PSA May Trigger Overtreatment of Prostate Ca

BY SUSAN LONDON

SAN FRANCISCO — Men on active surveillance for prostate cancer may be overtreated if clinicians rely strictly on certain commonly used prostate-specific antigen triggers for starting treatment, Dr. Andrew Loblaw said at a symposium on genitourinary cancers.

In a cohort of 315 such men who had no evidence of disease progression, the percentage in whom treatment would have been falsely triggered ranged widely—from 14% to 84%—depending on which of nine PSA measures was used for monitoring. The lowest value seen was with a PSA threshold of 20 ng/mL.

"For patients managed on active surveillance, this raises what we believe is a cautionary tale that strict follow-up with

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DR. LOBLAW

the definitions of either linear regression, threshold, or velocities may lead to a false rate of treatment for patients on surveillance who don't need it," said Dr. Loblaw, a radiation oncologist at the Sunnybrook Health Sciences Centre in Toronto.

Research shows that active surveillance can achieve good outcomes in men with low-risk prostate cancer, he said. This surveillance typically entails PSA monitoring, with initiatation of treatment often based on a PSA trigger.

The researchers tested the performance of various PSA triggers in 315 men with localized prostate cancer who declined radical treatment, were enrolled in an active surveillance program, and did not have any evidence of disease progression after a median follow-up of 6.8 years (7.2 years for survivors).

At enrollment, the patients' PSA levels were all less than 15 ng/mL. Their monitoring had consisted of periodic physical examination, digital rectal examination, blood work, transrectal ultrasound, bone scans, and repeated prostate biopsies.

"All of the triggers or definitions that we looked at had a false or high trigger for treatment," Dr. Loblaw reported at the symposium, which was sponsored by the American Society of Clinical Oncology, American Society for Radiation Oncology, and Society of Urologic Oncology.

The false trigger rate was lowest for a PSA threshold of 20 ng/mL (according to which 14% of the men would have been treated) and highest for a successive PSA velocity of greater than 2 ng/mL (84%).

The rate was intermediate for a PSA threshold of 10 ng/mL (38%), first-last PSA doubling times of less than 2 and less than 3 years (39% and 50%), linear regression PSA doubling times of less than 2 and less than 3 years (37% and 48%), overall PSA velocity of greater than 2 ng/mL per year (42%), and a 1-year PSA velocity of greater than 2 ng/mL (51%).

The findings suggest that only a PSA threshold of 20 ng/mL has a low false trigger rate and that men on active surveillance may be overtreated when clinicians rely on the other PSA triggers, Dr. Loblaw said.

To assess PSA changes, he said, clinicians at his center have started using and are validating a general linear mixed model that is freely available online (www.asure.ca).

"It allows us to smooth out these PSA variations and helps us interpret the PSA undulations over time," Dr. Loblaw said. "We are hoping that this will be a beneficial tool … to use in terms of managing patients on active surveillance." ■

VITALS

Major Finding: Common PSA triggers would have led to overtreatment of prostate cancer in 14%-84% of men on active surveillance.

Data Source: Prospective study of 315 men with localized prostate cancer and PSA levels less than 15 ng/mL at enrollment in monitoring program.

Disclosures: Dr. Loblaw reported having no conflicts of interest related to the study.

MY TAKE

Many Patients and Clinicians May Not Accept 20 ng/mL as Threshold

Active surveillance is a hot topic. Many men with localized prostate cancer may be candidates, but questions remain, including these:

► Is it prudent to offer active surveillance to young, healthy men who have a very long life expectancy?

► Does a patient on active surveillance need repeat prostate biopsies every year or two, or can we rely on PSA?

► As Dr. Loblaw and his colleagues asked, what is the best PSA change determinant to suggest a switch from active surveillance to active treatment?

The researchers found that a PSA above 20 ng/mL may be the most appropriate marker for switching to active treatment. But many patients would be very uncomfortable letting their PSA go as high as 20 before considering a repeat biopsy or treatment. With that strategy, we will be treating only high-risk patients who have progressed on active surveillance. This may be unacceptable to many clinicians and patients.

We need more randomized trials—such as the multicenter START trial—that address active surveillance. I congratulate the researchers on excellent work, and look forward to further studies of and new information about active surveillance.

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