Do Omega-3 Fatty Acids Cause Prostate Cancer? NO!

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A more thorough overview of the pertinent literature suggests that increased omega-3 fatty acid consumption does not increase prostate cancer risk, and notably decreases prostate cancer mortality.

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There has been recent controversy as to whether fish oil increases the risk of prostate cancer. The concern stems from a paper published recently by Brasky and colleagues concluding that increased blood levels of long-chain omega-3 in plasma phospholipids are associated prospectively with an increased risk for total as well as high-grade prostate cancer.[1] They reached this conclusion based on their own retrospective analysis of serum samples and data derived from the SELECT trial, as well as a meta-analysis of previous pertinent prospective epidemiological studies. The authors speculate that this finding may reflect a pathogenic role for fish oil omega-3s in the induction of prostate cancer. Widespread publicity given to this speculation through the popular media has triggered both consternation and skepticism among the public.

It must be emphasized that this study cannot prove that fish oil causes prostate cancer, as it is observational; it was not a controlled trial in which patients were randomized to receive fish oil supplements or placebos. Furthermore, dietary consumption of fish or fish oil was not assessed in this study, so, even as epidemiology, it cannot establish an association between fish oil consumption per se and prostate cancer risk. Rather, it only establishes a correlation of prostate cancer risk with omega-3s in plasma phospholipids. Whether this correlation reflects a pathogenic role for omega-3s is hypothetical, and there is considerable reason to believe that this hypothesis is incorrect. Conceivably, if their observation proves to be confirmable in subsequent research, the modest elevations of plasma phospholipid omega-3s observed in subjects who went on to develop prostate cancer may reflect some metabolic factor influencing omega-3 partitioning and/or oxidation that also influences prostate cancer induction.

It should be noted that the test used by Brasky and colleagues to assess "omega-3 status" – plasma phospholipid omega-3s – is not the most accurate way to assess long-term omega-3 dietary intake. Rather, the percentage of EPA + DHA in erythrocyte membranes as defined by Harris as the "omega-3 index,"[2] is more useful in this regard. The parameter measured by Brasky et al. is highly susceptible to day-to-day variation in omega-3 fatty acid intake, rendering it less than optimal as a surrogate for the characteristic omega-3 intakes or tissue levels of the subjects studied.

More importantly, a substantial number of epidemiological studies, both prospective and case-control, have previously examined the association between fish or fish oil ingestion and prostate cancer risk, and these findings clearly do not

incriminate long-chain omega-3 ingestion as factor in prostate cancer induction.[3-9] A recent meta-analysis of these studies indicates that fish consumption has a null or slightly protective impact on prostate cancer incidence, but is strongly protective with respect to prostate cancer mortality.[4] Moreover, the limited prospective epidemiology that has evaluated the association of fish oil supplementation with prostate cancer risk – including one study by Brasky's own group – does not provide any grounds for concern in this regard.[3] With respect to patients who already have prostate cancer, frequent fish consumption has been associated with improved survival.

Prior evidence has shown that patients with a higher mean baseline blood level of omega-3 fatty acids are at a lower risk of cardiac sudden death.[10] Indeed, one study found that relatively high omega-3 blood levels (5.63% and 6.87%) were associated with a 72% and 81% lower risk of sudden death, respectively, compared to patients with a mean omega-3 blood level of 3.58%.[10] Brasky and colleagues report a 43% increased risk of total prostate cancer with an omega-3 blood level $>$ 5.31% vs. $<$ 3.68% (hazard ratio [HR] 1.43, 95% conference interval [CI]: 1.09-1.88, p=0.007).[1] Hence, even in the unlikely event that Brasky and colleagues are correct in their speculation that omega-3 increases prostate cancer risk, one would need to balance a 43% increased risk of prostate cancer associated with replete omega-3 status, against a 72% higher risk of sudden cardiac death associated with low omega-3 status.

If fish omega-3 did indeed boost prostate cancer risk, then populations with high omega-3 fatty acid intakes could be expected to have a relatively high risk for prostate cancer; this does not seem to be the case. The intake of fish in Japan is one of the highest in the world,[11-13] being around eight times more than that of American men,[2] and yet the age-adjusted mortality from prostate cancer in Japan was approximately seven times lower than that in the U.S. in the 1950s.[14] Additionally, omega-3 fatty acid levels in red blood cells are approximately 8 to 10% in Japanese patients,[15] around twice that of those in the combined cancer group (4.66%) and controls (4.48%) in the paper by Brasky and colleagues.[1] Thus, the mean omega-3 fatty acid blood levels in the Brasky study are rather low from the standpoint of cardiovascular (CV) protection, and only differed by 0.18% in cases vs. controls - a negligible difference from a clinical perspective.

The very high omega-3 intake of the traditionally-living Inuit, evoked as a likely reason for their low risk for CV disease, first brought omega-3 nutrition to popular attention several decades ago. Less well known is the fact that the Inuit were also at very low risk for prostate cancer incidence and mortality.[15, 16]

Japanese men have a two-fold higher serum level of omega3-fatty acids than whites and Japanese Americans in the United States (U.S.),[11] and coronary heart disease in Japan is about half as common as in the U.S.[17] Contributing to the evidence that a higher omega-3 intake is associated with a reduction in coronary heart disease is JELIS, a randomized controlled trial which showed that adding 1.8 grams of eicosapentaenoic acid (EPA) daily as an adjunct to statin therapy in men with a relatively high baseline intake of omega-3s (Japanese patients) causes a significant reduction in the risk of major coronary heart disease events as well as stroke.[18, 19] Unlike the study by Brasky and colleagues, this trial could prove causation, demonstrating that fish oil reduces the risk of CV disease. It would be a shame if patients stopped taking their fish oil supplements, owing to an unwarranted fear regarding prostate cancer, and subsequently experienced a CV event or sudden death.

A possible indication that Brasky's paper is seriously flawed is that their data showed that the risk of prostate cancer decreased as the amount of pack-years of smoking increased.[1] Compared to non-smokers, there was a 3%, 13% (trend for reduction) and significant 19% lower risk for prostate cancer in those who smoked $\leq$ 12.5 pack-years, 12.5-25 pack-years and $\geq$ 25 pack-years, respectively (relative risk [RR] 0.97, 95% CI:0.84-1.11, p=0.63, RR 0.87, 95% CI:0.74-1.02, p=0.09, RR 0.81, 95% CI:0.69-0.95, p = 0.01). Moreover, those with diabetes had a 33% lower risk of developing prostate cancer compared to those who were not diabetic (RR 0.67, 95% CI:0.54-0.83, p=0.0003). However, a lower risk for prostate cancer in diabetics is, in fact, a well established phenomenon.[20]

In conclusion, the Brasky paper only demonstrates an association between plasma phospholipid omega-3s and subsequent prostate cancer risk; it cannot prove that omega-3 fatty acids (and particularly fish oil) cause prostate cancer. A more thorough overview of the pertinent literature suggests that increased omega-3 fatty acid consumption does not increase prostate cancer risk, and notably decreases prostate cancer mortality – and most certainly decreases risk for sudden death and CV events.

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Disclosure

CJL and JHO have previously served as speakers and consultants to GlaxoSmithKline. JHO is the Chief Medical Officer and Founder of CardioTabs, a nutraceutical company that sells products containing omega-3. MM