June 13, 2012

Re: “Serum vitamin D and risk of bladder cancer in the Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial”

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To the Editor:

The recent study by Mondul and colleagues failed to find a significant correlation between prediagnostic serum 25-hydroxyvitamin D [25(OH)D] concentration and incidence of bladder cancer in a study in the United States (1). This finding is in contrast to the inverse correlations found in many ecological studies of solar UVB doses and bladder cancer mortality rate (2) and to the finding in an earlier study in Finland [Ref. 4 in (1)] which found a direct correlation between prediagnostic serum 25(OH)D concentration and incidence of bladder cancer. In (1), the follow-up time was 13 years, while in Ref. 4 in (1), the follow-up time was 17-20 years. The assumption made in such studies is that serum 25(OH)D concentration measured at time of enrollment is a good measure of serum 25(OH)D during the entire follow-up period. This assumption is, however, faulty. A recent analysis found that a linear fit to correlation coefficients of serum 25(OH)D concentrations measured at different times changed from 0.7 at zero years to 0.42 at 14 y (3). In addition, the longer the follow-up time, the lower the correlation in studies of all-cause mortality rate (3) and cancer incidence rates [Ref. 10 in (3)].

There is another problem with long follow-up times, namely that those with low serum 25(OH)D concentrations at the time of enrollment may be told later by their physicians that they have osteoporosis and should take higher doses of vitamin D supplements. This is apparently what happened in the United States in a study of women aged 71 years and older at time of serum 25(OH)D concentration measurement: they were found to have a U-shaped relation with respect to serum 25(OH)D concentration and frailty status 4.5 years later (4). However, for men aged 65 years and older at time of 25(OH)D measurement, there was a monotonic decrease in frailty
status with respect to serum 25(OH)D concentration 4.6 years later (5). Case-control studies of 25(OH)D and bladder cancer incidence would be useful.

Case-control studies, with no interval between serum 25(OH)D concentration measurement and cancer diagnosis have found strong significant inverse correlations between serum 25(OH)D concentration and breast cancer incidence (4). Since cancer patients are unaware of their cancer until diagnosed, the undiagnosed cancer should not have affected serum 25(OH)D concentrations. In the future, cohort studies should measure serum 25(OH)D concentrations every few years as well as evaluate the effect of follow-up time.

References


Cancer Epidemiology, Biomarkers & Prevention

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William B Grant

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