

## Quality of Life Significantly Decreased with Aggressive Treatment for Prostate Cancer

Hoffman RM, Barry MJ, Stanford JL, et al. Health outcomes in older men with localized prostate cancer: results from the Prostate Cancer Outcomes Study. *Am J Med* 2006;119:418–25.

### Study Overview

**Objective.** To compare differences in health-related quality of life outcomes and survival among elderly men with localized prostate cancer who were treated with aggressive versus conservative management.

**Design.** Population-based cohort study.

**Setting and participants.** Men aged 75 to 84 years from 1 of 6 sites of the National Cancer Institute’s Surveillance, Epidemiology, and End Results (SEER) program who were diagnosed with localized prostate cancer between 1994 and 1995.

**Main outcome measures.** General and disease-specific health-related quality of life (ie, urinary, bowel, and sexual function) as well as overall and disease-specific mortality.

**Main results.** Of 465 patients, 175 (37.7%) received aggressive therapy (either radical prostatectomy or radiotherapy), and the remaining 290 patients were managed conservatively (watchful waiting or hormone therapy). After 2-year follow-up, men who were treated aggressively were much more likely to report being bothered by urinary problems (odds ratio [OR], 5.1 [95% confidence interval {CI}, 1.3–19.1];  $P = 0.02$ ) and sexual problems (OR, 2.8 [95% CI, 1.2–6.3];  $P = 0.01$ ). Patients who received aggressive therapy were twice as likely to report bowel dysfunction (9.4% versus 4.4%),

but this difference was not statistically significant ( $P = 0.12$ ). Five-year survival rates were 82% in the aggressive treatment group and 63% in the conservative treatment group ( $P < 0.001$ ), and 5-year prostate cancer-specific survival was also better in the aggressive treatment group (98% versus 92%;  $P = 0.01$ ).

**Conclusion.** Aggressive treatment of prostate cancer among elderly men is associated with greater urinary and sexual dysfunction but is likely associated with a better disease-free survival. Treatment for men in this age-group must be tailored to the individual patient.

### Commentary

Prostate cancer is the most common non-skin cancer in American men and is a major cause of morbidity and mortality. Population-based estimates suggest that a majority of men who live into their seventh decade of life will be diagnosed with prostate cancer. Given the aging population, understanding how to manage this highly prevalent disease is critical.

In addition to having prostate cancer, many men aged 75 years and older have other comorbid conditions, such as coronary artery disease or other malignancies, raising the question of whether one should even treat prostate cancer in such patient settings [1]. One way to better understand the risks and benefits of different treatment strategies for

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prostate cancer is to determine if there is substantial harm to the patient from aggressive treatment with surgery or radiotherapy. Hoffman and colleagues provide compelling evidence that aggressive treatment for prostate cancer leads to substantially higher rates of urinary, sexual, and, most likely, bowel complications. One important aspect of these results is the magnitude of the effect: the differences in urinary complications, sexual dysfunction, and even bowel dysfunction between the aggressive therapy and conservative therapy groups were substantial. Men who received aggressive therapy were at two- to fourfold higher risk for developing these life-altering complications. These results also do not take into account the morbidity and discomfort from surgery (or radiotherapy), which are usually substantial in this age-group.

Hoffman et al also found lower rates of disease-specific and overall mortality among men treated aggressively. However, these findings must be interpreted with caution. Because this was not a randomized trial, physicians and patients together chose which treatment approach to use. Those given aggressive treatment were usually healthier with fewer comorbidities than those managed conservatively. Concerned about this potential selection bias, the authors used a propensity score, which attempted to adjust for differences between the 2 treatment groups. However, this technique is inadequate in adjusting for factors that might influence mortality but for which data are not collected. The degree to which this bias is important is obvious

from the results: among those who received conservative treatment, 8% died of prostate cancer over the subsequent 5 years (versus 2% in the aggressive group), while another 29% died of a cause other than prostate cancer (versus 16% in the aggressive group). Clearly, men who were treated conservatively were much sicker, thereby creating bias in the mortality results.

### **Applications for Clinical Practice**

Prostate cancer is a common disease among elderly men and its importance is likely to grow over time. Understanding the best management strategy for prostate cancer, especially in elderly men with comorbidities, is critical. Well-conducted randomized trials are needed to help address many of the clinical uncertainties. Until these studies are completed, observational studies can be helpful. Hoffman et al's study suggests that although there may be a small survival advantage in using aggressive therapy among men older than 75 years, there is substantial morbidity with such a treatment approach. Decisions about treatment in this age-group should include patient preferences and a realistic appreciation for the substantial harm that can come from aggressive treatment.

—Review by Ashish K. Jha, MD, MPH

### **Reference**

1. Johansson JE, Andren O, Andersson SO, et al. Natural history of early, localized prostate cancer. *JAMA* 2004;291:2713–9.

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