Chapter 6

25-Hydroxyvitamin d is not associated with carotid intima-media thickness in older men and women*


Recent prospective studies highlighted vitamin D deficiency as a significant risk factor for cardiovascular events, but the underlying mechanisms remain unclear [1]. In their recent work among 650 Old Order Amish persons, Michos et al. have demonstrated that 25-hydroxyvitamin D (25(OH)D) levels are not associated with carotid intima-media thickness (cIMT) and coronary artery calcification [2]. These important findings suggest that the increased cardiovascular risk observed in persons with a poor vitamin D status is unlikely to be mediated by subclinical vascular disease. Considering, however, that 25(OH)D levels were significantly and inversely correlated with cIMT in another study among 390 patients with type 2 diabetes [3], there still exists a need to address further the issue of 25(OH)D levels and cIMT.

We therefore evaluated the latter research question in the Hoorn Study, a population-based study among older men and women [4, 5]. 25(OH)D levels were measured in 614 persons during a follow-up visit in 2000–2001 which included ultrasonographic evaluations of the common cIMT [4], and we have recently published that low 25(OH)D serum levels were significantly associated with an increased risk of all-cause and cardiovascular mortality in that study cohort [5]. Consistent with the statistical analyses used by Michos et al. [2] and in order to consider the seasonal variations of 25(OH)D levels, we calculated the residual of each subject’s 25(OH)D level (nmol/l) from the mean of each season and formed quartiles of these residuals. Regression analysis adjusted for age and gender showed no significant association of these seasonally adjusted 25(OH)D levels with cIMT (in mm) (β-coefficient = −0.011, \(p = 0.794\)). Regression analysis with multivariable adjustment according to Michos et al. [2], including age (years), gender (female/male), body mass index (kg/m²), current smoking (yes/no), hypertension (yes/no), diabetes mellitus (yes/no), total cholesterol (mmol/l), HDL-cholesterol (mmol/l), use of lipid-lowering medications (yes/no), and history of cardiovascular disease (yes/no), did not reveal a significant association either (β = 0.004, \(p = 0.919\)). In an analysis of covariance (ANCOVA) adjusted for age and gender, there was also no significant trend across seasonally adjusted 25(OH)D quartiles to be associated with cIMT (\(p = 0.891\)) and there was no significant difference in the first versus the fourth quartile (\(p = 0.588\); mean adjusted cIMT [with 95% CI] was 0.878 [0.851–0.906] mm in the first and 0.868 [0.841–0.894] mm in the

fourth quartile). Similar results were obtained after multivariable adjustments (as indicated above) for the trend across the quartiles ($p = 0.868$) as well as for the comparison of the first and the fourth quartile of seasonally adjusted $25$(OH)D levels ($p = 0.915$; mean adjusted cIMT [95% CI] was 0.871 [0.843–0.899] in the first and 0.869 [0.842–0.896] in the fourth quartile). No regression analyses showed any significant association of $25$(OH)D status with cIMT when stratified by gender and presence or absence of diabetes mellitus or prior cardiovascular disease (range of $\beta$-coefficients, −0.038 to 0.085; $p \geq 0.4$ for all).

In conclusion, our results confirm the findings of Michos et al. that $25$(OH)D serum levels are not associated with common cIMT. Hence, the mechanisms that link low $25$(OH)D levels to cardiovascular diseases remain to be further explored in detail but might, in our opinion, hypothetically be related to vitamin D effects on, e.g., blood pressure or myocardial structure and function [1, 6, 7].

References

2 Michos ED, Streiten EA, Ryan KA, Rampersaud E, Peyser PA, Bielak LF, Shuldiner AR, Mitchell BD, Post W. Serum $25$-hydroxyvitamin D levels are not associated with subclinical vascular disease or C-reactive protein in the Old Order Amish. Calcif Tissue Int 84:195–202, 2009