

Prostate Cancer Tx Side-Effects Study: New 15-Year Data

Fran Lowry

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Men with localized prostate cancer who elect to have prostatectomy or radiotherapy will experience problems with urinary, bowel, and sexual function in the long term, according to a [new study](#) published today in the *New England Journal of Medicine*.

Data from the Prostate Cancer Outcomes Study (PCOS) show that in the short term, men who have had surgery will have more urinary incontinence and sexual dysfunction, and those who have had radiotherapy will have more bowel dysfunction, but by 15 years, dysfunction in all domains is not significantly different.

"Whatever the reason, it could be aging, it could be the treatment, it could be secondary treatments, but in the long run, there are not a lot of differences between the 2 primary treatments for localized disease, whether they are surgery or radiation," senior author David F. Penson, MD, from Vanderbilt University, Nashville, Tennessee, told *Medscape Medical News*.

The results from PCOS should give men with localized prostate cancer pause before they choose a treatment, Dr. Penson said.

"A significant proportion of these men are not going to die from their disease and I think if a man has low grade prostate cancer, these data should really make him think carefully before he signs on to have any surgery or radiation because a lot of these quality of life side effects could be avoided by choosing active surveillance."

Dr. Penson and his team compared long-term urinary, bowel, and sexual function after radical prostatectomy or external-beam radiation therapy in a cohort of 1655 men who were diagnosed with localized prostate cancer in 1994 or 1995, when they were between the ages of 55 and 74 years.

Most (1164) of the men had undergone surgery, and 491 had radiotherapy. Functional status was assessed at baseline and at 2, 5, and 15 years after diagnosis.

Men who had surgery were significantly more likely than those who had radiotherapy to report urinary leakage at 2 years (odds ratio [OR], 6.22; 95% confidence interval [CI], 1.92 - 20.29) and at 5 years (OR, 5.10; 95% CI, 2.29 - 11.36).

At 15 years, 18.3% of men in the prostatectomy group and 9.4% of men in the radiation group had urinary incontinence, but this did not amount to a significant between-group difference in the odds of urinary incontinence.

Men who had radiotherapy had higher rates of bowel urgency compared with men who had prostatectomy at 2 years (OR, 0.39; 95% CI, 0.22 - 0.68) and at 5 years (OR, 0.47; 95% CI, 0.26 - 0.84).

At 15 years, the prevalence of bowel urgency in the prostatectomy group was 21.9% vs 35.8% in the radiotherapy group. But again, this did not amount to a significant between-group difference in the odds of bowel urgency.

Erectile dysfunction was significantly more likely in men who had prostatectomy than in those who had radiotherapy at 2 years (OR, 3.46; 95% CI, 1.93 - 6.17) and at 5 years (OR, 1.96; 95% CI, 1.05 - 3.63).

However, at 15 years, erectile dysfunction was "nearly universal," affecting 87.0% of those in the prostatectomy group and 93.9% of those in the radiotherapy group.

Only 43.5% of men in the prostatectomy group and 37.7% of those in the radiotherapy reported being bothered by their sexual dysfunction.

"For a lot of these guys, even though they are impotent, it doesn't bother them that much. It may be because they are older and weren't working that well to begin with, or it may be because they are cancer free, and so feel better anyway. The bottom line is you have a high risk of being impotent with whatever treatment you choose," Dr. Penson said.

Is It Treatment or Aging?

Commenting on this study for *Medscape Medical News*, Charles Catton, MD, from the Princess Margaret Cancer Centre, University Health Network, Toronto, Ontario, Canada, called it an "important study, as it is the first time that very long-term side effects of surgery and radiotherapy for prostate cancer have been compared prospectively in real time."

Dr. Catton agreed with Dr. Penson that the information in the study is important to help men with localized prostate cancer decide which treatment is best for them, "especially if we expect these treatments to be otherwise similar in cancer control benefit."

He also pointed out that surgery and radiation techniques have improved since the PCOS patients were treated in the mid-1990s. "The nature of the side effects may not have changed, but it is possible that the risk and severity of these side effects are less now than were shown in this study."

Matthew Cooperberg, MD, from the University of California, San Francisco, also called the findings important, although not surprising.

"With longer term follow up in an aging population, urinary and sexual functions tend to decline, and differences between treatments attenuate," he told *Medscape Medical News*. "This is consistent with clinical observations and other epidemiologic evidence, as noted by the authors."

Dr. Cooperberg added that an "important caveat" with respect to urinary function is that the authors reported only incontinence urinary leakage symptoms, which tend to be worse with surgery than with radiation.

"Urinary irritation symptoms including urgency, frequency, and bleeding, tend to be worse with radiation. The authors note they collected these data in the 15-year follow up survey but not in the earlier ones, so they did not include these data in the longitudinal analysis. Hopefully we will see them published in the future."

The fact that the patients in this analysis are drawn randomly from a population sample is the strength of the study, in terms of the reliability of its conclusions, Dr. Cooperberg also noted.

"Far better functional outcomes are routinely achieved in centers of excellence which treat high volumes of prostate cancer patients, so these results are in a sense a 'worst case scenario' in terms of absolute rates of dysfunction," he said.

James Mohler, MD, from the Roswell Park Cancer Institute, Buffalo, New York, and chair of the Guidelines Panel for Prostate Cancer of the National Comprehensive Cancer Network [NCCN], told Medscape Medical News that the information from the study "should cause men to remember that having either radical prostatectomy or radiation therapy is not without risk, and that that risk is lifelong."

However, he noted, it is difficult to sort out how much of these functional problems are due to aging or to the effect of treatment.

"The men in the trial were 55 to 74 years at the start and at 15 years of follow-up they are between 70 and 89, so they are going to be having a lot of issues, and in fact many had died," Dr. Mohler said.

He also pointed out that improvements in treatments since the mid-1990s could improve outcomes.

"This was done prior to the use of IMRT [intensity modulated radiation therapy] to decrease the side effects of radiation, and prior to anatomic prostatectomy, and it would be our hope that if this study were re-done that the side effects would be less, but that's only a hope. This is real data and it should certainly give men pause," he said.

Dr. Mohler stated that the NCCN prostate panel is concerned that men with low-risk prostate cancer are being unnecessarily treated.

"It is estimated that between 40 and 50 percent of the men treated for prostate cancer in America don't need to be treated, they would be better off with active surveillance or observation. Men need to understand that if you don't need to be treated in the first place, you certainly don't need to be treated unnecessarily with a treatment that is going to adversely impact your quality of life," he said.

"We need a test that will distinguish the potentially fatal prostate cancer from the indolent prostate cancer and we don't have that," Dr. Mohler added. "There are lots of people working on this, and I'm a huge believer in PSA velocity to help guide men's decision making process."

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