Letter to the Editor

Vitamin D and Cancer Mortality

To the Editor: Pilz et al. (1) found that low levels of 25(OH)D were associated with an increased risk of fatal cancer in patients referred to coronary angiography in the Ludwigshafen Risk and Cardiovascular Health (LURIC) study, with 3,316 study subjects and 95 cancer deaths. They contrast their results with the null findings in the NHANES III study, with 16,818 participants and 536 cancer deaths (2). Pilz et al. (1) suggest a number of possible explanations for the discrepant findings: (a) the association may have been confounded/modified by race in the multiracial NHANES III cohort, in contrast to the homogeneously Caucasian LURIC population; (b) the relationship between 25(OH) and season and region may require classifying 25(OH) by monthly blood levels; and (c) the association may reflect a threshold effect discernible in LURIC (in one analysis), but not NHANES III, because of the low distribution of 25(OH)D levels in LURIC.

Here, we review the NHANES III data set against these proposed explanations. We note first that the NHANES III study evaluated the 25(OH)D/cancer mortality relationship separately in non-Hispanic Whites (n = 6,835; cases = 298) and found no association (2). We also reanalyzed the NHANES III data, assessing risk by quintile of 25(OH)D based on month of blood draw in non-Hispanic Whites in 2 season/latitude groups: those providing blood from November through March (largely southern latitudes) and then, for April through October (largely northern latitudes), adjusting for age, gender, and smoking history, as in the original study. In the winter the relative risks were as follows: 1.0 [n (cases) = 19], 1.47 (95% confidence interval, 0.71-3.03), 1.37 (0.49-3.83), 1.03 (0.46-2.32), 1.25 (0.48-3.22); and, in the summer: 1.0 [n (cases) = 52], 1.02 (0.62-1.69), 0.75 (0.46-1.24), 0.83 (0.47-1.46), and 1.01 (0.55-1.86). Thus, there was no association with cancer mortality, although the ranges for the lowest quintile were higher than in the LURIC study, V50.7 (winter) and V9.2 (summer) compared with <38 nmol/L.

We attempted to create a reference group more comparable with that used in the LURIC study. Again, limiting NHANES III to non-Hispanic Whites and using the covariates identified above, we established 5 quantiles based on monthly blood draws throughout the year: lowest, 5%; next, 20%; followed by the top 3 quartiles. The range of 25(OH)D values for the lowest 5% was similar, ≤41.2 nmol/L (NHANES III) compared with <38 nmol/L (LURIC). The relative risks for the 5 groups were as follows: 1.0 [n (cases) = 23]; 0.84 (95% confidence interval, 0.52-1.34); 0.85 (0.49-1.34), 0.83 (0.50-1.37), and 0.78 (0.42-1.43), respectively, P_trend = 0.49, based on assigning a value for the median of each category and modeling the resulting variable as continuous. Comparing the lowest 5th percent (reference) to all other participants showed a risk ratio of 0.83 (0.52-1.32). In the full multiracial cohort, the risks for each of the upper quantiles, even after adjusting for race/ethnicity, were nonsignificantly higher than for the 5% reference group. Thus, reanalysis of the data does not support an association between 25(OH)D and total cancer mortality, although small numbers with depressed 25(OH)D levels limit the power of the study to discern effects at particularly low concentrations. In addition, we do not know if differences between the population-based NHANES III and LURIC, which is a nonrepresentative population with serious health concerns, may play some role in the differing results.

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References

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