Acta Oncologica Vol. 30 No. 2 1991

FROM THE DEPARTMENT OF UROLOGY, ÖREBRO MEDICAL CENTER, ÖREBRO, SWEDEN.

DEFERRED TREATMENT IN LOCALIZED PROSTATIC CANCER

J.-E. JOHANSSON and S.-O. ANDERSSON

Abstract

The natural history of early prostatic cancer has been evaluated in 223 patients with localized (T0-2, NX, M0), newly diagnosed, untreated prostatic cancer in a population-based study. No initial treatment was given and after an observation time of 66–150 months, 73 patients (33%) have progressed (25 with metastases) and 109 died but only 17 of prostatic cancer. Cumulative progression-free survival after 5 and 10 years was 73.1% and 64.3% respectively. Observed survival after 5 and 10 years was 67.3% and 44.1% respectively and the corresponding corrected survival 93.8% and 88.7%. Fifty-eight of the 223 patients filled the present criteria for radical prostatectomy. With only hormonal manipulation after symptomatic progression the corrected survival was very high, 98.0% after 5 years and 89.1% after 10 years among these 58 patients. As a result of this study a randomized trial comparing deferred treatment with radical prostatectomy in this group of patients has been started in Finland and Sweden.

Key words: Prostatic cancer, natural history, survival epidemiology.

The natural history of early prostatic cancer needs to be elucidated further. This knowledge is of crucial importance in choosing between observation alone, radical prostatectomy or curative radiation treatment as well as in deciding whether or not to introduce mass-screening for prostatic cancer.

In a population-based study, disease progression and survival were evaluated in untreated patients with newly diagnosed cancer of the prostate without distant metastases. From March 1977 to February 1984, totally 654 new consecutive cases of prostatic cancer were diagnosed from a well-defined catchment area. Two hundred and twenty-seven of these were localized (T0–2, NX, M0) and thus eligible for a study of the natural history in early stages. No initial treatment was given and complete follow-up was achieved in 223 (98%) patients. After 5 years the cumulative progression-free survival was 71.8% and survival corrected for causes of death other than prostatic cancer 93.8%. Univariate and multivariate analysis showed no association between age at diagnosis and the natural course. Local progression was less common in localized, non palpable tumours than in larger tumours. The rate of progression was 18.7 times higher and that of disease-specific death 216.0 times higher in patients with poorly than in those with well differentiated tumours. These results were obtained after an observation time of 36–120 months and were published in April 1989 (1).

The observation time is now 66–150 months and the results are in agreement with the earlier presentation. Seventy-three (33%) have progressed and 109 died but only 17 of prostatic cancer. The number of patients with progression and death according to T-stage and grade are shown in the Table. Twenty-five patients have progressed with a generalisation (M1) and 48 with only a local progression through the capsule (T3). Four of 72 patients in T0-local (= cancer in $<25\%$ of the total specimen) have died of prostatic cancer compared to 5 of 9 patients with grade 3 tumours.

Cumulative progression-free survival was 73.1% after 5 years and 64.3% after 10 years. Cumulative observed (OS) and corrected survival (CS) in the whole group of 223 patients by age at diagnosis are shown in Fig. 1. Of course age had pronounced effect on OS in this material of elderly men with a mean age of 72 years. OS after 5 and 10 years (with 95% confidence interval) was 67.3% (61.0–73.6) and 44.1% (35.9–52.3) respectively and the corresponding CS was 93.8% (90.2–97.4%) and 88.7% (83.2–94.1). There was no tendency for the CS to level off after 8–10 years after diagnosis. Tumour differentiation was strongly associated with CS (Fig. 2). Most patients with poorly differentiated tumours had rapidly fatal disease (5 years

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 17 September 1990.

Table

Study group of 223 patients with early prostatic cancer without initial treatment distributed by tumour stage and grade. Number of patients with progression and death after an observation time of 66–150 months

	n	Progression			Death	
		T3	M1	Total (%)	PC	Total
Tumour stage[1]						
T0 local	72	4	6	10 (14)	4	34
T0 diffuse	34	9	5	14 (41)	5	19
T1–2	117	35	14	49 (42)	8	56
Grade[2]						
1	148	21	10	31 (21)	5	72
2	66	26	10	36 (55)	7	29
3	9	1	5	6 (67)	5	8
Total	223	48	25	73 (33)	17	109

[1] T0 = clinically occult, incidental; T0 local = T0p T local (cancer < 25% of the total specimen); T0 diffuse = T0p T diffuse (cancer > 25% of the total specimen). T1–2 = confines to prostate gland; T1 = nodule surrounded by normal prostatic tissue; T2 = large nodule or multiple nodules.
[2] 1 = well, 2 = moderately, 3 = poorly differentiated.

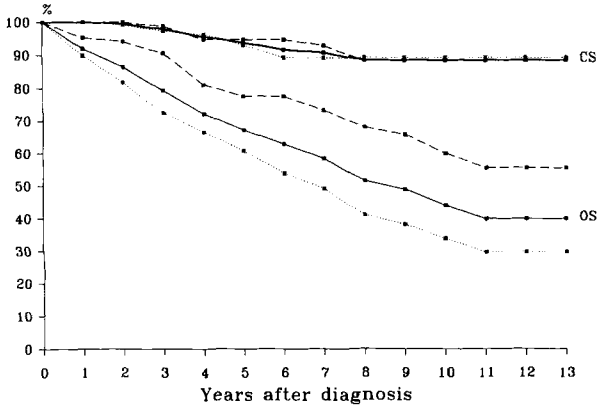

Fig. 1. Cumulative observed (OS) and corrected (CS) survival in whole group of 223 patients and by age at diagnosis. —— total; · · · >70 years; – – –<70 years.

CS = 28.5%). The rate of disease-specific death was also significantly higher in moderately compared to well differentiated tumours.

Fifty-eight of the 223 patients filled the present criteria for radical prostatectomy (i.e. under 70 years of age, T0 diff-T2, and with a well or moderately differentiated tumour) and were thus candidates for radical prostatectomy (Fig. 3). The nodal status among these patients was unknown. OS among these patients levelled off and was 77.6% after 5 years and 62.2% after 10 years. However, the CS was very high, 98.0% after 5 years and 89.1% after 10 years. The only therapy given to these patients was hormonal manipulation after symptomatic progression.

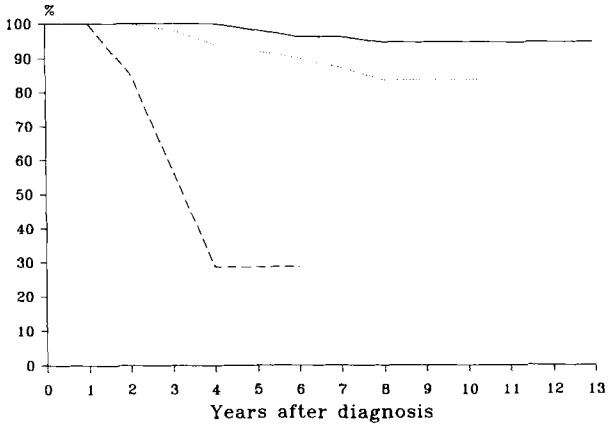

Fig. 2. Cumulative corrected survival by tumour grade. — G1; · · · G2; – – – G3.

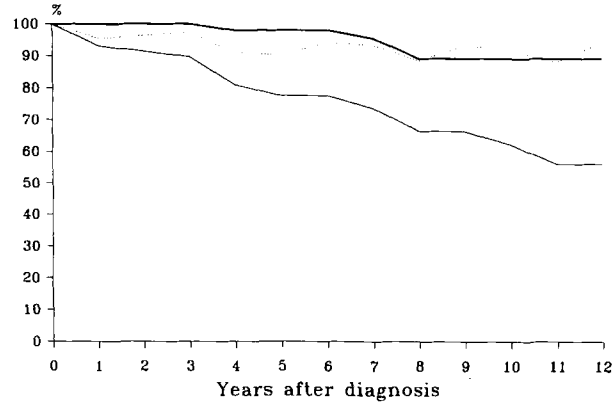

Fig. 3. Cumulative observed (OS—), corrected (CS—), and relative (RS · · ·) survival in 58 candidates for radical prostatectomy. (G1–2, T0 diffuse-T2, <70 years.)

The low death rate, especially in patients with well and moderately differentiated tumours, means that any local or systemic therapy intended for patients with early prostatic cancer must be evaluated in clinical trials with untreated controls for comparison. Two such studies have been started in the Nordic countries. In Denmark a randomized study comparing external irradiation versus observation in patients with confined prostatic cancer was started in February 1989. The Scandinavian Prostatic Cancer Group initiated another study comparing deferred treatment with lymph node dissection and radical prostatectomy in patients free from metastases in the lymph

nodes. This study was started in October 1989 in Sweden and patients will be recruited also from Finland.

ACKNOWLEDGEMENTS

This work was supported by grants from the Swedish Cancer Society and from Örebro County Council Research Committee. The study was started in co-operation with Dr Gunnar Lingårdh, assistant professor.

Corresponding author: Dr Jan-Erik Johansson, Department of Urology, Örebro Medical Center, S-701 85 Örebro, Sweden.

REFERENCES

1. Johansson J-E, Adami H-O, Andersson S-O, Bergström R, Krusemo U-B, Kratz W. Natural history of localized prostatic cancer. Lancet 1989; 1: 799–803.