Study Backs Active Surveillance for Prostate Ca

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BY SUSAN BIRK

CHICAGO — A strategy of active surveillance was associated with low prostate cancer mortality in a long-term study of 453 men with a favorable disease risk profile at baseline.

The study offers evidence for the use of active surveillance, based on changes in disease risk over time, as a means of addressing the significant problem of overdetection and overtreatment of prostate cancer in patients with indolent disease, said Dr. Laurence H. Klotz of the University of Toronto.

Dr. Klotz presented the results of the prospective, single-arm study in a poster at the annual meeting of the American Urological Association.

The AUA's recently updated best practice guidelines for prostate-specific antigen (PSA) testing strongly support informing patients that active surveillance is an option "in lieu of immediate treatment for certain men newly diagnosed with prostate cancer." (The guidelines are available at www.auanet.org; search for psa09.pdf. See also INTERNAL MEDICINE NEWS, May 15, 2009, p. 1.)

In the present study, patients (median age 70 years; range, 45-86 years) with a PSA level of 10 ng/mL or less and a Gleason score of 6 or less were managed with active surveillance (median follow-up 7.2 years; range, 1-13 years). The surveillance consisted of a PSA test every 3 months for 2 years and then every 6 months, a confirmatory biopsy at 1 year to rule out higher-grade disease that may have been missed on the initial biopsy, and a biopsy every 3-4 years thereafter.

Patients were reclassified as higher risk and offered more aggressive treatment if they had a PSA doubling time of less than 3 years, progression to a Gleason score of 4 + 3 or greater, or unequivocal clinical progression.

The study began in 1995. Initially, men over the age of 70 with a Gleason score of 3 + 4 or a PSA of 10-15 ng/mL were included, but starting in 2000, the researchers limited enrollment to patients with a favorable risk profile.

To date, overall survival among the cohort is 83%. Prostate cancer survival is 99%; five patients (1%) have died of prostate cancer.

Also, 35% of patients have been reclassified as higher risk and offered definitive therapy. The biochemical failure rate was 52% (15% of the overall cohort) among the 137 patients who underwent surgery or radiation.

Follow-up has been completed in 95% of participants, "so we know what has happened with almost all of the patients," Dr. Klotz said at a press briefing.

All five patients who died of prostate cancer progressed rapidly, were treated within 6-12 months of diagnosis, developed metastatic disease within 1 year of treatment, and died approximately 2 years later, Dr. Klotz noted. "It's safe to say, in looking back, that early treatment would have made no difference in these patients," he said.

The fact that roughly half of the treated patients had biochemical failure indicates that using PSA doubling time and repeat biopsies as active surveillance parameters identifies patients at higher risk of disease progression, Dr. Klotz said. "The ones who are treated do represent a fairly high-risk cohort, and we're going to need longer follow-up to see what happens to those patients."

Although about one-third of the patients eventually required definitive treatment, "roughly two-thirds remained untreated … and among these untreated patients, zero have gone on to metastatic disease or prostate cancer death," he said.

Dr. Klotz stressed the distinction between active surveillance and the more passive approach of watchful waiting, which he noted was a common practice in the United Kingdom and Scandinavia before the development of PSA testing. Scandinavia had the highest prostate cancer mortality in the world, presumably related to this policy, he said.

With active surveillance, "we actively monitor, we read biopsies, we try to get as accurate a sense of the extent of disease and the risk of progression as possible, and treat the subset that looks as if they are actually at higher risk," he said.

"It's all about risk assessment. … The moment we find a significant amount of Gleason 4 we say, 'This patient does not have the kind of indolent, very slow-growing disease we expected.' "

Funding for the study was provided by the Prostate Cancer Research Foundation of Canada. Dr. Klotz is a consultant for AstraZeneca and Sanofi-Aventis and has participated in research supported by GlaxoSmithKline. ■

Use of Statins Associated With Lower Prostate Cancer Risk

BY SUSAN BIRK

CHICAGO — Statins may have a protective effect against prostate cancer, according to recent study findings.

The research, presented at the annual meeting of the American Urological Association, adds weight to a growing body of evidence that statins may do more than help to lower cholesterol.

In an observational study of 2,447 men followed for 15 years, patients taking statins had one-third the risk of developing prostate cancer, compared with nonusers.

"We also found that the men who were taking statin medications the longest … had the greatest reduction in prostate cancer risk," Dr. Rodney H. Breau of the Mayo Clinic, Rochester, Minn., reported in a press briefing. The study analyzed prostate cancer risk in men aged 40-79 years, starting in 1990 using data from the Rochester Epidemiology Project.

Statin use was associated with a reduced likelihood of exceeding the prostate-specific antigen threshold for age and a reduced risk of prostate biopsy. In a randomly chosen subset of 618 patients who agreed to undergo PSA testing every other year, 11 (6.3%) statin users exceeded age-specific PSA thresholds, compared with 65 (14.7%) nonstatin users, for an age-adjusted hazard ratio of 0.35.

Among a group of 616 statin users, 75 (12.2%) underwent a prostate biopsy and 30 (4.9%) were diagnosed with prostate cancer. Age-adjusted hazard ratios for prostate biopsy and prostate cancer diagnosis were 0.39 and 0.38, respectively, compared with nonstatin users.

"We have to be very careful about looking at the data more closely to make sure we can't find some alternative explanation," Dr. Breau said. "Our data indicate you probably need to be on these medications for a prolonged period of time and possibly starting at the right age to prevent cancer from developing."

In another study presented at the meeting, there was a 30% reduction in the risk of a recurrence in PSA elevation following radical prostatectomy among statin users versus nonusers. "If these findings are confirmed in larger studies and/or randomized trials, it may be prudent to prescribe a statin to all men undergoing radical prostatectomy," said Dr. Robert J. Hamilton of the University of Toronto.

The researchers analyzed the Shared Equal Access Regional Cancer Hospital (SEARCH) database to assess the risk of biochemical recurrence in 1,325 men who had undergone radical prostatectomy. At the time of surgery, 237 (18%) of the men were taking statins.

Statin users were 2 years older than nonusers and had undergone surgery more recently (median year of surgery, 2004 vs. 2002). At the time of the diagnosis, statin users also had lower clinical stages of disease (67% vs. 58% with T1 disease) and with lower PSA levels (6.2 vs. 6.9 ng/mL).

After adjusting for differences between the two groups, statin use appeared to reduce the risk of biochemical recurrence by 30%.

A randomized, controlled trial is now needed, Dr. Hamilton said. He and his colleagues plan to analyze additional data on this group of patients to look at cholesterol levels, duration of statin use, and dose and statin use after surgery.

Findings from a third study presented at the meeting suggest a potential mechanism of action. The study of 254 men examined levels of prostate tumor inflammation in statin users vs. nonusers who were undergoing radical prostatectomy. A single pathologist graded tumors based on levels of white blood cells. Statin use was associated with a 72% reduction in the risk of tumor inflammation, reported Dr. Lionel L. Bañez of Duke University, Durham, N.C. Although statin users were significantly more likely than nonusers to be overweight or obese, statin use was associated with a lower risk for any tumor inflammation.

Dr. Breau, Dr. Hamilton, and Dr. Bañez had no financial disclosures related to their studies. ■

Statins Improve Male Urologic Health

New studies add weight to the possibility of a connection between statins and various aspects of male urologic health.

In addition to studies showing decreased risk of prostate cancer in men taking statins, a Mayo Clinic study using data on 2,447 men aged 40-79 from the Rochester Epidemiology Project revealed an inverse relationship between erectile dysfunction and statin use. A total of 729 (30%) of the men reported taking statin medications. Starting with the sixth year of follow-up and biennially thereafter, patients were asked questions from the Brief Male Sexual Function Inventory. The inverse association was strongest in the oldest men in the study, according to Dr. Ajay Nehra, of the urology department at Mayo. The association was strengthened after adjustment for age at baseline, diabetes, hypertension, coronary heart disease, smoking status, and weight.

In another Mayo Clinic study of the same cohort, statins were associated with a decreased risk of lower urinary tract symptoms and benign prostatic enlargement, as well as a decreased peak urinary flow rate. The combined use of statins and NSAIDs lowered these risks further, Dr. Jennifer L. St. Sauver, also of the Mayo Clinic, and her colleagues reported in a poster.

Dr. St. Sauver had no financial disclosures related to the study. Dr. Nehra is a consultant for Pfizer, GlaxoSmithKline, and Sanofi-Aventis.