Recently, Brasky et al. (1) reported an elevated risk of prostate cancer (PC) and high-grade PC, especially in people with high plasma phospholipid compositions (PPLCs) of long-chain (LC) omega-3 (n-3) polyunsaturated fatty acids (PUFAs), including eicosapentaenoic acid (EPA), docosapentaenoic acid (DPA), and docosahexaenoic acid (DHA), and a reduced PC risk in individuals with high linoleic acid, a major component of n-6 PUFAs. The observations, although challenging, are incompatible with our hypotheses. Comments should be made in view of PPLCs vs absolute consumption, supplements vs dietary intake, observational epidemiologic findings, and biological plausibility.

Although PPLC values may be more accurate than dietary consumption estimated by dietary records/recall/questionnaire and well correlated with medium-term dietary intakes, they are still relative proportions, not absolute intakes/concentrations, and although discussed by the authors, they may yield spurious results.

The authors did not mention dietary intakes of the subjects. Because Americans only occasionally consume fish/shellfish, the high PPLCs of LC n-3 PUFAs may be presumably attributable to recent intake from supplements. Even though they found a trend between PPLCs of LC n-3 PUFAs and the risk of PC, LC n-3 PUFAs may not be causal factors because the cancer, as is well known, has a long latency period from onset to overt cancer. Sufficiently long past and long-term dietary studies and follow-up are needed to pinpoint the etiologic factors.

Because there are certain fallacies in descriptive epidemiologic studies, such as time trend, migration, and ecological studies, they are considered less convincing than analytical research, but they are basic and robust. The recent growing incidence of PC in Japan may be largely attributable not only to the spread of prostate-specific antigen screening but also to the changes in lifestyle, including declining intake of fish/shellfish and soy, and increased intake of deep-fried food and red meat. The latter observations may coincide with findings of migration studies, in which Japanese migrants to the United States have an elevated incidence of PC (2).

LC n-3 PUFAs play ultimate competitive inhibitory bioactive roles as n-3 series leukotrienes, thromboxanes, and prostaglandins against respective n-6 family chemicals in lipoxigenase and cyclooxygenase pathways (3). EPA, DPA, and DHA may be milder COX inhibitor analogs without adverse effects, such as gastrointestinal bleeding, bleeding diathesis, and cardiac toxicity, typically caused by aspirin or nonsteroidal anti-inflammatory drugs. LC n-3 PUFAs have long been thought to have anti-inflammatory and anticarcinogenic properties, but, as also mentioned by the authors, the findings were counter to their expectations.

Although the World Cancer Research Fund/American Institute for Cancer Research (2) has categorized fish as one of the inconclusive factors of PC, we hypothesize that increased dietary consumption of marine food and reduced intake of vegetable oils, yielding lower ratios of n-6 PUFAs/n-3 PUFAs or arachidonic acid/LC n-3 PUFAs (4), may suppress inflammation and prevent the onset of cancers, including PC.

References

Notes
All authors contributed to this article, read, and approved the final manuscript. The authors have no conflicts of interest to declare.

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