

## Fish, Shellfish Associated with Advanced Prostate Protection

By Todd Neale, Staff Writer, MedPage Today  
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SAN FRANCISCO, March 24 -- Omega-3 fatty acids, particularly those found in dark fish and shellfish, are associated with protection against aggressive prostate cancer, a case-control study showed.

Men who consumed the greatest amount of long-chain omega-3 polyunsaturated fatty acids had a 63% reduced risk of advanced prostate cancer compared with those who ate the least (OR 0.37, 95% CI 0.25 to 0.54), John Witte, Ph.D., of the University of California San Francisco, and colleagues reported in *Clinical Cancer Research*.

The relationship was strengthened in men who had a specific variation on the COX-2 gene: those with the genetic variation and low omega-3 consumption had a substantially increased risk of aggressive cancer (OR 5.49, 95% CI 1.80 to 16.7).

Action Points

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- Explain to interested patients that this study found that men who ate the most dark fish and shellfish were the least likely to develop advanced prostate cancer, and that the relationship was affected by a genetic variation.
  - Point out that this study cannot determine causality.

"Previous research has shown protection against prostate cancer, but this is one of the first studies to show protection against advanced prostate cancer and interaction with COX-2," Dr. Witte said.

Consuming omega-3 fatty acids may reduce inflammation, thereby decreasing the risk of prostate cancer development and progression, the researchers said.

Most studies looking at the association have found a reduced risk of prostate cancer with greater dietary intake, and there is some evidence that the relationship is modified by COX-2, which is involved in the metabolism of fatty acids, they said.

To explore the association with aggressive disease, the researchers recruited 466 men diagnosed with advanced prostate cancer, which was defined as a Gleason score of 7 or higher, a tumor-node-metastasis stage of T<sub>2c</sub> or higher, or a prostate-specific antigen level greater than 10 ng/mL.

As controls, they enrolled 478 men who were free from cancer.

Increasing consumption of any and total long-chain omega-3 polyunsaturated fatty acids -- assessed using a food frequency questionnaire -- was associated with a reduced risk of aggressive prostate cancer ( $P \leq 0.0001$  for trend).

Specifically, men who ate boiled or baked dark fish (such as salmon, mackerel, and bluefish) one to three times a month had a 36% reduced risk of aggressive disease compared with those who never ate it (OR 0.64, 95% CI 0.48 to 0.86).

Men who ate dark fish at least once a week had an even greater reduction in risk (OR 0.43, 95% CI 0.29 to 0.63).



There were similar findings for non-fried shellfish consumption ( $P < 0.0001$  for trend).

Of nine single nucleotide polymorphisms on *COX-2* that the researchers evaluated for an effect on the association, only one -- rs4648310 -- had a significant modifying effect ( $P = 0.02$ ).

Among men with the variation, those with low intake of omega-3 fatty acids had a greater risk of aggressive prostate cancer and those with high intake had a reduced risk.

"Our findings . . . suggest that, although carriers of the variant polymorphism had an overall increased risk of aggressive prostate cancer, this deleterious effect was found only in men consuming low levels of long-chain omega-3 fatty acids," the researchers said.

They said this supports "the hypothesis that long-chain omega-3 fatty acids may impact prostate inflammation and carcinogenesis through the *COX-2* enzymatic pathway."

However, they acknowledged, "more clinical and biological studies are needed to decipher how dietary long-chain omega-3 fatty acids and other factors involved with inflammation, such as *COX-2* genotypes, affect aggressive prostate cancer."

The study was limited, they said, by a small sample size for detecting gene-diet interactions and possible recall bias. In addition they noted the possibility of prognostic selection bias and confounding "because a majority of our cases were diagnosed by screening and screening, a health-conscious behavior, may be associated with the consumption of a healthier diet, fish, and long chain fatty acids."