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Dietary Fat and Reduced Prostate Cancer Mortality:

Does the Type of Fat Matter?

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There are 3 well-established risk factors for prostate cancer: race (specifically, African American race), family history, and age. Unfortunately, we cannot change our race or our parents nor can we stop time. Given this reality, there is much interest in identifying modifiable risk factors for prostate cancer. In a landmark study, Calle and colleagues followed up more than 900 000 persons for more than 16 years and found that obesity was linked with death from 17 different cancer types.¹ Although prostate cancer was one of the cancers identified, its association with obesity was modest, with mildly obese (body mass index [calculated as weight in kilograms divided by height in meters squared], 30-34.9) and moderately obese (body mass index, 35-39.9) men being 20% and 34% more likely, respectively, to die of prostate cancer. Even so, given the large number of men who die annually of prostate cancer (258 100 worldwide and 32 600 in North America in 2008)² and the high prevalence of obesity (35% in the United States in 2012),³ the association means that tens of thousands of men die annually of obesity-related prostate cancer. While the exact links between obesity and prostate cancer are complex, diet and lifestyle invariably play a role.

Further support for the role of lifestyle in prostate cancer comes from geographic differences in prostate cancer incidence, with Western countries having dramatically higher rates of prostate cancer than developing countries.² While these data suggest that a “Western” lifestyle may promote prostate cancer, it is difficult to discern which specific aspect is responsible, as a “Western” lifestyle involves low levels of physical activity and a diet high in calories, saturated fats, refined carbohydrates, and animal protein and low in fresh fruits, vegetables, and whole grains, resulting in lower intake of essential minerals and phytochemicals and excess intake of other factors. All of these factors have, in one study or another, been linked with prostate cancer, although a large amount of conflicting data exist.⁴

Given this uncertainty and a growing interest in the role of nutrition and prostate cancer, the article by Richman et al⁵ is both timely and informative. The authors examined 4577 men with nonmetastatic prostate cancer, followed up from before diagnosis until death. Using data from food frequency questionnaires completed every 4 years during follow-up, they

found that men who consumed more vegetable fat had a lower risk of prostate cancer death ($P=.04$). No other fat sources were linked with prostate cancer mortality.

In examining epidemiological data, one's first question should be whether unaccounted-for differences between groups could explain the results. Indeed, men who consumed more vegetable fat did have small baseline differences that would favor better prostate cancer survival (lower prostate-specific antigen levels at diagnosis, fewer high-grade cancers, and more prostate-specific antigen screening). While these variables were adjusted for in multivariable analysis, other unaccounted-for differences may have contributed to the better outcomes. For example, these same factors may correlate with increased rates of secondary treatments, such as earlier use of hormone therapy or more aggressive secondary radiotherapy for surgical failures, both of which may lower risks of metastatic and fatal prostate cancer. Thus, in the absence of randomized trial data, it is impossible to use these data as "proof" that vegetable intake lowers prostate cancer risk, and the authors have carefully avoided such statements.

Given that residual confounding is always possible, what if we accept these data at face value? What does it mean that vegetable fat intake was associated with lower prostate cancer mortality? A key point in all statistics is that they are relative. In other words, these data suggest that men who consumed more vegetable fat had lower prostate cancer mortality than men who ate less vegetable fat. Given that the results were adjusted for calories, one must ask what the men eating fewer vegetables ate instead. In this case, they ate carbohydrates. The authors state that "replacing 10% of calories from carbohydrates with vegetable fat was associated with a 29% lower risk of lethal prostate cancer." In other words, eating vegetable fat is better than eating carbohydrates. The key question is whether this is due to vegetables being beneficial, or "good"; carbohydrates being harmful, or "bad"; or a combination of both.

Increasing data suggest that carbohydrate intake and the resultant increases in serum insulin levels may promote aggressive prostate cancer. In animal models, lowering carbohydrate intake slows prostate cancer growth.⁶ In men with prostate cancer, higher levels of C-peptide (a marker of insulin secretion) before diagnosis is strongly predictive of death from prostate cancer.⁷ Moreover, a recent cohort study found that, whereas total carbohydrate intake may not be related to prostate cancer risk, excess intake of sugar-sweetened beverages was associated with increased risk of symptomatic prostate cancer.⁸ Thus, like fats, not all carbohydrates may be created equal, but collectively these data support the hypothesis that excess intake of carbohydrates—refined carbohydrates specifically—may be harmful in their association with prostate cancer.

Given that increased vegetable intake was at the expense of carbohydrates, which as noted may be harmful, we must then ask whether vegetables are beneficial. Richman et al⁵ found that "the magnitude of the association [between vegetable fat intake and lower prostate cancer mortality] was similar, but not statistically significant, when animal fat was replaced with vegetable fat." In other words, vegetable fat was more beneficial than animal fat. Of note, replacing carbohydrates with animal fat had no effect on prostate cancer mortality, suggesting that animal fat was as harmful as carbohydrates. However, animal fat is a

complex mixture of multiple types of fat. Moreover, fats are consumed not alone but as part of whole foods, and consumption of animal fats entails consumption of animal meats. This is relevant because charring of red meat creates heterocyclic amines, which can cause genomic instability and are linked with prostate cancer both in rat models and in human epidemiological studies.⁴ Thus, it remains possible that animal fat is not harmful in itself but that how meat is prepared leads to prostate cancer risks similar to those associated with carbohydrates.

Ultimately, this leaves us with the question of whether vegetables are beneficial. Certainly, these data suggest that they are. Moreover, they suggest that carbohydrates and animal fats may both be harmful. Indeed, a longitudinal study in women using heart disease as the outcome found that, while a low-carbohydrate diet was not linked with heart disease (positively or negatively), when vegetable fats and proteins were the predominant protein and fat source, this dietary pattern was linked with a lower heart disease risk.⁹ Given many shared etiological factors for heart disease and prostate cancer (eg, inflammation, high cholesterol, and obesity), a heart-healthy diet is probably a prostate-healthy diet. Indeed, the data by Richman et al⁵ suggest this in that dietary patterns linked with lower prostate cancer mortality were linked with lower all-cause mortality. One key limitation of their data is the inability to determine what type of vegetable fat may be most beneficial (eg, corn vs olive vs canola oil).

When counseling patients, I remind them that obesity is the only known modifiable risk factor linked with prostate cancer mortality to date. Thus, avoiding obesity is essential. Exactly how this should be done remains unclear, although the data by Richman et al⁵ suggest that substituting healthy foods (ie, vegetable fats) for unhealthy foods (ie, carbohydrates) may have a benefit. Determining whether this benefit is due to reduced consumption of carbohydrates or greater intake of vegetables will require future prospective randomized trials.

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