**CORRESPONDENCE**

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

Brasky et al. recently reported a positive association between high plasma long-chain omega-3 polyunsaturated fatty acids (LCo-3PUFAs) reflecting fish consumption and risk of total and high-grade prostate cancer in a case-cohort study nested within the SELECT Trial (1). However, of the 909 case patients, only four were diagnosed with advanced-stage disease (T3). Consequently, the vast majority of case patients in the study by Brasky et al. had localized cancers. Even high-grade disease, defined here as Gleason 4+3 or higher, is common on autopsy, and hence cannot serve as a surrogate for potentially lethal prostate cancer. Limitations in the use of localized (even high-grade) cancers as a surrogate of lethal prostate cancer has been discussed previously (2). Most important, small localized prostate cancers, including high-grade ones, are highly prevalent beginning early in life and most generally progress slowly. Dietary factors in middle-aged and elderly men, if at all relevant, probably act largely on progression of localized cancers to lethal forms rather than on initiation. The potential influence of such progression factors may be completely missed if the endpoint is localized prostate cancer.

In fact, many studies indicate that risk factors for advanced (T3 or T4) or fatal prostate cancer differs from total prostate cancer or high-grade disease, and this has been observed in a study by Crowe et al. where no positive association was found between plasma LCo-3PUFAs and advanced disease (3). Furthermore, this pattern is also seen in dietary studies, as a recent meta-analysis found no association between total fish consumption and overall prostate cancer incidence but a significant reduction in prostate cancer mortality (4). The National Institutes of Health–AARP Diet and Health Study showed an inverse association between fish and omega-3 fatty acids consumption and risk of fatal prostate cancer, adjusting for multiple confounding factors (5). A prospective study that assessed baseline fish intake in 1983 with mean follow-up time of 19 years showed reduced prostate cancer mortality among men consuming high levels of fish and seafood LCo-3PUFAs, and the inverse association became stronger when prostate-specific antigen (PSA)–detected cases were excluded from the analysis (6). An analysis using blood levels of fatty acids in the same cohort showed similar results, with a statistically significant inverse relation of higher LCo-3PUFA levels with more aggressive prostate cancer [cited in (6)]. A prospective population-based study from Iceland (7), where there is a long tradition of fish oil consumption, found that fish oil consumption in later life was inversely associated with advanced prostate cancer. Although measurement error is likely to attenuate associations in studies based on dietary recall, this type of error is unlikely to produce protective associations if LCo-3PUFAs from fish actually enhance prostate carcinogenesis.

In the PSA screening era, studies of total prostate cancer incidence are of little value; because perhaps half of all older men have latent prostate cancer, incidence largely reflects the propensity for PSA screening intensity and having a biopsy. Thus, any public health recommendations for prostate cancer should be based on potential effects on lethal disease.

**References**


**Notes**

The authors have no conflict of interest to declare.

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