

LITERATURE REVIEW

Radical Prostatectomy Versus Watchful Waiting in Early Prostate Cancer

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Prostate cancer continues to be a significant factor in morbidity and mortality. Due to high prevalence (most common cancer in U.S. males) and mortality (second most common cause of cancer deaths in males), prostate cancer is one of the most crucial health problems in men.

The discussion of managing early prostate cancer is not only common, but also complicated. Treatment decisions involve scant survival data and quality of life issues such as impotence and urinary incontinence. Watchful waiting has also had to fight the paradigm of surgery curing cancer.

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STUDY DESIGN

The study¹ was designed to address the question of the management of early prostate cancer. Men were entered into 1 of 2 arms of the study; watchful waiting or radical prostatectomy. There were 695 patients enrolled by 14 centers in Scandinavia between 1989–1999. To be enrolled, the patients must have been less than 75 years old and surgical candidates. Additional criteria included:

- Previously untreated prostate cancer
- Tissue proven cancer
- “Early” prostate cancer; T1, T2
- World Health Organization (WHO) defined well or moderately well differentiated pathology
- Bone scan negative
- Prostate-specific antigen (PSA) <50

Symptomatic treatment of obstruction in the watchful waiting group included transurethral prostatectomy (TURP). Symptomatic local progression in the prostatectomy group

was treated with orchiectomy or gonadotropin—releasing hormone analogues. Treatment of disseminated disease was the same in both groups. Follow-up was scheduled at 6-month intervals, in which labs were also performed. Bone scan and chest x-rays were performed yearly.

STUDY RESULTS

There were 115 deaths during the follow-up period with 62 in the watchful waiting arm and 53 in the radical prostatectomy group. Of the deaths, 47 were attributed to prostate cancer. Of these, 31 were in the watchful waiting arm and 16 in the radical prostatectomy group. There were 37 deaths in the radical prostatectomy group due to ‘other causes’ and 23 in the watchful waiting arm.

In evaluating the cumulative rate of distant metastasis, there was no significant difference at 5 years (both under 10%). At 8 years there was an absolute decrease in the rate of de-

veloping distant metastasis by 14% in the prostatectomy arm (27% vs. 13%). The difference in the disease specific death rate was not significant at 5 years (4.6% for watching vs. 2.6% prostatectomy). At 8 years the difference, was 6% lower in the prostatectomy arm although still not statistically significant ($p = 0.02$). Overall survival was not significant at 5 years with 10.3% in the watchful waiting and 8.7% radical prostatectomy. At the 8-year interval, the overall mortality data was 28% deaths in the waiting group versus 22% in the radical prostatectomy group.

DISCUSSION

Headlines of "Surgery benefits patients" made all of the national news media, even though all-cause mortality was not statistically significant.

Some concern about this study may relate to the fact that it was designed before routine screening with PSAs. Of U.S. men who receive a diagnosis of prostate cancer, 75% have non-palpable tumor and undergo a biopsy because of an elevated PSA. This study is almost obsolete by design, as it was designed before the era of PSA screening. The increase in lead-time presumably gained by screening PSAs would conceivably show increased surgical benefits at a later time frame. A longer study design would be necessary to demonstrate this benefit.

The sheer number of prostate cancer patients and the implications of treatment recommendations seem to warrant a study with a large number of patients. This study had a relatively small number of patients for the disease studied. The radical prostatectomy will be performed 100,000 times this year in the United States. A study with 16 deaths in

the prostatectomy group appear to be statistically light.

The study used WHO tissue grades. When one examines Gleason scoring, some disconcerting data emerges. Thirty percent of the watchful waiting arm had Gleason scores of 7 or greater. This is hardly a group in which U.S. physicians would recommend watching. The radical prostatectomy group had 4% fewer patients in the Gleason 7 or greater category. Given that the disease specific death rate data was only 6% lower in the prostatectomy group, this difference in the Gleason scores could be very significant.

Would a longer follow-up time period show a more significant difference in the disease specific survival experience? Dr. Lars Holmberg, the lead author, was quoted in a news interview on CNN.com September 12, 2002. "We now have better evidence that radical prostatectomy diminishes your prostate cancer recurrence. And so now we have a possibility to alter the natural course of the disease by radical surgery." Unfortunately, the study does not address who would benefit the most or least from the surgery. A presumption that the younger the patient the more benefit over time; however, this is mere speculation.

The Veterans Administration has just finished enrolling patients in a more definitive study in the era of screening PSAs. Of course, the data will not be available for years. Until a large, randomized study is available, presumption and extrapolation of data will be the standard.

REFERENCE

1. Holmberg L, Bill-Axelsson A, Helgesen F, et al. A Randomized Trial Comparing Radical Prostatectomy With Watchful Waiting In Early Prostate Cancer. *NEJM*. 2002;347:781-789.