

Omega-3 Fatty Acids and Risk for Prostate Cancer

On July 11, 2013 a paper was published online by Brasky et al. in the *J Natl Cancer Institute* entitled, "Plasma Phospholipid Fatty Acids and Prostate Cancer Risk in the SELECT Trial." The authors found that higher plasma omega-3 fatty acid levels were associated with increased risk for developing prostate cancer. In this study, plasma phospholipid omega-3 levels were measured in 834 men who eventually developed PC (the time between plasma sampling and diagnosis is not available from the abstract), and 1393 men who did not. Using standard statistical methods, they found that men in the highest quartile of omega-3 had a 43% to 71% increased risk for prostate cancer (depending on severity). This is the same conclusion that the same group reached in 2011 in a study in another cohort entitled, "Serum Phospholipid Fatty Acids and Prostate Cancer Risk: Results from the Prostate Cancer Prevention Trial" (1). So with two studies reaching the same conclusion, it is important to seriously consider its findings.

I will be the first to admit that had this study turned out the "right" way, I would have embraced its findings and had no criticism of its design or methods. It is disingenuous, therefore, for me to find fault with the way the study was conducted just because I don't agree with the findings. Nevertheless, we should examine the methods to be clear on the context of the conclusions.

First, the reported EPA+DHA level in the plasma phospholipids in this study was 3.62% in the no-cancer control group, 3.66% in the total cancer group, 3.67% in the low grade cancer group, and 3.74% in the high-grade group. These differences between cases and controls are very small and would have no meaning clinically as they are within the normal variation. Based on experiments in our lab, the lowest quartile would correspond to an HS-Omega-3 Index of <3.16% and the highest to an Index of >4.77%). These values are obviously low, and virtually none of the subjects was in "danger" of having an HS-Omega-3 Index of >8%. So to conclude that regular consumption of 2 oily fish meals a week or taking fish oil supplements (both of which would result in an Index above the observed range) would increase risk for prostate cancer is extrapolating beyond the data. This study did not test the question of whether *giving* fish oil supplements (or eating more oily fish) increased PC risk; it looked only at blood levels of omega-3 which are determined by intake, other dietary factors, metabolism and genetics.

But even granting that the associations they reported are real, the findings of this study do not mean that EPA and DHA play any role in the development of prostate cancer. Associations do not imply causation. For example, it is possible that some component of whatever fish these patients were consuming was carcinogenic, in which case the serum omega-3 levels were just a marker of fish (i.e., carcinogen) intake.

It is important to put these findings into perspective (which the authors failed to do). First consider the risk of dying from prostate cancer vs ischemic heart disease (IHD). Based on the National Vital Statistics Report for deaths in the US in males in 2010, (http://www.cdc.gov/nchs/data/dvs/deaths_2010_release.pdf), there were about 28,500 deaths from prostate cancer and 207,500 deaths from IHD: a 7.3x higher rate of death for heart

disease. If one assumes (conservatively) that higher fish intake reduces risk for death from heart disease by only 10%, and (liberally) increases risk for death from PC by 50%, then the chances of dying from CHD are still 4.4x higher than from PC. This very crude analysis suggests that even in the worst case scenario, the benefit of higher omega-3 intakes/levels still outweighs the risk.

The authors also failed to present the fuller story taught by the literature. The same team reported in 2010 that the use of fish oil supplements was *not* associated with any increased risk for prostate cancer (2). 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 (3). Terry et al. in 2001 (4) reported higher fish intake was associated with lower risk for prostate cancer incidence and death, and Leitzmann et al. in 2004 (5) reported similar findings. Higher intakes of canned, preserved fish were reported to be associated with reduced risk for prostate cancer (6). Epstein et al. found that a higher omega-3 fatty acid intake predicted better survival for men who already had prostate cancer (7), and increased fish intake was associated with a 63% reduction in risk for aggressive prostate cancer in a case-control study by Fradet et al (8). So there is considerable evidence actually FAVORING an increase in fish intake for prostate cancer risk reduction.

Another piece of the picture is to compare prostate cancer rates in Japan vs the US. Here is a quote from the World Foundation of Urology*:

“[Prostate cancer] incidence is really high in North America and Northern Europe (e.g., 63 X 100,000 white men and 102 X 100,000 Afro-Americans in the United States), but very low in Asia (e.g., 10 X 100,000 men in Japan).”
<http://www.prostatecancerprevention.net/index.php?p=prostate-cancer>

Since the Japanese typically eat about 8x more omega-3 fatty acids than Americans do and their blood levels are twice as high, you'd think their prostate cancer risk would be much higher... but the opposite is the case.

In summary, the work of Brasky et al does add to the evidence-base for omega-3 fatty acids and PC, which taken as a whole (not even getting into animal studies which are typically positive) support a neutral, if not beneficial, effect of fish oil in prostate cancer. There will always be mixed findings in studies of “diet” and “disease” since both predictor and outcome entail so many variables, known and unknown. Higher omega-3 levels are associated with lower rates of death from any cause (9, 10), from sudden cardiac arrest (11), and with slower rates of cellular aging (12). The risk benefit for fish oils remains very favorable.

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