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ARTICLES

A Nested Case–Control Study of Plasma 25-Hydroxyvitamin D Concentrations and Risk of Colorectal Cancer

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Background: Low vitamin D status has long been implicated in colorectal carcinogenesis. We investigated this relationship in a nested case–control study within the Health Professionals Follow-up Study (HPFS), a large ongoing study of male health professionals living in the United States.

Methods: Between 1993 and 2002, 179 colorectal cancer patients were diagnosed and matched to 356 control subjects by age and by month and year of blood collection. Results were also pooled with previously published results from the Nurses' Health Study (NHS) cohort, a large female cohort. Conditional logistic

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regression was used to analyze the association between plasma 25-hydroxyvitamin D [25(OH)D] and colorectal cancer, and pooled estimates were calculated using the method of DerSimonian and Laird. All statistical tests were two-sided.

Results: In the HPFS, we observed a non–statistically significant inverse association between higher plasma 25(OH)D concentration and risk of colorectal cancer and a statistically significant inverse association for colon cancer (highest versus lowest quintile: odds ratio [OR] = 0.46, 95% confidence interval [CI] = 0.24 to 0.89; $P_{\text{trend}} = .005$). After pooling the results from the HPFS and NHS, higher plasma 25(OH)D concentrations were statistically significantly associated with decreased risks of both colorectal cancer (highest versus lowest quintile, OR = 0.66, 95% CI = 0.42 to 1.05; $P_{\text{trend}} = .01$) and colon cancer (highest versus lowest quintile, OR = 0.54, 95% CI = 0.34 to 0.86; $P_{\text{trend}} = .002$). Inverse associations with plasma 25(OH)D concentration did not differ by location of colon cancer (proximal versus distal), but the number of patients was small and none of the associations was statistically significant. Opposite relationships between plasma 25(OH)D levels and risk of rectal cancers were found among men (positive) and women (inverse).

Conclusion: Our data provide additional support for the inverse association between vitamin D and colorectal and, in particular, colon cancer risk.

CONTEXT AND CAVEATS

Prior knowledge

A possible association has been noted between low vitamin D status and colorectal carcinogenesis.

Study design

Nested case–control study of plasma vitamin D, measured as 25(OH)D, and risk of colorectal cancer among male participants in the Health Professionals Follow-up Study (HPFS). Pooled analyses were also performed with previous results from the Nurses' Health Study.

Contribution

Higher plasma 25(OH)D concentrations were associated with a decreased risk of colon cancer among participants in the HPFS and with decreased risks of colon and colorectal cancer in the pooled analysis.

Implications

There is an inverse association between vitamin D and risk for colon cancer in these study populations.

Limitations

They study follow-up period was only 8 years in the HPFS and 11 years in the Nurses' Health Study. Plasma vitamin D concentrations were determined from blood samples that were provided at only one time point.

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