RE: Plasma Phospholipid Fatty Acids and Prostate Cancer Risk in the SELECT Trial

Brasky et al. (1) reported that higher plasma omega-3 fatty acid levels were associated with increased risk for developing prostate cancer. The authors inappropriately implicated the dietary intake of omega-3 (fish and/or supplements) as potentially causal for prostate cancer, and they failed to consider other potential explanations for their observation. For example, He et al. (2) and Azordegan et al. (3) both provide evidence that in precancerous tissues early changes in fatty acid metabolism (eg, increases in the activity of delta-6-desaturase [D6D]) could increase tissue (and possibly plasma) levels of long-chain n-3 fatty acids. Hence, it is possible that metabolic changes (eg, upregulation of D5D and D6D, which produce long-chain from short-chain omega-3 fatty acids) associated with the carcinogenic process could have raised omega-3 levels. Second, higher levels of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) are also observed in individuals with common polymorphisms in the FADS1 and FADS2 genes (that code for D5D and D6D, respectively). FADS1 polymorphisms have also been linked to increased risk for prostate cancer (4), and D6D inhibition can suppress tumor growth in mice (2). Because an increased intake of long-chain omega-3 fatty acids can suppress D6D by product inhibition (5), dietary or supplemental EPA and DHA could potentially reduce the risk of prostate cancer, as others have described.

The authors also failed to present the fuller story. The same team reported in 2010 that the use of fish oil supplements was not associated with any increased risk for prostate cancer (6). A 2010 meta-analysis of fish consumption and prostate cancer reported a reduction in late-stage or fatal cancer among cohort studies but no overall relationship between prostate cancer and fish intake (7). In other studies, higher fish intake has been associated with lower risk for prostate cancer incidence and death. In addition, a higher omega-3 fatty acid intake predicts better survival for men who already had prostate cancer, and increased fish intake was associated with a reduction in risk for aggressive prostate cancer in another case–control study. So there is considerable evidence actually favoring an increase in fish intake for prostate cancer risk reduction. International comparisons are also informative. Prostate cancer rates in the Japanese population (who typically eat about 8 times more omega-3 fatty acids than Americans) are markedly lower than rates in the United States. Obviously, this is counter to the expectations from Brasky et al. (1).

The EPA and DHA levels reported by Brasky et al. (1) are well below those seen in individuals who take fish oil supplements (eg, in Framingham), and the differences in levels between control subjects (3.66%) the most extreme case patients (3.74%) was de minimus, far too small to be explained by differences in fish oil supplementation.

In summary, the authors’ conclusion that the intake of omega-3 fatty acids increases prostate cancer risk represents an inappropriate extrapolation far beyond their data. The overall risk/benefit ratio for fish and fish oils remains very favorable.

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References

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