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Prostate Cancer: Weighing Options

By MELINDA BECK



You've been diagnosed with prostate cancer and after the shock comes confusion.

Should you treat it fast with surgery but face an immediate risk of sexual and urinary problems? Or should you opt for weeks of daily radiation treatments and side effects that set in more slowly? Should you also use hormone therapy that may shrink the cancer -- and your sex drive along with it? Or should you just monitor your cancer and hope you'll catch it if it starts to spread out of control?

Today's Health Journal is the second in a two-part series on the many dilemmas that prostate cancer poses. Last week's column looked at imaging and biopsy techniques that can help clarify the diagnosis. This week's column explores the bewildering array of treatment options. A related column -- on living with "watchful waiting" -- will appear in the Journal's Encore supplement on April 18.

Some 185,000 men will be diagnosed with prostate cancer this year in the U.S., and many will get conflicting advice. There's little consensus on how or even whether to treat prostate cancer, which can be slow-growing and harmless or aggressive and lethal.

When the New England Journal of Medicine recently asked readers how they would treat a hypothetical 63-year-old man with a low-grade cancer and a rising PSA (for prostate-specific antigen), the more than 3,720 physicians who responded split almost evenly among surgery, radiation therapy and monitoring the cancer to see if it grew.

With doctors so divided, how can patients know who to believe and what to do?

The first step is to find out as much information you can about your own cancer.

You've been given a Gleason score, based on the pattern of abnormal cells seen in the biopsy. A Gleason 6 or below is considered low-grade. Gleason 7 and above is more worrisome. But traditional biopsies that sample the prostate at random can miss cancers in about 20% of cases, and may miss the most advanced spots. Ask how many biopsy samples were taken -- and whether imaging is available as well. MRI scans or a color Doppler ultrasound, used at some major cancer centers, can provide more information about suspicious areas.

"Don't stop until you have clarity on the location, the extent and the aggressiveness," says Faina Shtern, a former official at the National Cancer Institute, who now heads the AdMeTech Foundation, which is lobbying for more federal funding for imaging research.

It's reassuring to know that with early-stage cancers that are still confined to the prostate, there is a 90% "cure" rate -- which means patients are free of cancer for at least five years -- no matter which treatment they choose. And many prostate cancers are so slow-growing they may not require treatment at all.

But every man's cancer is different, as is his general health, family history, life situation and mindset. Make sure you understand your own priorities. Some men want the cancer out as fast as possible; others want to avoid surgery at all costs. Some want the best chance for a long-term cure; some care as much or more about avoiding incontinence or erectile dysfunction.

Here's a look at the options:

Surgery

Men diagnosed with prostate cancer in their 40s and 50s are often steered toward surgery (called a radical prostatectomy), since it's thought to offer the best chance for long-term survival. What's more, removing the prostate and examining it in a lab is the only way to know for sure how much cancer was there and how likely it is to return.

"I present the choice very simply: either you are damaging the prostate or removing it," says Randy Fagin, who performs robot-assisted surgeries in Austin, Texas. "If you damage it and leave it there, what if the cancer comes back? If you have surgery, it's gone."

Surgeries using the daVinci Robotic System now account for over 50% of prostatectomies. The surgeon sits at a console about six feet from the patient and, while watching on a video screen, manipulates miniature, flexible tools that perform the surgery through small incisions. It's minimally invasive, which reduces pain, recovery time and blood loss. Most patients go home the next day.

"If you have a well-trained robotic surgeon, there's absolutely no reason to filet patients open and go through all the mess we used to have," says David Samadi, chief of robotic and minimally invasive surgery at Mount Sinai Medical Center in New York City who has performed over 1,800 robotic prostatectomies.

Doctors who practice traditional "open" surgeries say there are no reliable studies showing that robotic surgery has higher cure rates or fewer side effects than conventional surgery.

Both camps agree that having a highly experienced surgeon is far more important than the method he or she uses. How can patients find one? Jan Manarite, a counselor of the Prostate Cancer Research Institute, a nonprofit patient education group, suggests joining a local support group and asking for recommendations. "Some surgeons will also give you a list of their patients to talk to -- that's a sign of honesty and transparency," she says.

Removing the prostate does carry a high risk of side effects, since many delicate nerves and blood vessels involved in urination and ejaculation run through the gland. Depending on where and how big the cancer is, surgeons may be able to use "nerve-sparing" procedures that preserve much of those functions. Most men need a urinary catheter for a week or two after surgery. Some need to wear absorbent pads for a few weeks, but most are fully continent within a year.

Sexual function after surgery depends largely on the age of the patient, his potency before surgery and the skill of the surgeon. "Whatever you start out with, even in the hands of an artist, you will probably come away with a little bit less," Ms. Manarite says.

Radiation

Men over 70, those with other health problems or those whose cancer has spread beyond the prostate are usually counseled to have radiation. External-beam radiation therapy, or EBRT, requires no incisions, no hospitalization and no anesthesia. But it can be inconvenient: Patients generally undergo 40 or more treatments over six to eight weeks.

High-energy beams damage the ability of cancer cells to replicate. The entire prostate slowly withers as well.

Radiation has fewer immediate side effects than surgery, but urinary discomfort and loss of sexual potency often set in gradually.

The goal of all EBRT is to maximize the radiation hitting the prostate and minimize its impact on surrounding tissue. The field took a big leap in recent years with intensity-modulated radiation therapy, which allows doctors to sculpt the radiation beam to fit the contours of the individual patient's prostate.

One variation, TomoTherapy, takes a new CT scan at the start of each treatment and adjusts the beam accordingly. CyberKnife condenses the standard number of radiation sessions from 40 down to just a handful, at higher doses, so treatment is often completed in a single week.

Traditional radiation oncologists argue that there is no evidence to prove that such innovations offer better outcomes.

The lack of evidence has been a particular issue for proton-beam therapy, which fires super-accelerated atomic particles, rather than X-rays, at prostate and other cancers. Proponents say proton-beam therapy causes fewer side effects because protons can be made to peak at the target area and then stop, minimizing collateral damage on the way out of the body.

But proton accelerators cost \$125 million to \$225 million each and are the size of two football fields. There are currently only five in the U.S., with several others in the works. The therapy costs patients -- in most cases, Medicare -- about four times what traditional radiation costs. Critics say there is no conclusive evidence that the added cost is justified.

In another form of radiation called brachytherapy, doctors insert 70 to 80 tiny radioactive pellets into the prostate that gradually dissolve and destroy cancer cells internally. Many patients like the convenience: It requires just one minimally invasive procedure that lasts about an hour.

One downside is that patients are advised to avoid prolonged contact with pregnant women and children to minimize a slight risk of radiation exposure to them. In high-dose brachytherapy, a radioactive source is placed in the prostate only temporarily, with no risk to others. Studies have shown that brachytherapy carries a higher risk of urinary problems than other therapies.

'Male Lumpectomy'

About 20% of prostate cancer patients have very small localized tumors. One new option for them is focal ablation, in which doctors destroy the individual tumor while leaving the rest of the gland intact, much like a lumpectomy for breast cancer.

Of several ablation techniques, cryotherapy has been in use the longest. Doctors insert metal prongs into the prostate to surround the tumor and freeze it with liquid nitrogen. In a study presented last month at the Society for Interventional Radiology, Gary M. Onik, director of the Center for Safer Prostate Cancer Therapy in Orlando, Fla., reported that of 120 men who had focal cryoablation over 12 years, 93% of men had no evidence of cancer recurrence, and 85% retained sexual function.

Another focal technique used in Europe, Canada and Mexico is high-frequency ultrasound, or HIFU, which involves heating localized prostate tumors rather than freezing them.

A key to focal therapy is knowing the precise size, shape and location of tumors. It's frequently used with three-dimensional mapping biopsies that can supply that data after taking 50 or more samples.

Critics argue that prostate tumors that are small and localized enough for focal therapy could be safely watched instead. Dr. Onik says that's just the point: Focal cryosurgery offers a middle ground between watchful waiting and more aggressive therapies. "Let's ablate the cancers we know about, and then do watchful waiting," he says. Meanwhile, the minimally invasive procedure can be repeated if the cancers recur.

Watchful Waiting

At least 50% of men diagnosed with prostate cancer in the U.S. have a low-grade form of the disease that experts say doesn't need immediate treatment and may never. But less than 10% opt to put treatment off and just monitor their cancer. That's in part because it can be psychologically difficult to live with untreated cancer, and in part because the medical system is geared toward active treatment.

"Some patients tell me that their doctors never mentioned this as an option," says oncologist Jeri Kim, the principal investigator of a watchful waiting trial at M.D. Anderson's Multidisciplinary Prostate Cancer Clinic in Houston. It's one of a few academic centers where patients consult doctors from all the rival disciplines to arrive at the best option.

The big risk with watchful waiting is that a cancer will spread from a highly curable early stage to a more advanced stage, growing outside the prostate, that is far more difficult to treat. Some tumors that have been stable for years can suddenly start to spread.

That's why Dr. Kim and others stress that patients and doctors alike need to do active monitoring, with PSA tests every three to six months, digital rectal exams annually, and repeat biopsies if the PSA starts to rise. "You can't have a patient who will disappear on you. If the guy moves to Florida and five or six years from now his PSA hits 90, then it's over," Dr. Samadi says.

A handful of doctors in the U.S. -- and many more in Europe -- use color Doppler ultrasound imaging to monitor prostate cancer patients. Real-time ultrasound imaging can be done painlessly in a doctor's office. Areas of increased blood flow that signify cancer show up in color. "The ultrasound differentiates not just cancer, but which cancers are lethal," says Robert L. Bard, a radiologist in New York City, who has been monitoring about 3,000 prostate-cancer patients.

Other doctors who use Doppler ultrasound caution that nothing is 100% accurate -- but it can provide more reassurance for patients monitoring their cancer. A biopsy targeted at suspicious areas can help verify whether a tumor is changing.

Diet and Exercise

Besides being conscientious about followup exams, patients can help their own cause by maintaining a healthy diet and lifestyle. "Active surveillance also means you are going to change your life and do things that can slow the cancer down," says Charles Myers, former chief of clinical pharmacology at the National Cancer Institute and a prostate-cancer survivor himself who now treats patients in Charlottesville, Va.

Dr. Myers says it's critical to maintain an adequate level of vitamin D, which can help keep cancers in check. Many older people are deficient. Studies have also shown that a Mediterranean diet -- with plenty of fish, olive oil and vegetables -- can slow cancer growth, along with vitamin E, selenium, lycopene, omega 3 fatty acids and green tea polyphenol, as well as avoiding animal fat.

Getting exercise and minimizing stress can go a long way as well. Stress hormones epinephrine and norepinephrine help prostate-cancer cells grow and impair the immune system.

"I'm proud of what I'm doing," says Ronald Zaza, who was diagnosed with prostate cancer in 1996, six weeks after having quadruple bypass surgery. He has since abandoned meat and chicken for vegetables and tofu, started running

marathons and is monitoring his cancer once a year with a color Doppler ultrasound. So far, it's not showing any suspicious areas, and Mr. Zaza says, "I'm 71 and just ran a marathon. I feel like I'm 35."

Late-Stage Cancer

Not all prostate-cancer patients can control their cancer with diet and exercise. For those whose cancer has metastasized, a variety of hormone therapies that block testosterone can often stop the progression very successfully, at least for a while. The downside is a high risk of osteoporosis, hot flashes, depression, breast enlargement, diabetes, obesity and high blood pressure. Using hormone therapy intermittently can help reduce such side effects.

A number of new drug therapies are under investigation -- including drugs that block the androgen receptors on cancer cells. Results of a clinical trial on Avodart, a medication for enlarged prostates, as a treatment to slow cancer growth, are expected this spring. Doctors and patients also have high hopes for Provenge, which could offer the first immunotherapy agent approved to fight cancers.

In the past, chemotherapy drugs have not been as successful against prostate cancers as other cancers. But Taxotere is showing promise, particularly when combined with other drugs that fight blood-vessel growth in tumors.

Patients with advanced prostate cancer often find that medications can be effective in a variety of combinations, and when one stops working, it may be effective again in a few months. "Somewhere between cure and death is a middle road where you are keeping a cancer suppressed or under control," says Ms. Manarite, whose husband, Dominic, has had metastatic prostate cancer for nine years.

Some experts also urge men with prostate cancer -- at any stage -- to join clinical trials if possible. "That's how we made all the progress in breast and colon cancer," says Jonathan Simons, president of the Prostate Cancer Foundation, which funds clinical research. "We have some very important ideas to test that might lengthen your life."

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