.0). The prevalence rate of vitamin D deficiency (serum 25-OH vitamin D <10 ng/mL) was 18.7% (95% confidence interval [CI]: 16.1%–21.5%).

The median total cholesterol level was 163 (IQR: 140–191) mg/dL. The median LDL-cholesterol level was 85 (IQR: 65–107) mg/dL. The median HDL-cholesterol level was 50 (IQR: 39–61) mg/dL. The median triglycerides level was 107 (IQR: 75–155) mg/dL. The median systolic BP was 117 (IQR: 108–128) mmHg, and the median diastolic BP was 73 (IQR: 66–81) mmHg. According to the Framingham Risk Score algorithm, 730 (86.3%) of the 846 participants had low risk of CAD.[20]

There were significant (or borderline significant) differences between those with and without the presence of CAC, not only in terms of traditional risk factors, including age, sex, family history of CAD, cigarette smoking, alcohol consumption, hypertension, systolic and diastolic BP, total cholesterol, LDL-cholesterol, HDL-cholesterol, triglycerides, and Framingham Risk Score, but also in vitamin D deficiency, cocaine use, year of ART initiation, duration of exposure to NRTIs, duration of exposure to PIs, and duration of exposure to ARTs. There were no significant differences in hsCRP, CD4 cell count, and plasma viral load levels between those with and those without the presence of CAC (Table 1).

Prevalence of the presence of CAC

The overall prevalence of the presence of CAC was 28.1% (95% CI: 25.1%–31.3%). The prevalences of the presence of CAC were 16.9% and 23.1% in those without and with vitamin D deficiency, respectively ($P = 0.038$).

Factors associated with the presence of CAC

According to univariate logistic regression analyses, traditional risk factors associated with the presence of CAC included age, male sex, family history of CAD, cigarette smoking, years of cigarette smoking, systolic BP, diastolic BP, total cholesterol, serum LDL-cholesterol concentration, serum HDL-cholesterol concentration, triglycerides, and Framingham Risk Score. Nontraditional risk factors associated with the presence of CAC included cocaine use, years of cocaine use, year of ART initiation, exposure to any NRTIs, exposure to any PIs, exposure to any ARTs, and vitamin D deficiency. Specifically, univariate logistic regression analyses showed that, compared to those without vitamin D deficiency, those with vitamin D deficiency were almost 50% more likely to have CAC (odds ratio [OR]: 1.47; 95% CI: 1.02–1.72).

The final model indicated that the presence of CAC was associated with previously described traditional risk factors, including age (adjusted OR: 1.11; 95% CI: 1.08–1.14), male sex (adjusted OR: 1.71; 95% CI: 1.18–2.49), family history of CAD (adjusted OR: 1.53; 95% CI: 1.05–2.23), serum total cholesterol concentration (adjusted OR: 1.006; 95% CI: 1.002–1.010), and serum HDL-cholesterol concentration (adjusted OR: 0.989; 95% CI:0.979–0.999). The analysis also showed that years of cocaine use (adjusted OR: 1.02; 95% CI: 1.001–1.04), duration of exposure to PIs (adjusted OR: 1.004; 95% CI: 1.001–1.007), and vitamin D deficiency (adjusted OR: 1.98; 95% CI: 1.31–3.00) were independently associated with the presence of CAC. If

Table 1 Characteristics of study participants by the presence of coronary calcification[a]

Characteristic	Total	Coronary calcification		*P*-value
	(N = 846)	No (N = 608)	Yes (N = 238)	
Age (years)	46 (41–51)	44 (39–49)	50 (46–54)	<0.0001
Male (%)	63.1	59.1	73.5	<0.001
Family history of CAD (%)	23.8	20.1	30.7	0.003
Cocaine use (%)	76.2	73.6	82.8	0.005
Cocaine use >15 years (%)	37.6	33.2	47.9	0.04
Cigarette smoking (%)	83.2	81.6	87.4	0.04
Cigarette smoking >15 years (%)	65.4	61.4	75.6	<0.0001
Alcohol use (%)	86.3	84.9	89.9	0.06
hsCRP ≥2 mg/dL (%)	45.7	44.1	50.0	0.12
hsCRP (mg/dL)	1.65 (0.6–4.7)	0.6 (0.2–1.6)	2.1 (0.6–5.0)	0.34
Serum 25-OH vitamin D (ng/mL)	18.0 (11.0–27.0)	18.0 (11.0–27.0)	18.0 (10.0–26.0)	0.06
Vitamin D deficiency (%)	18.7	16.9	23.1	0.038
Systolic BP (mmHg)	117 (108–128)	116 (107–125)	121 (111–132)	<0.0001
Diastolic BP (mmHg)	73 (66–81)	73 (66–81)	74 (68–83)	0.03
Fasting glucose (mg/dL)	85 (78–93)	85 (78–93)	86 (79–94)	0.38
Hypertension (%)	12.4	10.7	16.8	0.015
Diabetes (%)	4.0	3.5	5.5	0.18
BMI (kg/m^2)	25.1 (22.1–29.1)	25.0 (22.2–29.1)	25.4 (22.0–29.5)	0.64
Baseline CD4 (cells/mm^3)	368 (221–583)	374 (222–575)	347 (213–610)	0.85
Baseline viral load[b] (copies/mL)	1,311 (202–32,950)	2,721(202–40,943)	462 (202–15,240)	0.06
Total cholesterol (mg/dL)	163 (140–191)	161 (139–186)	168 (141–199)	0.01
LDL-C (mg/dL)	85 (65–107)	84 (64–103)	90 (66–113)	0.02
HDL-C (mg/dL)	50 (39–61)	50 (40–61)	49 (36–62)	0.09
Triglycerides (mg/dL)	107 (75–155)	103 (72–147)	118 (84–178)	<0.0001
Year of enrollment (%)				0.19
2003–2005	12.4	13.2	10.5	
2006–2007	12.5	13.0	11.3	
2008–2009	34.8	32.6	40.3	
2010–2011	37.8	40.2	37.8	
Year of ART initiation				0.0007
Never initiated	20.8	23.2	14.7	
Before 1996	11.0	9.2	15.6	
1996–2003	30.3	28.8	34.0	
2004–2007	22.8	21.9	25.2	
2008–2010	15.1	16.9	10.5	
Duration of NRTI use (months)	26.0 (2.9–26.0)	24.0 (0.9–66.0)	36.0 (7.9–93.0)	0.002
Duration of NNRTI use (months)	0 (0.0–14.0)	0.0 (0.0–12.0)	0.0 (0.0–24.0)	0.15
Duration of PI use (months)	12.0 (0.0–52.5)	7.9 (0.0–48.0)	15.0 (0.0–72.0)	0.005
Duration of ART use (months)	36.0 (6.9–86.0)	32.2 (4.9–80.0)	48.0 (15.0–115.1)	<0.0001
Framingham risk score	4.0 (2.0–7.0)	3.0 (2.0–6.0)	6.0 (4.0–10.0)	<0.0001
Framingham risk score <10.0 (%)	86.3	90.5	75.6	<0.0001

Notes: [a]Median (interquartile range) for continuous variables, proportion (%) for categorical variables; [b]HIV RNA quantification.
Abbreviations: 25-OH, 25-hydroxy; ART, antiretroviral therapy; BMI, body mass index (kg/m^2); BP, blood pressure; CAD, coronary artery disease; HDL-C, high-density lipoprotein cholesterol; hsCRP, high-sensitivity C-reactive protein; LDL-C, low-density lipoprotein cholesterol; NNRTI, non-NRTI; NRTI, nucleoside reverse transcriptase inhibitor; PI, protease inhibitor.

the categorized serum 25-OH vitamin D (<10 ng/mL as the reference group) instead of vitamin D deficiency was included in the final model, the higher 25-OH vitamin D levels were independently associated with a lower risk of having CAC (Table 2). Thus, after controlling for traditional and nontraditional risk factors identified in this population, vitamin D deficiency is associated with a two-fold increase in the prevalence of CAC.

Interactions between vitamin D deficiency and other factors were not statistically significant in the multiple logistic regression models.

Discussion

This study estimated the prevalence of CAC in HIV-infected AAs without clinical cardiovascular disease or symptoms, and investigated whether vitamin D deficiency and other

Table 2 Demographic, laboratory, and clinical factors in relation to the presence of coronary calcification: logistic regression analysis[a]

Variable	Subclinical CAD	
	Crude OR (95% CI)	Adjusted OR (95% CI)
Age	1.12 (1.09–1.15)	1.11 (1.08–1.14)
Sex		
Female	1.00	1.00
Male	1.92 (1.39–2.68)	1.71 (1.18–2.49)
Family history of CAD		
No	1.00	1.00
Yes	1.66 (1.18–2.33)	1.53 (1.05–2.23)
Cigarette smoking		
Never	1.00	
Ever	1.57 (1.01–2.42)	
Alcohol use		
No	1.00	
Yes	1.59 (0.99–2.56)	
Cocaine use		
Never	1.00	
Ever	1.72 (1.18–253)	
Duration of cigarette smoking (years)	1.03 (1.01–1.04)	
Duration of cocaine use (years)	1.03 (1.01–1.04)	1.02 (1.001–1.04)
hsCRP >2 mg/dL		
No	1.00	
Yes	1.27 (0.94–1.72)	
Serum 25-OH vitamin D (ng/mL)		
<10.0	1.00	1.00
10.0–19.9	0.68 (0.42–0.97)	0.53 (0.33–0.85)
20.0–29.9	0.64 (0.41–0.99)	0.40 (0.24–0.68)
≥30.0	0.83 (0.52–1.32)	0.61 (0.36–1.05)
Systolic BP (mmHg)	1.02 (1.01–1.03)	
Diastolic BP (mmHg)	1.02 (1.01–1.03)	
Fasting glucose	1.004 (0.999–1.009)	
BMI (kg/m^2)	1.00 (0.98–1.03)	
Baseline CD4 count		
≥350 cells/mm^3	1.00	
<350 cells/mm^3	1.14 (0.70–1.85)	
Baseline viral load[b]		
≥400 copies/mL	1.00	
<400 copies/mL	0.65 (0.39–1.07)	
Total cholesterol (mg/dL)	1.005 (1.002–1.009)	1.006 (1.002–1.010)
LDL-C	1.005 (1.001–1.010)	
HDL-C	0.993 (0.985–1.001)	0.989 (0.979–0.999)
Triglycerides (mg/dL)	1.003 (1.001–1.004)	
Year of ART initiation		
Never initiated	1.00	
Before 1996	2.66 (1.53–4.64)	
1996–2003	1.87 (1.18–2.94)	
2004–2007	1.82 (1.13–2.94)	
2008–2010	0.98 (0.55–1.73)	
Year of enrollment		
2003–2005	1.00	
2006–2007	1.09 (0.58–2.05)	
2008–2009	1.55 (0.93–2.59)	
2010–2011	1.15 (0.69–1.91)	
Duration of NRTI use (months)	1.005 (1.003–1.008)	
Duration of NNRTI use (months)	1.004 (0.999–1.008)	
Duration of PI use (months)	1.006 (1.003–1.009)	1.004 (1.001–1.007)
Duration of ART use (months)	1.006 (1.003–1.008)	
Framingham risk score	1.015 (1.11–1.20)	

Notes: [a]subclinical CAD was coded as yes (1) or no (0); [b]viral load, HIV RNA quantification.

Abbreviations: 25-OH, 25-hydroxy; ART, antiretroviral therapy; BMI, body mass index (kg/m^2); BP, blood pressure; CAD, coronary artery disease; CI, confidence interval; HDL-C, high-density lipoprotein cholesterol; hsCRP, high-sensitivity C-reactive protein; LDL-C, low-density lipoprotein cholesterol; NNRTI, non-NRTI; NRTI, nucleoside reverse transcriptase inhibitor; OR, odds ratio; PI, protease inhibitor.

factors are independently associated with the presence of CAC, a significant marker of subclinical CAD.

There are several major findings of our study. The overall prevalence rate of CAC in this population was 28.1% (95% CI: 25.1%–31.3%). This rate is high, considering that almost 90% of the population was at low risk based on the Framingham Risk Score.[20] Even among those with CAC, the median Framingham Risk Score was only 6 with an IQR of 4.0–10.0, suggesting that nontraditional risk factors are likely to significantly contribute to disease in this patient population. The study found that, among cardiovascularly asymptomatic AAs with HIV infection, vitamin D deficiency was independently associated with a two-fold increase in the risk of the presence of CAC. In addition, the study found that age, male sex, duration of cocaine use, total cholesterol, and duration of PI use were associated with an increase in risk of CAC as well.

We also demonstrated that ART (PI) use was linearly associated with the presence of CAC. Although these results are consistent with our previous observations,[21–32] a dose–response relationship between duration of PI use and CAC has never been reported. Studies have suggested that PIs may induce dyslipidemia and lipodystrophy, leading to elevated incidence of atherosclerosis in patients.[33–35] Animal and cell line studies have suggested that PIs may also have a direct adverse effect on vascular endothelial cells rather than an indirect influence via dyslipidemia.[36,37] It is worth mentioning that, although year of ART initiation was significant in the univariate logistic regression model, suggesting that earlier

generations of ART (including PIs) may be associated with a higher risk of CAC, the independent effect of year of ART initiation disappeared in the multivariate model, implying that all generations of PIs may be less cardiovascular-friendly.

It has been reported that highly active antiretroviral therapy (HAART) containing PIs can cause hyperlipidemia, hyperglycemia, and central obesity.[38] Cardiovascular risk is increased by these metabolic derangements, and premature atherosclerotic vascular disease may be the consequence. Impairment of glucose transport and phosphorylation may contribute significantly to impaired systemic glucose uptake in patients receiving HAART.[39] In addition, some PIs, such as ritonavir, indinavir, and amprenavir, upregulate CD36, a scavenger receptor mediating cholesterol uptake in macrophages.[40] Furthermore, PIs may directly damage endothelium-dependent vasodilation, a marker of vascular damage preceding atherosclerotic changes.[38] One study showed that patients treated with PIs had a higher prevalence of atherosclerotic lesions in the carotid arteries than did HIV-infected patients naïve of PI treatment.[41]

Cocaine use was previously implicated as being independently associated with CAC;[24,29] nevertheless, a dose–response relationship between duration of cocaine use and CAC has not been demonstrated before. The mechanism by which cocaine promotes atherosclerosis remains unclear. The effect of cocaine use on atherosclerosis has been investigated in animal studies.[42–46] In one animal study[45] in which rabbits were fed a high-cholesterol diet, cocaine appeared to accelerate the development of atherosclerosis: rabbits were fed a 0.5% cholesterol diet for 60 days and administered either cocaine (0.25 mg/kg twice a day) or saline. Atherosclerotic plaque area of the intimal surface of the aorta was shown to be significantly greater in the rabbits that received cocaine.[45] Another animal study showed that incubation of rabbit platelet-rich plasma increased platelet aggregation and thromboxane production to arachidonic acid, suggesting that cocaine may alter platelet function.[46]

The prevalence of vitamin D deficiency was 18.7% (95% CI: 16.1%–21.5%). This was based on our working definition of vitamin D deficiency as 25-OH vitamin D $<$10 ng/mL. However, the US Endocrine Society guideline defines vitamin D deficiency as 25-OH vitamin D less than 20 ng/mL.[47] If the US Endocrine Society's definition is used, the prevalence of vitamin D deficiency in this population would be 54.5% (95% CI: 51.1%–57.9%) – indicating that more than half of the study population suffered from vitamin D deficiency. Humans get most of their vitamin D from cutaneous synthesis following exposure to ultraviolet B light.[48] The prevalence of vitamin D deficiency is much higher in AAs than in other racial/ethnic groups, possibly due to multiple factors, including increased pigmentation in darker skin suppressing cutaneous vitamin D synthesis.[12,39,49]

Although growing evidence suggests that vitamin D deficiency may be associated with clinical CAD[12,49,50] and subclinical CAD,[14–16] the relationship between vitamin D deficiency and CAC has not been well characterized. A large prospective study recently demonstrated that lower vitamin D levels were independently associated with increased risk of developing new-onset CAC during a 3-year follow-up study in a large, community-based, multiethnic population without preexisting clinical CAD;[51] however, the association between vitamin D deficiency and CAC in people with HIV infection has not been reported.

New evidence links vitamin D deficiency and endothelial dysfunction, suggesting a possible mechanism linking deficiency with CAD.[52–54] An animal study reported that early-life vitamin D deficiency is associated with endothelial vasodilator dysfunction as well as elevated BP.[55] Studies have suggested that vitamin D suppresses the endothelial inflammation process[56,57] and may play an active role in protecting against vascular calcification.[56–58]

This study has several limitations. First, because all of the study participants were AA and were not a random sample of those with HIV infection, the results should be interpreted with caution. Second, although the overall investigation is a cohort study, the data presented here are cross-sectional only, and causality cannot be determined with a cross-sectional study. Third, due to the nature of cross-sectional design, some hidden confounding factors, such as socioeconomic status, were not adjusted for. Fourth, since this study was performed in AAs living in inner-city Baltimore, where cocaine use is often intertwined with other drug addictions, the effects of these drugs (or multiple-drug interactions) on CAC could not completely be controlled for by statistical analyses. Lastly, we only discussed CAC as a marker for atherosclerosis. In addition to being a marker of atherosclerosis, coronary calcification may be influenced by other factors, such as calcium levels.[59] Calcium supplementation may be associated with elevated vascular disease risk.[60]

Despite its limitations, this study's findings highlight the importance of investigating prevention strategies in cardiovascularly asymptomatic HIV-infected AA populations. In order to reduce the risk for CAD in HIV-infected AAs, this study suggests that vitamin D levels should be closely monitored. Identifying and successfully treating vitamin D deficiency may be much easier than managing

some traditional risk factors for CAD, including cigarette smoking cessation and achieving and maintaining optimal BP control. Our study also suggests that clinical trials should be conducted to examine whether vitamin D supplementations reduce the risk of CAC in this AA population.

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Disclosure

The authors report no conflicts of interest in this work.

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