Active Surveillance Does Not Raise Mortality in Elderly Men

BY BETSY BATES
Los Angeles Bureau

Vancouver, B.C. — Men live longer when a "watchful waiting" prostate cancer strategy is followed by treatment later in the course of the disease, compared with aggressive initial treatment, Dr. Li Li said at the annual meeting of the North American Primary Care Research Group.

Dr. Li and his associates from Case Western Reserve University, Cleveland, conducted a survival analysis using 1991-2001 Medicare–Surveillance, Epidemiology, and End Results (SEER) linked data, reviewing the disease course of 138,670 men diagnosed with prostate cancer. A follow-up analysis was performed in 2004. Survival was analyzed based on whether patients were followed by various cancer management strategies, including:

► Watchful waiting, in which patients received no initial treatment, but follow-up examinations after their diagnosis.

► Watchful waiting with delayed treatment, in which active hormone treatments were instituted during some follow-up point based on disease course.

► No treatment, in which patients did not receive any subsequent examinations or active treatments after the initial cancer diagnosis.

Overall survival and prostate-cancer specific survival rates were adjusted for age, ethnicity, comorbidity, screening, socioeconomic status, and cancer stage/grade.

Opting for no treatment or follow-up was associated with a "huge, almost fourfold increase in dying," even among men who were older than 80 years, in all likelihood because the strategy prevented identification and treatment of competing causes of mortality, said Dr. Li.

However, even prostate-specific survival was strongly adversely affected by a lack of treatment or follow-up in men of all ages.

Watchful waiting with no subsequent treatment led to nearly 25% higher overall mortality than did aggressive treatment for men who were younger than 80 years, with a hazard ratio of 1.24 (1.19-1.28), whereas the strategy did not significantly increase mortality over aggressive treatment in older men (hazard ratio 1.04 (0.99-1.09).

Watchful waiting followed by treatment if necessary conferred a survival benefit regardless of mens' ages at diagnosis, said Dr. Li during an oral presentation at the meeting.

Men followed by watchful waiting who did eventually receive treatment for prostate cancer had lower all-cause mortality than any other strategy: watchful waiting without treatment, hormone therapy only, or no treatment or follow-up.

In men under age 80, the relative risk for survival with this strategy was 0.88 (0.85-0.92); in men 80 and older, it was 0.72 (0.68-0.77), representing a 12% and 28% survival advantage, respectively.

When Dr. Li and his associates studied the 64% of men in the cohort who had low to intermediate risk prostate cancer, age became a factor as a strategic consideration.

In this group, watchful waiting without subsequent treatment led to slightly lower overall survival rates than did aggressive treatment in men over age 80, with a relative risk of 1.13 (1.06-1.22). The survival difference was greater for men aged 80 or younger, with a relative risk of 1.28 (1.22-1.33).

In both age groups of men at low to intermediate risk, watchful waiting followed by treatment led to higher survival rates than any other strategy. Prostate cancer-specific survival was highest in low to intermediate–risk men who were followed by watchful waiting without subsequent treatment.

Among the oldest men (over age 80) in this risk group, watchful waiting with delayed treatment prolonged disease-specific survival at about the same rates as aggressive treatment.

However, men under age 80 had diminished prostate-specific survival rates of nearly 40% when their treatment was delayed compared with initial aggressive treatment. ■

Statin Use Is Tied to Fewer Relapses in Prostate Cancer

BY JANE SALODOF MacNEIL
Senior Editor

Los Angeles — Men who were on statins when given radiotherapy for prostate cancer were significantly more likely to be disease free 10 years later, said researchers who reviewed 871 patients treated from 1994 to 2000 at a New York City cancer center.

Based on prostate-specific antigen levels, 76% of statin users, but only 66% of men who did not take the cholesterol-lowering drugs, were relapse free, Dr. Michael J. Zelefsky, lead author, reported at the annual meeting of the American Society for Therapeutic Radiation and Oncology.

The greatest benefit was seen in 221 men with high-risk disease, who were threefold more likely to have long-term biochemical control and to be free of distant metastases if they used statins.

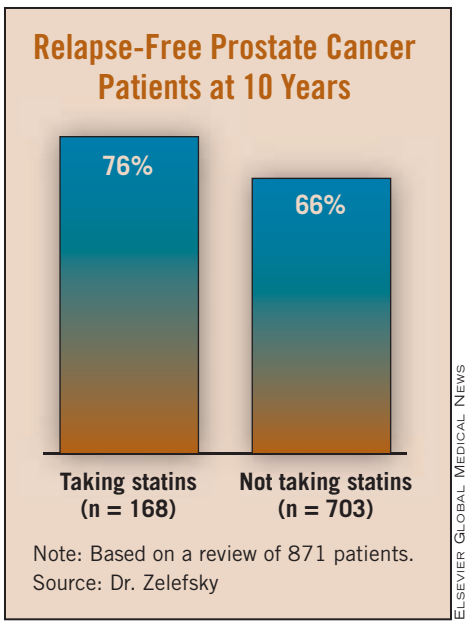
"These results … will have to be tested carefully," cautioned Dr. Zelefsky, a radiation oncologist at Memorial Sloan-Kettering Cancer Center, where the study was conducted. "We still don't know … the appropriate duration of taking these medications, or the appropriate dose, or which particular statin is more beneficial."

That statins can lower risk of heart disease is well established. Dr. Zelefsky said the team conducted the retrospective study because published studies had suggested statins also may have an apoptotic effect, may act as a radiation sensitizer, and may reduce cancer risk.

They selected patients with T1c-T3 prostate cancer who received high-dose radiotherapy, 75.6-86.4 Gy, at Memorial Sloan-Kettering during the study period. A records review determined that 168 men, 19%, used statins and 703 men, 81%, did not. The population had been followed for a median of 7 years. PSA relapse was defined as nadir +2.

Overall survival was not significantly different at 10 years, with 78% of the statin users and 71% of the nonusers still alive. All told, 72% of the entire population lived 10 years.

Introducing Dr. Zelefsky at a press briefing, Dr. Anthony Zietman, professor of radiation oncology at Harvard Medical School, Boston, said cancer treatment is "not just about the therapy and the cancer—it's about the environment. … We are treating the patients with whatever they are putting inside their body. By the time a man gets to 70 years of age, he is almost certainly taking at least one prescription medication. That prescription medication interacts with our therapy." ■



Brachytherapy Trumps Watchful Waiting in Local Prostate Ca

BY JANE SALODOF MacNEIL
Senior Editor

Los Angeles — A study of 11,453 men diagnosed with local prostate cancer from 1999 to 2001 found that brachytherapy reduced their relative risk of dying from the disease by 55%, compared with watchful waiting.

Radical prostatectomy was the best option and hormone therapy was the worst in the complex analysis reported by Dr. Esther H. Zhou at the annual meeting of the American Society for Therapeutic Radiology and Oncology. External beam radiation therapy also was better than watchful waiting (sometimes known as active surveillance), but the difference was not statistically significant.

"The results indicate brachytherapy is better than watchful waiting for the patient, even after we adjust for age, comorbidity, and…Gleason score," Dr. Zhou, an epidemiologist at Case Western Reserve University, Cleveland, told reporters at a press briefing. "We want to emphasize that brachytherapy is as good as radical prostatectomy and better than watchful waiting."

She described the study as the first large, population-based comparison of brachytherapy with watchful waiting, and said the researchers were surprised to find that brachytherapy produced a higher rate of disease-specific survival. The best choice among prostate cancer treatments is highly controversial, with options ranging from surgically removing the prostate to doing nothing while monitoring the slow-moving disease for signs of progression.

Brachytherapy involves small radioactive seeds that are placed into the prostate by a radiation oncologist. Unlike external beam radiation therapy, the procedure can be done in one visit. It also is less arduous and has a faster recovery than does radical prostatectomy, which is often reserved for patients who are relatively young and physically fit.

Dr. Zhou and her colleagues examined the records of newly diagnosed prostate cancer patients aged 65 years and older in the Ohio Cancer Incidence Surveillance System and linked them with Medicare and death certificate files. She said that the Ohio database is comparable to the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) registry. The investigators assigned patients who did not receive a curative therapy within 6 months of diagnosis to the watchful waiting category.

At 7 years, disease-specific survival—the percentage of patients who didn't die of the disease—was highest for radical prostatectomy (97.9%), followed closely by brachytherapy (96.6%) and external beam radiation (94.2%). Watchful waiting (89.8%) and androgen deprivation therapy (88.1%) were not as effective, according to Dr. Zhou.

When the investigators conducted a multivariate analysis taking into account age, disease stage, comorbidities, and Gleason score, they found that radical prostatectomy (hazard ratio 0.25) and brachytherapy (HR 0.45) were significantly better than watchful waiting, which was assigned a hazard ratio of 1. "For the same age of patient with the same Gleason score with the same stage, [those who receive brachytherapy] tend to have better survival" than do those treated with watchful waiting, Dr. Zhou said.

External beam radiation therapy also was better than watchful waiting (HR 0.66), she added, but the difference was not statistically significant. Again, androgen-deprivation therapy produced the worst results (HR 1.32), compared with watchful waiting.

Dr. Zhou noted, however, that the database did not include information on prostate-specific antigen levels, which would be a factor in the choice of treatment.

The investigators had no disclosures. ■