Serum phospholipid fatty acids, genetic variation in myeloperoxidase, and prostate cancer risk in heavy smokers : a gene-nutrient interaction in the carotene and retinol efficacy trial

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Abstrak

The authors investigated associations of serum phospholipid n-3 and n-6 polyunsaturated fatty acids (PUFAs) and trans-fatty acids with prostate cancer risk, and whether myeloperoxidase G-463A (rs2333227) modified the associations in the Carotene and Retinol Efficacy Trial (CARET) (Seattle, Washington; Irvine, California; New Haven, Connecticut; San Francisco, California; Baltimore, Maryland; and Portland, Oregon, 1985-2003). Prerandomization sera were assayed for fatty acids among 641 men with incident prostate cancer (368 nonaggressive and 273 aggressive (stage III/IV or Gleason score ≥ 7)) and 1,398 controls. Overall, dihomo-γ-linolenic (quartiles 4 vs. 1: odds ratio (OR) = 0.66, 95% confidence interval (CI): 0.49, 0.95; P(trend) = 0.024) and docosatetraenoic (OR = 0.69, 95% CI: 0.46, 1.02; P(trend) = 0.011) acids were inversely associated with nonaggressive and aggressive prostate cancer risks, respectively. Among men with MPO GG, the genotype upregulating oxidative stress, quartiles 4 versus 1 eicosapentaenoic plus docosahexaenoic acids were suggestively associated with an increased risk of aggressive prostate cancer (OR = 1.66, 95% CI: 0.95, 2.92; P(trend) = 0.07). However, the association was the inverse among men with MPO GA/AA genotypes (P(interaction) = 0.011). Interactions were also observed for docosapentaenoic acid, total n-3 PUFAs, and arachidonic acid. MPO GA/AA vs. GG was associated with a 2-fold increase in aggressive prostate cancer risk among men with low (quartile 1) n-3 PUFAs. This study adds important evidence linking oxidative stress with prostate carcinogenesis.