Acta Oncologica Vol. 30 No. 2 1991

FROM THE UROLOGIC-ONCOLOGIC GROUP, UNIVERSITY OF CHICAGO, CHICAGO, ILLINOIS, USA.

TREATMENT OF EARLY PROSTATIC CANCER

G. CHODAK

Abstract

The therapeutic management of early prostatic cancer is discussed with background of recent reports and trials. For an old patient with localized, well differentiated cancer deferred treatment can be the best alternative especially if he has significant cardiovascular disease. Advantages and disadvantages of the different local treatment methods (radical prostatectomy, external beam irradiation, interstitial irradiation) are discussed. The author concludes that present information does not permit any recommendations regarding the most effective treatment. The physician should carefully explain all the risks and benefits of each option and then help the patient decide which therapy he would be most willing to accept.

Key words: Prostatic cancer, early, localized, deferred therapy, radical prostatectomy, radiation therapy.

The management of early prostate cancer continues to be a controversial topic. Recommendations by physicians appear to be based more on personal bias and the country in which physicians practice than on data which justify any recommendation. Moore et al. (1) reported that 92% of Americal radiation oncologists but only 8% of American urologists would select radiation therapy if they had a localized cancer whereas 79% of American urologists but only 8% of American radiation oncologists would choose radical prostatectomy. This bias means that patients will encounter significant difficulty when they try to decide on the optimum therapy.

In the US, current philosophy is that localized prostate cancer can be cured either by radical prostatectomy or external beam radiation therapy. There is also agreement that the two treatments yield equivalent results at 10 years after treatment (2). This belief, however, is not based on any well conducted study. One randomized clinical trial has been performed in which aggressive treatment was compared to no treatment. The Veterans Administration cooperative study randomized patients with clinical stage A or B cancer to receive either radical prostatectomy plus placebo versus placebo alone (3). Although the study had several important problems, there was no significant difference in prostate cancer mortality between the two groups.

In regards to radiation treatment versus radical prostatectomy there also has been only one well-designed trial. Patients with negative pelvic lymph nodes and stage A2 or B cancer were randomized to either external beam irradiation or radical retropubic prostatectomy (4). At 5 years follow-up the surgery group had a significantly higher disease-free survival rate. Despite an appropriate design, however, several methologic problems invalidate the conclusions.

In the face of such uncertainty, how does a patient and physician make a decision regarding management? Any option is probably appropriate for some but not all patients with localized disease. The actual choice will be based on several factors including the patient's age and overall health, the grade and possibly the DNA content of the tumor, the patient's willingness to accept the side effects of treatment and his ability to accept uncertainty. Each of the management options will now be reviewed.

Deferred therapy, although unpopular in the US, may be quite appropriate for many patients. Johansson et al. (5) studied patients with localized prostate cancer who received delayed therapy and found that patients with a grade I cancer had only a 5% disease specific mortality at 10 years after diagnosis. This occurred in men who were both younger and older than age 70 at diagnosis (Personal communication). A patient with a localized well-differentiated tumor may require approximately 10 years to die from this disease if he does not receive aggressive treatment. Since the average life expectancy of a 75-year-old

Presented at the Conference on Early Prostatic Cancer. The WHO Collaborating Centre for Urological Tumours, Karolinska Hospital, Stockholm, March 21–23, 1990.

Accepted for publication 29 June 1990.

man is only 6 years, treatment may be unnecessary unless he has a longer than normal life span, since he is far more likely to die of another disease before suffering from the tumor. Similarly a patient with significant cardiovascular disease at age 70 may also not benefit from immediate treatment. In contrast, a 60-year-old otherwise healthy individual has a life expectancy of 17.5 years so he has far more to lose by not having aggressive treatment.

The obvious risks of observation are that the tumor may metastasize and lead to death whereas the benefit of observation is that the patient may be spared from the adverse affects of treatment. The ideal candidate for this management is a patient who 1) has a well differentiated, diploid tumor, 2) a life expectancy less than 15 years, 3) can cope with the risk of not receiving treatment, and 4) wants to avoid the potential adverse affects of treatment.

For those patients who are not appropriate candidate for observation, the choice of therapy may be quite difficult. Surgery is clearly the most aggressive therapy which offers a greater potential for cure. The reason is that approximately 30–50% of patients with clinically localized disease have pathologic stage C disease. Following radiation therapy for clinical stage C disease the 5-year survival is 58–72% and the local recurrence rate is 19–25% (6). In contrast, patients with pathologic stage C disease who receive postoperative radiotherapy have a 5-year survival rate of 73–94% and a local recurrence rate of 0–9% (7, 8). Thus, in patients who would like the maximum opportunity to control the disease, the best choice may be surgery followed by postoperative radiotherapy for selected cases because either surgery or radiation alone may not control the disease. Longer follow-up will be needed before more definitive data are available, however. Until then, the combination would seem appropriate for the motivated patient. Another advantage of surgery is that immediate information is obtained about the lymph node status and extent of tumor. If lymph node metastases are present, the patient probably derives little benefit from either surgery or radiation treatment. Thus, a patient who is irradiated without a lymph node dissection could receive an ineffective and unnecessary treatment along with its potential side effects. Another concern about irrradiation is the fact that complete eradication of disease may not occur. Several studies have found that patients with a positive biopsy 18–24 months after radiotherapy have a significantly higher risk of disease progression than a patient with a negative biopsy (9, 10). Furthermore, residual cancer may be found by ultrasound-guided biopsy in a high percentage of patients with a normal rectal examination following radiotherapy (11). Thus, the patient accepting radiation treatment must be willing to accept the probability that irradiation may not eradicate the disease which could lead to a local recurrence or distant metastases at a later date. Although salvage prostatectomy can be performed following radiotherapy, the complication rate is significantly higher than following immediate radical prostatectomy. Furthermore, a high percentage of patients will have extracapsular disease which cannot be removed by the operation.

To summarize then, the ideal candidate for radical prostatectomy is a patient who 1) has a moderate or poorly differentiated tumor, 2) has a life expectancy of at least 15 years, 3) wants the best chance for cure, 4) is willing to accept the risks of surgery, and 5) is willing to have postoperative radiotherapy, if necessary.

Over the past few years, several improvements in surgical technique have resulted in decreased blood loss, less incontinence and less impotence. In particular, potency may be spared in as many as 75% of patients who are less than age 70, have small tumors not adjacent to the pelvic nerves and have normal erections prior to surgery. These developments have resulted in increased enthusiasm for surgery by US urologists.

Improvements in technique have also resulted in reduced morbidity following radiotherapy. Radiation treatment clearly has a lower risk of death (approxiamtely 1% for surgery versus 0.07% for irradiation) and a lower risk of impotence. Thus, the ideal candidate for external beam radiotherapy 1) has a moderately differentiated tumor, 2) a life expectancy of 10 years, 3) wants to avoid the complications of surgery, and 4) can accept the uncertainty about the persistence of cancer.

The final option for therapy which has received increased attention in the US is interstitial irradiation. Previously, radioactive seeds were placed during an open surgical procedure which resulted in uneven seed distribution and variable dosimetry. Although this treatment was effective for very small tumors, larger tumors were not well controlled. The development of transrectal sonography now permits more even seed distribution without the need for surgery. Although the nodal status is not assessed, the procedure is easier and less costly. Also, newer radionuclides are being used which have theoretical advantages over ^{125}I. Unfortunately there are no data showing that interstitial irradiation using ultrasound guidance yields comparable results with radical prostatectomy or external radiation therapy for larger size tumors. Thus, patients need to be aware of the fact that this method could be less effective. The ideal candidate for interstitial irradiation 1) wants to receive some treatment, 2) has a survival of less than 10 years, 3) wants to maximize his chance for potency, 4) does not have a poorly differentiated tumor, and 5) understands that this treatment may not be as effective as the alternatives.

In summary, the information to date about treatment of localized prostate cancer does not permit any recommendations regarding the most effective therapy. Furthermore, physicians may be far too biased to select therapy for the patient. Therefore, the most appropriate role for the physician is to carefully explain all the risks and benefits of each

option and then help the patient decide which therapy he would be most willing to accept because the patient must live with the consequences of his choice. To avoid bias, perhaps all patients should consult with a radiotherapist and a urologist before selecting treatment.

Corresponding author: Dr Gerald Chodak, Urologic-Oncology Group, University of Chicago, P.O. Box 403, Chicago, IL 60637, USA.

REFERENCES

1. Moore MJ, O'Sullivan B, Tannock IF. How expert physicians would wish to be treated if they had genitourinary cancer: J Clin Oncol 1988; 6: 1736–45.
2. Grayhack JT. The management of clinically localized prostate cancer, National Institutes of Health Consensus Development Conference. J Urol 1988; 138: 1369–75.
3. Byar DP, Corle DK. Vacurg randomized trial of radical prostatectomy for stages I and II prostate cancer. Urology 1981; 17: 7–11.
4. Paulson DR. Randomized series of treatment with surgery versus radiation for prostate adenocarcinoma. J Urol 1979; 7: 127–31.
5. Johansson JE, et al. Natural history of localized prostatic cancer. Lancet 1989; 15: 799–803.
6. Hanks GE. The role of radiation therapy in the treatment of prostate cancer: Cancer of the prostate. Co Med Communicationos 1989.
7. Hanks GE, Dawson AK. The role of external beam radiation therapy after prostatectomy for prostate cancer. Cancer 1986; 58: 2406–10.
8. Gibbons RP, Cole BS, Richardson RG, et al. Adjuvant radiotherapy following radical prostatectomy. Results and complications. J Urol 1986; 135: 65–8.
9. Scardino PT, Wheeler TM. Prostatic biopsy after irradiation therapy for prostatic cancer: 1985; 25: 39–48.
10. Jacobi GH, Hohenfellner R. Staging, management, and post-treatment re-evaluation of prostate cancer: dogma questioned. In: Jacobi GH, Hohenfellner R, eds. Prostate cancer. Baltimore: Williams and Wilkins, 1982; 45–46: 212–4.
11. Kabalin JN, Hodge KK, McNeal JE, Freiga FS, Stamey TA. Identification of residual cancer in the prostate following radiation therapy. Role of transrectal ultrasound guided biopsy and prostate specific antigen: J Urol 1989; 142: 326–31.