

Prostatitis Can Confound Cancer Risk Assessment

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SAN FRANCISCO — Prostatitis can quickly lead to surges in prostate-specific antigen levels, potentially undermining the use of the biomarker's rate of change to help detect cancer, Dr. Scott Eggener said at a symposium on prostate cancer sponsored by the American Society of Clinical Oncology.

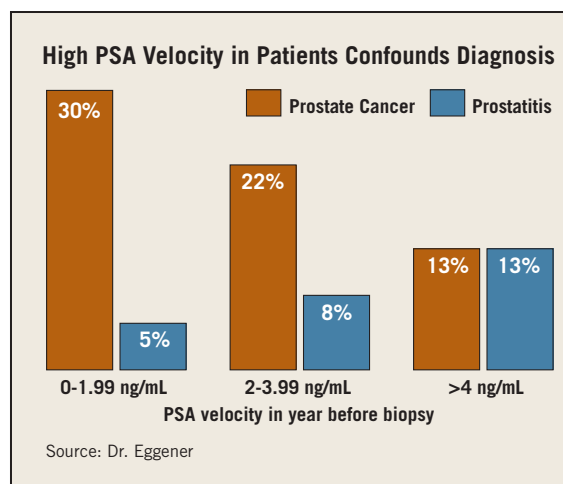
Previous studies have shown that prostate-specific antigen (PSA) velocity can be a valuable tool for assessing prostate cancer risk. Specifically, PSA velocity elevations of 2.0 ng/mL per year or higher have been identified as significant with respect to the risk of dying of prostate cancer, said Dr. Eggener of Memorial Sloan-Kettering Cancer Center in New York. It has also been suggested, however, that certain conditions, such as prostatitis and benign prostatic hyperplasia, could be confounding variables for rising PSA velocities.

Dr. Eggener and his colleagues analyzed records from 1,851 men enrolled in a community-based prostate cancer screening trial. At the time of their first biopsy, 468 men were diagnosed with prostate cancer, and 135 were diagnosed with prostatitis.

All of the men had a normal digital rectal exam and a calculable PSA velocity for the year prior to biopsy.

"What we found, relative to rising PSA velocity, was a general trend for decreasing cancer detection rate and a corresponding trend for increasing prostatitis," Dr. Eggener said at the symposium, which was cosponsored by the Society of Urologic Oncology and the American Society for Therapeutic Radiology and Oncology.

Specifically, 30% of the men with a PSA velocity of 0-1.99 ng/mL in the year be-



fore biopsy had prostate cancer, and 5% had prostatitis. In comparison, among men with a PSA velocity of 2.0-3.99 ng/mL, 22% had cancer on first biopsy, and 8% had prostatitis.

Men whose PSA velocities were greater than 4.0 ng/mL were equally likely to have prostatitis or prostate cancer, with

13% being diagnosed with each condition.

The risk of cancer diagnosis peaked relative to PSA velocity increases of 0.3-0.5 ng/mL per year, and the risk of prostatitis diagnosis rose substantially with PSA velocity increases of more than 2.0 ng/mL per year, Dr. Eggener said.

"Men with prostatitis often have dramatic rises in PSA prompting biopsy, but subsequently have a significant drop in PSA in the year or two following biopsy," he said.

Men with a normal digital rectal exam, elevated PSA, and a high PSA velocity should therefore undergo repeat PSA testing. "If any symptoms or laboratory findings suggest prostatitis, they should undergo appropriate evaluation and treatment," he said.

Dr. Eggener stressed that PSA velocity continues to be "very useful in assessing prostate cancer risk," but that dramatic increases over short periods of time should raise suspicion of prostatitis, in addition to prostate cancer. ■

PSA Increase Over Time Predicts Survival in Some Prostate Cancers

SAN FRANCISCO — Among men with early-stage prostate cancer who choose watchful waiting as their primary treatment strategy, the rate of rise in their prostate-specific antigen level is more predictive of survival than any single PSA value, Dr. Jennifer Cullen said at a symposium on prostate cancer sponsored by the American Society of Clinical Oncology.

In a retrospective study of nearly 1,400 men with early prostate cancer being followed with watchful waiting rather than active intervention, those men with a PSA velocity (the rate of increase in PSA value) of less than 2 ng/mL per year during a mean follow-up time of nearly 5 years had a significantly better overall survival rate than did men whose PSA velocity was at least 2 ng/mL per year, said

Dr. Cullen of the Department of Defense Center for Prostate Disease Research (CPDR) in Rockville, Md.

The study sample consisted of military-care beneficiaries from the CPDR database who were diagnosed with biopsy-proven, clinically localized prostate cancer between January 1989 and December 2003 and who did not receive any clinical intervention for their cancer for at least 6 months after diagnosis. Of the 1,369 men who met these criteria, the survival analysis was limited to 830 men who had a record of at least one follow-up appointment in the first 3 years following diagnosis, "to be sure that no other therapy was chosen at some time point after their care in the [CPDR] database program," she said.

All of the subjects had at least three PSA values after diagnosis but not spaced within 3 months of each other, to minimize the potential for noise-related inaccuracies that could occur at shorter intervals. The mean age was 69 years, and

the mean follow-up time was nearly 5 years.

The investigators generated survival analyses for men with PSA velocities below 2 ng/mL versus 2 ng/mL or more—a distinction that is literature driven, according to Dr. Cullen.

After controlling for comorbidities, secondary treatment, and time to secondary treatment, "we observed significantly poorer survival for those men in the higher PSA velocity group, independent of PSA value at diagnosis," she said. "Only 56% of men in the higher-velocity category were alive at follow-up, compared with 87% of those with lower velocity values."

On the heels of the recent report by the Scandinavian Prostate Cancer Group Study No. 4, a long-term trial showing small but significant overall and disease-specific survival differences between watchful waiting and radical prostatectomy (N. Engl. J. Med. 2005;352:1977-84), the findings of this study shed light on how best to evaluate the survival potential of watchful waiting for a given patient, Dr. Cullen noted at the meeting, cosponsored by the Society of Urologic Oncology and the American Society for Therapeutic Radiology and Oncology.

The Scandinavian study "did not specifically investigate factors that might impact survival in men who choose watchful waiting," she said. "Our goal was to look for characteristics that might be predictive of better or worse outcomes."

Although limited by its retrospective design, "our database is so large that we have the ability to do robust subset analyses such as this one," Dr. Cullen said. The findings, though promising, still need to be replicated in a nonmilitary population. In addition, she said, "we want to look at the relative impact of other survival predictors, including patient age, specific tumor characteristics, and Gleason scores, as well as the optimal frequency of PSA testing." ■

Age-Adjusted PSA Velocity Can Detect More Prostate Cancers

SAN FRANCISCO — Adjustment of threshold values of prostate-specific antigen velocity for age can substantially improve prostate cancer detection among men younger than 70 years, Dr. Judd W. Moul said at a prostate cancer symposium sponsored by the American Society of Clinical Oncology.

In a review of data from more than 11,000 men who underwent PSA testing during a 7-year period, Dr. Moul and colleagues at Duke University Medical Center in Durham, N.C., tested the hypothesis that lowering the threshold for what's considered the "normal" PSA velocity for younger age groups would help detect disease sooner than current thresholds allow.

The investigators calculated PSA velocities from patients' PSA measures over time and correlated them to prostate biopsy status. They then normalized velocity percentiles to three different age categories (40-59 years, 60-69 years, and 70 years and older).

Conventional screening protocols consider a PSA velocity increase of 0.75 ng/mL or more per year to be an indicator of increased prostate cancer risk regardless of patient age.

After adjustment of the data for patient age, the threshold PSA velocity for men aged 40-59 years was lowered to 0.25 ng/mL per year.

For men aged 60-69 years, it was lowered to 0.50 ng/mL per year.

The threshold for men older than 69 remained 0.75 ng/mL, Dr. Moul said at the symposium, which was cosponsored by the Society of Urologic Oncology and the American Society for Therapeutic Radiology and Oncology.

In a comparison of the screening accuracy of the age-adjusted threshold with the traditional stan-



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dard, the prostate cancer detection rate in the study cohort increased from 19% to 35% among men in the youngest category and from 25% to 57% among men in the middle age group.

"The sensitivity of the age-adjusted PSA velocity for the younger group was 0.519, compared to 0.265 for the standard," Dr. Moul said. "For the middle age group, the sensitivity with the lower threshold was 0.398, compared to 0.306."

Specificity values in these two groups were only slightly and non-significantly diminished from those associated with the conventional threshold values, he said.

Based on the findings, "it's clear that age-adjusted PSA velocity could significantly improve our ability to detect early prostate cancer," he said. ■