Selenium- or Vitamin E-Related Gene Variants, Interaction with Supplementation, and Risk of High-Grade Prostate Cancer in SELECT.


Abstract

BACKGROUND: Epidemiologic studies and secondary analyses of randomized trials supported the hypothesis that selenium and vitamin E lower prostate cancer risk. However, the Selenium and Vitamin E Cancer Prevention Trial (SELECT) showed no benefit of either supplement. Genetic variants involved in selenium or vitamin E metabolism or transport may underlie the complex associations of selenium and vitamin E.

METHODS: We undertook a case-cohort study of SELECT participants randomized to placebo, selenium, or vitamin E. The subcohort included 1,434 men; our primary outcome was high-grade prostate cancer (N = 278 cases, Gleason 7 or higher cancer). We used weighted Cox regression to examine the association between SNPs and high-grade prostate cancer risk. To assess effect modification, we created interaction terms between randomization arm and genotype and calculated log likelihood statistics.

RESULTS: We noted statistically significant (P < 0.05) interactions between selenium assignment, SNPs in CAT, SOD2, PRDX6, SOD3, and TXNRD2, and high-grade prostate cancer risk. Statistically significant SNPs that modified the association of vitamin E assignment and high-grade prostate cancer included SEC14L2, SOD1, and TTPA. In the placebo arm, several SNPs, hypothesized to interact with supplement assignment and risk of high-grade prostate cancer, were also directly associated with outcome.

CONCLUSION: Variants in selenium and vitamin E metabolism/transport genes may influence risk of overall and high-grade prostate cancer, and may modify an individual man's response to vitamin E or selenium supplementation with regards to these risks.

IMPACT: The effect of selenium or vitamin E supplementation on high-grade prostate cancer risk may vary by genotype. Cancer Epidemiol Biomarkers Prev; 25(7); 1050-8. ©2016 AACR.

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