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# Dietary omega-3 fatty acids, cyclooxygenase-2 genetic variation, and aggressive prostate cancer risk.

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## Abstract

PURPOSE: Dietary intake of long-chain omega-3 (LC n-3) polyunsaturated fatty acids may reduce inflammation and in turn decrease risk of prostate cancer development and progression. This potential effect may be modified by genetic variation in cyclooxygenase-2 (COX-2), a key enzyme in fatty acid metabolism and inflammation.

EXPERIMENTAL DESIGN: We used a case-control study of 466 men diagnosed with aggressive prostate cancer and 478 age- and ethnicity-matched controls. Diet was assessed with a semiquantitative food frequency questionnaire, and nine COX-2 tag single nucleotide polymorphisms (SNP) were genotyped. We used logistic regression models to estimate odds ratios (OR) for association and interaction.

RESULTS: Increasing intake of LC n-3 was strongly associated with a decreased risk of aggressive prostate cancer (P(trend) <or= 0.0001). The OR (95% confidence interval) for prostate cancer comparing the highest with the lowest quartile of n-3 intake was of 0.37 (0.25-0.54). The LC n-3 association was modified by SNP rs4648310 (+8897 A/G), flanking the 3' region of COX-2 (P(interaction) = 0.02). In particular, the inverse association was even stronger among men with this variant SNP. This reflected the observation that men with low LC n-3 intake and the variant rs4648310 SNP had an increased risk of disease (OR, 5.49; 95% confidence interval, 1.80-16.7), which was reversed by increasing intake of LC n-3.

CONCLUSIONS: Dietary LC n-3 polyunsaturated fatty acids appear protective for aggressive prostate cancer, and this effect is modified by the COX-2 SNP rs4648310. Our findings support the hypothesis that LC n-3 may impact prostate inflammation and carcinogenesis through the COX-2 enzymatic pathway.

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