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 aggres-
sive initial treatment, Dr. Li Li said at the an-
nual meeting of the North American Primary Care Research Group.

Dr. Li and his associates from Case Western Reserve University, Cleveland, conducted a survivor 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 treated for local prostate cancer man-
gagement strategies, including:

- Watchful waiting, in which patients received no initial treatment, but follow-up examina-
tions after their diagnosis.
- Watchful waiting with delayed treatment, in which active hormone treatments were insti-
tuted during some follow-up point based on disease course.
- No treatment, in which patients did not re-
cieve any subsequent examinations or active treatments after the initial cancer diagnosis.

Overall survival and prostate-cancer specific sur-
vival rates were adjusted for age, ethnic-
ty, comorbidity, screening, socioeconomic sta-
tus, and cancer stage/grade.

Opting for no treatment or follow-up was as-
associated with a “huge, almost fourfold increase in dying,” even among men who were older than 80 years, in all likelihood because the strat-
egy 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 treat-
ment or follow-up in men of all ages.

Watchful waiting with no subsequent treat-
ment led to nearly 20% higher overall mortal-
ity than did aggressive treatment for men who were younger than 80 years, with a hazard ra-
tio of 1.24 (1.19-1.28), whereas the strategy did not significantly increase mortality over ag-
gressive treatment in older men (hazard ratio 1.04 (0.99-1.09).

Watchful waiting followed by treatment if nec-
necessary conferred a survival benefit regard-
less of men’s ages at diagnosis, said Dr. Li dur-
ing an oral presentation at the meeting.

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

In men under age 80, the relative risk of sur-
vival with this strategy was 0.88 (0.85-0.92); in men 80 and older, it was 0.72 (0.68-0.77), rep-
resenting 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 in-
termediate risk prostate cancer, age became a factor as a strategic consideration.

In this group, watchful waiting without sub-
sequent 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 inter-
mediate risk, watchful waiting followed by treat-
ment led to higher survival rates than any other strategy. Prostate cancer-specific sur-
vival 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 treat-
ment 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 this treatment was delayed compared with initial aggressive treatment.

Dr. Zhou and her colleagues examined the records of 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 re-
lapse 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 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 med-
ications, or the appropriate dose, or which particular statin is more beneficial.”

That strategy can lower risk of heart disease is well established.

Dr. Zelefsky said the team con-
ducted the retrospective study because published studies had suggested statins also may have an apopotic effect, may act as a radiation sensitizer, and may reduce cancer risk.

They selected patients with T1G3 prostate cancer who received high-dose radiothera-
py, 75.6-86.4 Gy, at Memorial Sloan-Kettering during the study period. A record 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 significa-
cantly 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, pro-

fessor of radiation oncology at Har-
vard 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 inter-
acts with our therapy.”

**Brachytherapy Trumps Watchful Waiting in Local Prostate Ca**

**By JANE SALODOF McNEIL**

**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 15%, 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 Ameri-
can Society for Therapeutic Radiology and Oncology. Ex-
ternal beam radiation therapy also was better than watch-
ful waiting (sometimes known as active surveillance), but other strategies were 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 epi-
demiologist at Case Western Reserve University, Cleve-
land, told reporters at a press briefing, “We want to em-
phasize 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 wait-
ing, 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 mon-
toring 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 anesthetic 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 to end linked to Medicaid death certificate files.

She said that the Ohio database is comparable to the Na-
tional Cancer Institute’s Surveillance, Epidemiology, and End Results (SEER) registry. The investigators assigned pa-
tients with Gleason score 7 or less to a watchful waiting category 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 rad-
ical prostatectomy (97.9%), followed closely by brachyther-
athy (96.6%) and external beam radiation (94.2%). Watch-
ful waiting (89.8%) and androgen deprivation therapy (88.1%) were not as effective, according to Dr. Zhou.

When the investigators conducted a multivariate analy-
sis taking into account age, disease stage, comorbidities, and Gleason score, they found that radical prostatecto-
my (hazard ratio 0.25) and brachytherapy (HR 0.45) were significantly better than watchful waiting, which was assigned a hazard ratio of 1.0. “For the same age of pa-
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tient with the same Gleason score with the same stage [those who receive brachytherapy] tend to have better sur-

ival” 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 depre-

tion therapy produced the worst results (HR 1.32), compared with watchful waiting.

It is noteworthy that the database did not in-
clude information on prostate-specific antigen levels, which would be a factor in the choice of treatment.

The investigators had no disclosures.