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Can We Eat Our Way to a Lower Prostate Cancer Risk, and If So, How?

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Within a few decades of moving to the United States, immigrants from countries with low cancer risk show a risk for several cancer types comparable to the average American [1]. These findings have long been used to argue that lifestyle factors play a strong role in cancer development. As such, it is logical to ask whether men living and working in the United States who adhere to "old world" diets (eg, Mediterranean) are at decreased risk of cancer.

To address this specific question in the context of prostate cancer (PCa), Kenfield et al. [2] in this issue of *European Urology* tested whether adherence to a Mediterranean diet (calculated using a Mediterranean diet score) among US men was associated with reduced risk of overall PCa or advanced PCa. During a 14-yr follow-up period of 47 867 men, they identified 6220 cases of PCa and found that the Mediterranean diet score was not associated with overall risk or risk of advanced PCa. They further examined 4538 men who were diagnosed with PCa and among these men found no association between the Mediterranean diet score and PCa-specific mortality. Of note, they did observe a significant association between a higher Mediterranean diet score and reduced overall mortality in men with nonmetastatic PCa.

Although these results are disappointing to the enthusiast for the role of diet and PCa, it is important to determine exactly what the authors meant by a "Mediterranean diet." Specifically, Table 1 in Kenfield et al. [2] is extremely informative. For example, the Mediterranean diet score was influenced by factors commonly associated with a Mediterranean diet, such as vegetables, fish, whole grains and "healthy fats" (ie, a high polyunsaturated-to-saturated fat ratio). However, the role of some of these factors in PCa risk is unclear. For example, one study suggested that whole grain intake may increase risk of PCa [3]. Similarly, while many studies suggest dietary fish may reduce PCa risk, a recent study showed plasma omega-3 fatty acid (i.e. a common fat present in fish) was associated with increased PCa risk [4]. Thus, the role of fish oil in altering PCa remains unclear. The relevance of this information is that it remains possible that certain factors Kenfield et al. [2] included in their Mediterranean diet score may reduce PCa risk, while others increase PCa risk, resulting in an overall null association.

Interestingly, Kenfield et al. recently analyzed the same data, but rather than looking at dietary patterns, they examined fat intake [5]. In that analysis, the authors found that increased vegetable fat intake reduced PCa mortality. In other words, eating more fat reduced PCa death, as long as it was the right kind of fat. As such, this finding highlights the complexity of examining diet, in that people do not eat nutrients but rather foods. Moreover, each person consumes a different variety of foods, thus computing total diet scores can be challenging. Moreover, simply labeling any one broad category of foods as "good" or "bad" may be too simplistic. Finally, when a person makes a choice to eat a given food, he or she is doing so at the expense of not eating some alternative food. In other words, diet is not like smoking or drinking, which is yes or no. We all must eat to live. Every day, three times a day, we are faced with making the choice of what to eat. Thus, when someone chooses a salad as a side dish instead of a simple carbohydrate side dish (ie, white rice), is the benefit from eating salad, from not eating the carbohydrates, or both?

Importantly, one should not take away from this study that diet has no role in PCa. On the contrary, diet may play a

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large role in PCa [6], but data are conflicting for many dietary factors, and thus finding a take-away message is not always easy. Nevertheless, what is clear is that excess caloric intake leads to obesity, which is known to be correlated with PCa mortality [7]. Thus, the strongest link between diet and PCa comes from the consistent findings linking obesity and PCa mortality.

Given all the difficulties in epidemiologic studies of diet, where is the field going? As in all of medicine, the future likely lies in personalized nutrition (ie, nutrigenomics) [8]. For example, one study suggested that higher plasma selenium levels were associated with lower PCa risk but only in men with a particular genotype of manganese superoxide dismutase [9], an enzyme that metabolizes reactive oxygen species and superoxide anions to oxygen and hydrogen peroxide, which are further converted to water via seleniumdependent enzymes. Thus, it is likely that your genotype influences how you metabolize your food, which ultimately affects your overall health. Sorting out how the complexities of diet interact with the complexities of the genome will not be an easy task, but this is clearly the future and ultimately where research needs to go.

Until that day, what can we take away from this study and similar studies? Importantly, the number one cause of death for men with PCa is heart disease. Thus, our advice to our patients should focus on these areas: Avoid obesity, exercise regularly, control your cholesterol, and don't smoke. Whether such advice reduces PCa risk remains to be determined, but such advice is unlikely to increase PCa risk and thus unlikely to cause harm. Finally, we need to remember the old adage that while genes may load the gun, lifestyle pulls the trigger.

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