Serum 25-Hydroxyvitamin D3 Concentrations and Prevalence of Cardiovascular Disease Among Type 2 Diabetic Patients

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A ccumulating research suggests that low 25-hydroxyvitamin D3 (25(OH)D) concentrations may be inversely associated with type 2 diabetes (1–3), metabolic syndrome (4,5), insulin resistance (6), and cardiovascular disease (CVD) (7).

Much remains to be learned, however, about the relationships between vitamin D status, metabolic syndrome, and CVD. Furthermore, the published data in humans arguing that hypovitaminosis D is a CVD risk factor remain conflicting (8,9).

Because this topic has received scant attention and the available information on associations between vitamin D status and CVD among type 2 diabetic adults was lacking, we examined the relationships between serum 25(OH)D concentrations and prevalent CVD in type 2 diabetic adults.

RESEARCH DESIGN AND METHODS — We studied 459 consecutive type 2 diabetic outpatients attending our clinic after exclusion of those with recent acute illness or advanced chronic liver or renal disease and those who were taking medications known to alter vitamin D metabolism. The control group consisted of 459 (64% men, age 61 ± 6 years) age- and sex-matched non-diabetic volunteers.

Biochemical blood measurements were determined by standard laboratory procedures. Serum 25(OH)D concentrations were measured during winter months using an automated chemiluminescence immunoassay (DiaSorin Liaison). Metabolic syndrome was defined according to the Adult Treatment Panel III criteria (10).

PREVALENCE — As shown in Table 1, diabetic patients with hypovitaminosis D were more likely to be women and had increased prevalence of higher values of A1C, triglycerides, CRP, and fibrinogen than their vitamin D–sufficient counterparts. The proportion using insulin, lipid-lowering, or antiplatelet drugs was higher among those with hypovitaminosis D, whereas the proportion using hypoglycemic drugs was similar in both groups. Age, BMI, waist circumference, diabetes duration, smoking, LDL cholesterol, creatinine, calcium, albuminuria, and metabolic syndrome components did not differ between the groups.

Overall, 143 (31.1%) of 459 patients were coded positive for CVD. Of these, 81 patients had coronary heart disease, 51 had cerebrovascular disease, and 41 had peripheral vascular disease; many subjects had CVD in multiple sites. As shown in Table 1, the prevalence of CVD was greater among those with hypovitaminosis D. Similarly, 25(OH)D was lower (P < 0.01) among those with CVD (17.9 ± 9 vs. 20.6 ± 10 ng/ml), coronary disease (17.9 ± 9 vs. 20.3 ± 10 ng/ml), and cerebrovascular disease (16.9 ± 7 vs. 20.10 ng/ml) than among those without CVD.

In logistic regression analysis, the association between hypovitaminosis D and prevalent CVD (odds ratio 1.70 [95% CI 1.1–2.6], P < 0.01) remained statistically significant after adjustment for classical risk factors, A1C, metabolic syndrome, renal function tests, calcium, and use of medications (1.77 [1.1–2.9], P = 0.023); additional adjustment for fibrinogen (or CRP) levels abolished this association (1.43 [0.9–2.3], P = NS). Almost identical results were obtained in models that included the individual components of
typically observed during winter months,ing elevations of CRP and fibrinogen levels with hypovitaminosis D is probably mediated by correlated elevations in plasma inflammatory markers. Moreover, since elevations of CRP and fibrinogen levels increase the risk for CVD (14), these findings could help to explain the CVD excess typically observed during winter months, a period in which vitamin D status tends to be poor (15), and suggest a rationale for vitamin D supplementation in prevention of CVD, especially in the elderly.

Our findings are supported by few available data in humans showing that 25(OH)D levels are inversely related to coronary artery calcifications (16,17) and are lower in patients with myocardial infarction (7) and by experimental studies (18–22) suggesting that low 25(OH)D influences the activity/expression of macrophages and lymphocytes in atherosclerotic plaques, thus promoting chronic inflammation in the artery wall. Interestingly, in two recent clinical trials (23,24), vitamin D supplementation markedly reduced serum levels of CRP, interleukin-6, and tissue matrix metalloproteinases. Additionally, low vitamin D3 concentrations result in elevations of parathyroid hormone, which has been linked to insulin resistance and significant increases in the serum levels of many acute-phase proteins (25).

Evidently, these findings are all consistent with the proposition that hypovitaminosis D and subsequent secondary hyperparathyroidism may promote the acute phase response and may help to explain how hypovitaminosis D might act as a risk factor for CVD.

This study has some limitations. Because our study was a cross-sectional one, the causative nature of the associations cannot be established. Additionally, parathyroid hormone and 1α,25(OH)D were not measured in this study. Further investigation is necessary to evaluate whether hypovitaminosis D is associated with incident CVD among type 2 diabetic adults and to determine possible mechanisms of any preventive effect from vitamin D supplementation against CVD.

CONCLUSIONS — We found a high prevalence of hypovitaminosis D and a strong inverse association between 25(OH)D concentrations and prevalent CVD among type 2 diabetic outpatients. Interestingly, our data suggest that the putative elevated CVD risk associated with hypovitaminosis D is probably mediated by correlated elevations in plasma inflammatory markers. Moreover, since elevations of CRP and fibrinogen levels increase the risk for CVD (14), these findings could help to explain the CVD excess typically observed during winter months, a period in which vitamin D status tends to be poor (15), and suggest a rationale for vitamin D supplementation in prevention of CVD, especially in the elderly.

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Vitamin D status and CVD in diabetes


