Prostate Cancer: The Big Picture

by Dr. Richard A. Saladino

According to the American Cancer Society, about 186,320 Americans will be diagnosed with prostate cancer this year, and 28,660 will die from the disease.

That makes prostate cancer the most common internal malignancy in American men, with a cancer death toll that trails only lung cancer. Researchers have made substantial progress in understanding the causes and basic biology of the disease, and clinicians have developed improved methods of diagnosis and therapy. Even so, basic questions remain unanswered; as a result, many important decisions about prostate cancer are not made by doctors but by patients.

The first decision a man faces is whether or not to have a blood prostate-specific antigen (PSA) test and a digital rectal exam (DRE) to screen for early prostate cancer. Although many men find the decision difficult, there is no wrong answer. Proponents of screening point out that PSA testing is the best way to diagnose prostate cancer in its earliest, most treatable stages. Skeptics counter that some men diagnosed by screening receive treatments that produce more ill effects than the disease itself. Odd as it sounds, both sides are right. In fact, informed decision-making is the approach recommended by every major medical organization that has weighed in on the question, ranging from the American Cancer Society and the American Urological Association to the American College of Physicians and the Academy of Family Physicians.

Once a man is diagnosed with prostate cancer, his decisions take on a new urgency. In the case of most malignancies, news of the diagnosis is accompanied by a crisp and confident treatment plan. Not so with prostate cancer; instead, the doctor who announces the diagnosis is likely to ask the patient what treatment he wants. That means the shock of a diagnosis followed by the shock of learning that, in many cases, doctors disagree about which treatment is best.

It's not that the doctors haven't tried to answer the questions themselves. In 1995 and again in 2007 the American Urological Association published reports by the authoritative Prostate Cancer Clinical Guidelines Panel.

In both cases, dozens of experts reviewed thousands of studies but were unable to establish standard-of-care recommendations. Instead, the experts recognized that there are many acceptable therapeutic options, and they suggested that doctors inform their patients about the advantages and disadvantages of each treatment, enabling every man to choose for himself. And a major 2008 review sponsored by the U.S. Agency for Healthcare Research and Quality agreed, concluding that "Assessment of the comparative effectiveness and harms of localized treatments is difficult because of lack of evidence."

First, let's ask why prostate cancer is different from other malignancies, and what makes studies hard to perform and tricky to interpret.

The natural history of prostate cancer

Scientists don't know how prostate cancer gets started or what causes it, but several factors are important. Genetics certainly play a role. Men with fathers or brothers who have had prostate cancer are 1.5 to 3 times more likely to get the disease than men with no family history, and if multiple relatives have been diagnosed before age 55, a man's risk rises further.

Hormones also play a role. Testosterone and other androgens (male hormones) stimulate the growth of prostate cells, both benign and malignant, but there is no simple link between testosterone levels and risk. Lifestyle is also important. Prostate cancer is vastly more common in white Americans than in Japanese or Chinese men—but when Asians move to the U.S. and adopt to Western habits, they quickly acquire the high risk of native-born Americans.

Diet is the most important lifestyle risk factor. Dietary fat—particularly saturated fat from animal products—appears to fuel the disease, and very high levels of calcium and alpha-linolenic acid (the omega-3 fat in flaxseeds and canola oil) may also have an adverse effect. In contrast, tomatoes and other vegetables, soy products, fish, and whole grains may be protective. Obesity increases risk. And although the evidence is mixed, exercise may be helpful, smoking harmful. Though factors contribute to prostate cancer, they act slowly. That's why age is the greatest predictor of risk.

It's a bit scary. If you live long enough, you will probably get prostate cancer. Remember, though, that most of the prostate cancers in these surveys are clinically unimportant—a few malignant cells discovered in the course of complete autopsies on men who died from other causes. In all, an American man's lifetime risk of developing early microscopic prostate cancer is at least 30%, but his risk of clinically diagnosed prostate cancer is only about 16%. A one-in-six chance of being diagnosed with prostate cancer is scary, but a white American's risk of dying from the disease is only about 3%; an African American's about twice that.

Why the debate?

In most forms of cancer, diagnosis and treatment go hand in hand; it may be hard for a doctor to diagnose a tumor, but once he know it's there, he can offer a clear plan of treatment based on solid scientific evidence that's backed by experts. Why is prostate cancer so different?

First, the disease is different. Most cancers behave predictably, but prostate cancer does not; sometimes it's aggressive and dangerous, but often it's indolent or even harmless.

Second, the cancer grows slowly. With many malignancies, a five year survival is tantamount to cure, so clinical trials can learn if a treatment is effective in a relatively short time. But more patients with prostate cancer can survive for more than five years with any form of treatment—or with no treatment at all. An important 1995 study found that most cases remain indolent for 10 to 15 years after diagnosis, even without therapy. After that, however, the prostate cancer death rate triples. As a result, it may take 10 to 15 years for a study to learn how well a treatment works.

Third, the diagnosis of prostate cancer has changed dramatically in the past 15 years. Before 1992, the disease was most often discovered as the result of a DRE or a pathological examination of tissue obtained during a transurethral resection of the prostate (TURP), performed to treat benign prostatic hyperplasia (BPH). At present, prostate cancer is most often diagnosed as the result of a PSA blood test. Widespread PSA testing has produced an explosive rise in the number of cases detected, particularly in young men with early disease. Doctors don't yet know if the cancers detected by PSA screening will behave the same way as the cancers detected by older methods.

Fourth, the treatment is also changing. For many years, the options for active therapy were limited to surgery, external beam radiation, and hormonal therapy. Doctors have developed greatly improved techniques for each of these standard treatments—and they have also developed entirely new approaches, such as brachytherapy with implanted radioactive seeds; cyrotherapy, which kills prostate cells by freezing them; and neoadjuvant therapy, which combines radiation with hormone treatment. It is heartening, but these advances make a man's decision even more complex.

Finally, and most importantly, only a tiny number of scientific trials that compare treatment have been completed. When the American Urological Association tried to compare the outcome of patients treated with active surveillance, surgery, or radiation, they found they were comparing apples to oranges. The vast majority of studies that have been completed to date differ so substantially in patient age, disease state, and follow up that comparisons are not possible. New studies to resolve these issues are already in progress, but they will not be completed for years. Until the results are in, the only option is to consider each treatment on its own merits.

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