

Radical prostatectomy as treatment for prostate cancer

Michael A.S. Jewett, Neil Fleshner, Lawrence H. Klotz, Robert K. Nam, John Trachtenberg

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Prostate cancer is the most common cancer in men and, after lung cancer, the second most common cause of death.¹ Although the lifetime risk of being diagnosed with prostate cancer is 12.3%, the lifetime risk of dying of prostate cancer is only 3.8%. Prostate cancer is clearly different in this respect from most other cancers. Prostate cancer is frequently diagnosed in elderly men with competing causes of mortality and often grows very slowly.²

The natural history of prostate cancer makes treatment decisions difficult and complicates the design and interpretation of clinical trials. Young men and those with high-grade cancer have a high risk of dying of their disease.³⁻⁵ Conversely, most low-grade tumours in older men probably need only be observed. However, treatment strategies cannot be assumed to convey benefit and must be subjected to sophisticated clinical trials that take into account the variable risk profiles of patients.

Canadian physicians and their patients should be aware that the Scandinavian Prostatic Cancer Group has just reported a landmark randomized trial comparing radical prostatectomy and watchful waiting in early prostate cancer (see In the Literature page 67).^{6,7} Over 10 years, almost 700 men with newly diagnosed prostate cancer that was either clinically inapparent, confined to the prostate or diagnosed by needle biopsy performed because of an elevated prostate-specific antigen (PSA) level and whose tumours were graded as well or moderately well differentiated were randomly allocated to receive a radical prostatectomy or watchful waiting. After a median 6.2 years of follow-up, death due to prostate cancer occurred in 4.6% of those assigned to radical prostatectomy and in 8.9% of those assigned to watchful waiting (relative risk 0.50, 95% confidence interval 0.27-0.91). Death due to prostate cancer was halved by radical treatment. This is conclusive proof that treatment markedly reduces the risk of death due to prostate cancer. Men assigned to radical prostatectomy also had significantly lower relative risks of distant metastases than men assigned to watchful waiting. However, fewer men in the watchful waiting group died of other causes than men assigned to radical prostatectomy, so overall survival in the 2 groups was similar.

Strong differences of opinion exist regarding the merits of these treatment alternatives. Those who regard prostate cancer as a disease of advanced age argue forcibly for watchful waiting, particularly in those with low-grade disease,⁸ while at the same time acknowledging that young pa-

tients with high-risk disease (characterized by intermediate to high-grade cytology and clinical or pathologic evidence for substantial volume of disease) warrant intervention. Similarly, proponents of an aggressive approach to therapy recognize that prognostic factors can identify a population of men, particularly older men with histologically well-differentiated small-volume tumours, who may just be observed, particularly those with limited life expectancy. A critical appraisal of the literature will confirm that these 2 schools of thought are not far apart.

There are a number of intriguing features of the Scandinavian study. First, the difference in rates of death from prostate cancer between the group assigned to radical prostatectomy and the group assigned to watchful waiting increased over time despite the fact that in the intent-to-treat analysis 15% of the patients assigned to radical prostatectomy did not receive curative treatment. Second, although the time to the development of distant metastases was similar for the first 5 years of follow-up, it then increased rapidly for those on watchful waiting compared with those who underwent radical prostatectomy. By 8 years of follow-up, twice as many men on watchful waiting as compared with those assigned radical prostatectomy developed distant metastases. The usual interval between development of metastatic prostate cancer and death is about 5 years. Thus, it is probable that with longer follow-up of these 2 groups of men, this difference in frequency of metastasis will result in greater overall survival in the patients undergoing radical prostatectomy. At the time of analysis, 17 radical prostatectomies had to be performed to prevent one death due to prostate cancer, however, this ratio will likely fall with further follow-up.

But what about the adverse effects of radical prostatectomy? Erectile function and urinary continence are adversely affected by all curative treatment modalities. Improvements in surgical technique and radiation have reduced the frequency of these effects, but they still occur. Many surgeons were involved in the Scandinavian study, and undoubtedly different technical modifications were used. Nerve sparing was not particularly emphasized in this group of patients with more locally advanced disease than is currently diagnosed in Canada. A companion report to the clinical results of the Scandinavian trial addresses quality of life.⁹ Erectile dysfunction (80% v. 45%) and urinary leakage (49% v. 21%) were more common in the group assigned to radical prostatectomy, however, anxiety, depres-

sion, sense of well-being and subjective quality of life were similar in the 2 groups.

There are several caveats to the findings of this important trial. These patients were identified over a 10-year period dating from the earliest era of PSA detection. Eighty percent of the patients had prostatic nodules or other abnormal digital rectal findings. Currently, the proportion of patients presenting with a prostatic nodule is low; most patients present with an abnormal screening PSA level. At the Princess Margaret Hospital, Toronto, Ont., of 1350 patients who presented for a prostate biopsy between 1998 and 2000, only 24.1% had a prostatic nodule and only 5.4% had a prostatic nodule with a normal PSA level.

The most controversial issue remains the role for screening.¹⁰ Although earlier detection of prostate cancer with PSA screening results in the diagnosis of cancers that are more amenable to treatment by either radiotherapy or surgery, this has not yet been proven to result in a fall in mortality.

What may be true in more advanced cancers may not be so in the early stages. Many men are now diagnosed at a younger age. These men have more to lose from the side effects of treatment. Furthermore, how many of the men on watchful waiting suffered side effects of the supportive and hormonal treatment prescribed for disease progression? This would skew the quality-of-life data in favour of prostatectomy. In addition, this trial compared surgery with watchful waiting. It did not compare surgery with radiotherapy. We will have to await further trial results to determine what treatment is best for the individual patient. In many ways, this is a more difficult question, especially with the rapid improvements being made in the delivery of precision radiation and in less invasive prostatectomy using laparoscopy and robotics.

This trial is the first of a number of well-designed and implemented studies of screening and treatment of localized prostate cancer that will be reported over next decade. It represents the dawn of a new era of evidence-based medicine in prostate cancer management. We await the results of these trials with interest. Patients with newly diagnosed prostate cancer can now look forward to relatively easier treatment decision-making. Women have long enjoyed the benefits of the large clinical trials of treatment for breast cancer initiated 30 years ago. The role for the different treatment modalities is much better defined for them. This is one field that experiences a reverse gender bias.

From the Uro-Oncology Program, Division of Urology, University of Toronto (all authors); the Princess Margaret Hospital (Jewett, Fleshner, Trachtenberg); and the Sunnybrook and Women's College Health Sciences Centre (Klotz, Nam), Toronto, Ont.

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Correspondence to: Dr. Michael A.S. Jewett, Ontario Cancer Institute, The Princess Margaret Site, 920-610 University Ave., Toronto ON M5G 2M9; fax 416 340-4275; m.jewett@utoronto.ca

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