

## Delayed versus Immediate Prostatectomy: The Question of Cancer Curability

Warlick C, Trock BJ, Landis P, et al. Delayed versus immediate surgical intervention and prostate cancer outcome. *J Natl Cancer Inst* 2006;98:355-7.

### Study Overview

**Objective.** To compare cure rates among patients with small, low-grade prostate cancers who underwent delayed versus immediate prostatectomy.

**Design.** Retrospective cohort study.

**Setting and participants.** 320 men with small, low-grade prostate cancer were enrolled in a delayed management (surveillance) program from 1995 to 2005. These patients underwent semiannual prostate-specific antigen (PSA) measurements (total and free PSA), semiannual digital rectal examinations, and annual surveillance prostate biopsies. Surgery was performed if there was a Gleason score  $\geq 7$  with a Gleason pattern grade  $\geq 4$ , more than 2 cores positive for cancer,  $> 50\%$  of any 1 core involved with cancer, or if a patient requested a change in management. Outcomes in the delayed surgical intervention cohort were compared with outcomes in a cohort of patients selected from an institutional database of 2266 consecutive patients surgically treated for newly diagnosed prostate cancer between 1975 and 2004. Of 420 patients who would have been eligible for delayed management, 150 were randomly selected and matched by age, PSA levels, and number of positive cores.

**Main outcome measures.** Rates of noncurable cancer (defined as the percentage of patients per cohort with adverse pathology associated with  $< 75\%$  chance of disease-free survival at 10 years).

**Main results.** Outcome data for 38 patients in the surveillance group who underwent delayed prostatectomy were compared with data for 150 similar patients who underwent immediate prostatectomy. 9 patients in the surveillance group elected to have surgery before other predefined criteria were met. The surveillance group had a higher PSA density and lower percentage of core involvement. In the surveillance group, the median time to surgery after diagnosis was 26.5 months (95% confidence interval [CI], 17-32 mo) compared with 3 months (95% CI, 2-4 mo) in the immediate prostatectomy group. 23% of patients in the surveillance

group were considered noncurable compared with 16% in the immediate prostatectomy group ( $P = 0.27$ ). Adjustments made for age, PSA levels, and PSA density (PSA/prostate volume) did not change this comparison (relative risk, 1.08 [95% CI, 0.55-2.12];  $P = 0.819$ ). Additional adjustment for other potential confounding factors did not alter this estimate (data not provided by the authors).

**Conclusion.** Delayed prostate cancer surgery for patients with small, low-grade prostate cancers does not compromise curability.

### Commentary

Prostate cancer is the most common nonskin malignancy in men. More than 230,000 men are diagnosed per year, with over 30,000 prostate cancer deaths annually [1]. The incidence of prostate cancer has risen over the last decade due in large part to the increasing frequency of PSA testing.

The optimal approach to treating newly diagnosed prostate cancer can be variable and is currently a matter of debate due to the fact that, for many patients, prostate cancer is an indolent disease that can often take years to progress. Subjecting patients to surgery or radiation for disease that may ultimately not threaten their lives offers patients no benefit and considerable risks, including impotence, incontinence, and pain. Indeed, elderly patients may die from other comorbid conditions before prostate cancer progresses [2]. Observation, also known as watchful waiting, is considered a reasonable alternative for patients with low-risk disease who may still benefit from curative therapy in the future.

In this retrospective analysis, Warlick and colleagues

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studied a unique population of patients who chose a surveillance strategy where surgery was deferred nearly 2 years relative to a matched cohort of patients. Patients in the surveillance group experienced similar rates of adverse pathology as those patients who underwent immediate prostatectomy at diagnosis. However, this trial has many limitations, including its small size, retrospective and nonrandomized design, and questionable endpoints. The authors chose to compare surgical strategies by examining rates of adverse pathology discovered. However, it is possible that earlier intervention for these patients ultimately led to improvements in survival—an endpoint not followed in this study. Nonetheless, the authors should be congratulated for attempting to investigate an approach to care that is uncommon in the United States but may have merit for some patients with indolent disease who could be spared unnecessary morbidity.

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### **Applications for Clinical Practice**

Presently, watchful waiting is a reasonable option for older men who are diagnosed with low-risk prostate cancer and who have a reduced life expectancy due to comorbid health conditions.

*—Review by David R. Spiegel, MD*

### **References**

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2. Albertsen PC, Hanley JA, Barrows GH, et al. Prostate cancer and the Will Rogers phenomenon. J Natl Cancer Inst 2005;97:1248–53.

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