PSA Velocity Can Guide Watchful Waiting Tack

BY DIANA MAHONEY
New England Bureau

San Francisco — Among men with early-stage prostate cancer who choose watchful waiting as their primary treatment strategy, the rate of rise in 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 those men whose PSA velocity was 2 ng/mL per year or greater, said Dr. Cullen of the Department of Defense Center for Prostate Disease Research (CPDR) in Rockville, Md.

'We observed significantly poorer survival for those men in the higher PSA velocity group independent of PSA value at diagnosis.'

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 following diagnosis. Of the 1,369 men who met these criteria, the survival analysis was limited to 830 men who had 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," Dr. Cullen said.

All participants had at least three PSA values recorded after diagnosis and were taken more than 3 months apart, to minimize the potential for noise-related inaccuracies that could occur in shorter intervals, she said. Mean patient age was 69 years, and mean follow-up time was nearly 5 years.

The investigators generated survival analyses for men with PSA velocities below 2 ng/mL and those with velocities equal to or greater than 2 ng/mL—a distinction that is literature driven, Dr. Cullen said.

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 statistically 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 associated with 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, 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." ■

Hydrogenated Vegetable Oil Intake Found Associated With Prostate Cancer Risk

Washington — High blood levels of a trans fatty acid found in partially hydrogenated vegetable oil were linked to an increased risk for nonaggressive prostate cancer in a review of data from the Physicians' Health Study, Dr. Jorge E. Chavarro reported at the annual meeting of the American Association for Cancer Research.

The association between prostate cancer and trans fatty acid type 18:2, which results from the hydrogenation of linoleic acid, was statistically significant but was limited to organ-confined tumors, noted Dr. Chavarro of Harvard University, Boston.

The investigators reviewed blood samples from more than 14,000 adults, and measured trans fatty acid levels in the blood of 479 men with prostate cancer and 491 age-matched controls. "We can't produce trans fatty acids, so measurements of tissue levels reflect our intake," he noted.

The risk of organ-confined prostate cancer was significantly greater among subjects in the highest quintile of type 18:2 trans fatty acid blood levels than among those in the lowest quintile.

In general, there were no differences in the median levels of other types of trans fatty acids between cases and controls, Dr. Chavarro said.

—Heidi Splete

Complexed PSA Tests Could Avert Needless Prostate Biopsies

BY JOHN R. BELL
Associate Editor

A prostate cancer–screening strategy using complexed prostate-specific antigen rather than total PSA would reduce the occurrence of needless biopsies without compromising sensitivity, according to a series of analyses that compared the detection accuracy of various cutoff values of the two biomarkers.

More accurate markers for detecting prostate cancer are needed, given that the current total PSA (tPSA) cutoff value of 4.0 ng/mL (the threshold at which prostate biopsy is recommended) misses the roughly 30% of cancers that occur in men with tPSA levels below that cutoff.

Dr. R. Joseph Babaian, of the University of Texas M.D. Anderson Cancer Center, Houston, and his coinvestigators compared biopsy findings with tPSA and complexed PSA (cPSA) in 467 men. Of that total, cancer was confirmed by biopsy in 147 (31.5%). Men with cancer had a mean age of 64 years, and those without cancer had a mean age of 62 years.

Using the Mann-Whitney U test, the investigators compared the number of men who had and did not have cancer in each tPSA and cPSA range.

They found that among men with tPSA scores in the broad range of 2.5-6.0 ng/mL, the cancer-detection rate was 31.5%. The cancer-detection rate was similarly 32.6% among men with cPSA values in the range of 2.2-5.1 ng/mL (J. Urol. 2006;175:897-901).

They concluded that among men with tPSA in the range of 2.5-6.0 ng/mL, determining biopsy decisions based on a cPSA cutoff value of 2.2 ng/mL—rather than a tPSA level of 2.5 ng/mL—would have eliminated 12% of needless biopsies but missed 2% of cancer cases. Using the same cPSA cutoff among men with tPSA of 2.5-4.0 ng/mL would have spared 20% of the patients unnecessary biopsies.

In a separate analysis involving 2,807 men who participated in a free cancer-detection program at M.D. Anderson, the investigators concluded that using a 2.2-ng/mL cutoff value for cPSA—rather than a tPSA cutoff of 2.5 ng/mL—would save roughly 3% of this population from undergoing unnecessary biopsies, or 32,000 biopsies per 1 million men.

Avoiding unnecessary biopsies would provide a significant money-saving opportunity for the health care industry. "The direct biopsy charges saved would be about $38 million per 1 million men undergoing a PSA test in the United States," the investigators wrote. They estimated that nationally, $190 million in direct, annual biopsy charges would be saved.

These study results confirm findings from previous investigations suggesting that cPSA might be a better initial diagnostic tool than tPSA, they wrote.

Their analyses, however, were limited by the fact that some participants came from referrals. A population-based study would, they said, provide stronger evidence of cPSA's superior accuracy.

In an editorial comment, Dr. J. Kellogg Parsons of the University of California, San Diego, wrote that "compared to tPSA, cPSA has increased specificity for prostate cancer detection at all clinically relevant sensitivities. Superior specificity decreases the number of false-positive results, which in turn potentially decreases unnecessary biopsies, health care expenditures, and patient anxiety."

The study was supported by Bayer Diagnostics. Dr. Babaian disclosed a financial interest and/or other relationship with Bayer and AstraZeneca. ■

Study Challenges Carotenoids' Role in Prostate Cancer Prevention

Washington — Contrary to previous findings, a high intake of lycopene and other carotenoids was not associated with a reduced risk of prostate cancer in a large case-control study, Ulrike Peters, Ph.D., said at the annual meeting of the American Association for Cancer Research.

To assess the association between the risk of prostate cancer and prediagnostic levels of serum carotenoids and serum retinol, Dr. Peters of the Fred Hutchinson Cancer Research Center in Seattle and her colleagues analyzed data from 692 cases of prostate cancer and 842 age-matched controls.

"Overall, there was no significant inverse association between carotenoids and prostate cancer risk," Dr. Peters said.

Previous research has shown a 10%-20% reduced risk of prostate cancer associated with a higher intake of lycopene and tomato products, but this study was not able to confirm such an association, Dr. Peters noted.

The study did show that high serum retinol levels were significantly associated with a reduced risk of advanced prostate cancer, but that association was not significant for prostate cancer overall.

The subjects were part of the multicenter Prostate, Lung, Colorectal, and Ovarian Cancer Screening trial, which included more than 150,000 adults aged 55-74 years. Levels of retinol and several carotenoids were measured in each subject when they entered the study. Prostate cancer cases were diagnosed during an 8-year follow-up.

Should physicians encourage their male patients to eat tomatoes? "I think the jury is still out about eating more tomatoes as a way to prevent prostate cancer," Dr. Peters said.

—Heidi Splete