Surveillance and Deferred Treatment for Localized Prostate Cancer. Population Based Study in the National Prostate Cancer Register of Sweden

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Purpose: To what extent active surveillance and deferred treatment for localized risk prostate cancer are used is unclear. We assessed the use of surveillance and of deferred treatment in a population based, nationwide cohort in Sweden.

Materials and Methods: In the National Prostate Cancer Register of Sweden, with a 98% coverage vs the compulsory Swedish Cancer Registry, we identified 8,304 incident cases of prostate cancer in 1997 to 2002 with age younger than 70 years, clinical local stage T1 or 2, N0 or Nx, M0 or Mx and serum prostate specific antigen less than 20 ng/ml. Data were extracted from medical charts for 7,782 of these men (94%) at a median of 4 years after diagnosis.

Results: Primary treatment was surveillance for 2,065 men (26%), radical prostatectomy for 3,722 (48%), radiotherapy for 1,632 (21%) and hormonal treatment for 363 (5%). Men on surveillance had lower local tumor stage, grade and prostate specific antigen, and were older than those who received active primary treatment ($p < 0.001$). After a median surveillance of 4 years 711 men (34%) on surveillance had received deferred treatment, which was radical prostatectomy for 279 (39%), radiotherapy for 212 (30%) and hormonal treatment for 220 (30%).

Conclusions: Surveillance was a common treatment for patients younger than 70 years with localized prostate cancer in Sweden in 1997 to 2002, 26% of men with localized prostate cancer started surveillance and after a median followup of 4 years, 66% of these men remained on surveillance.

Key Words: prostatic neoplasms, data collection, registries, therapeutics

Widespread testing of serum PSA has drastically increased the number of nonpalpable, well or moderately differentiated prostate cancers, ie T1c tumors with Gleason score 6 or less and small tumor volume in core biopsies.[1] As a consequence many men who undergo curative therapy today have a low risk of tumor progression and there is a growing concern of over treatment, in particular of elderly men.[2,3] Therefore, active surveillance as a treatment option for low risk prostate cancer has become increasingly attractive.[4,5] The aim of surveillance is to avoid side effects of active treatment by treating only men who experience disease progression during followup. However, relatively little is known to what extent surveillance is used and what proportion of men on surveillance subsequently receives deferred treatment. Some previous studies, notably 2 large register based studies in the United States[3,6] plus a number of modestly sized, mostly single institution series, have reported on the use of surveillance, and some have also reported the use of deferred treatment.[7–15] In this study we assessed the use of surveillance for localized prostate cancer and assessed the use of deferred treatment in a large, population based, nationwide cohort in Sweden.

MATERIALS AND METHODS

The Swedish Cancer Registry and the NPCR

In Sweden registration in the Cancer Registry of all cancer cases is mandatory, regulated by law, and the capture rate has been reported to be virtually complete at approximately 98% for solid tumors in patients younger than 75 years.[16,17] Currently 98% of all incident prostate cancer cases in the Cancer Registry are also registered in the NPCR which contains data on TNM stage, tumor differentiation, serum PSA at the date of diagnosis and primary treatment within 6 months from the date of diagnosis. Expectancy was one of the treatment options that could be actively indicated in the registration.[1,18] In NPCR clinical local tumor stage T2 is

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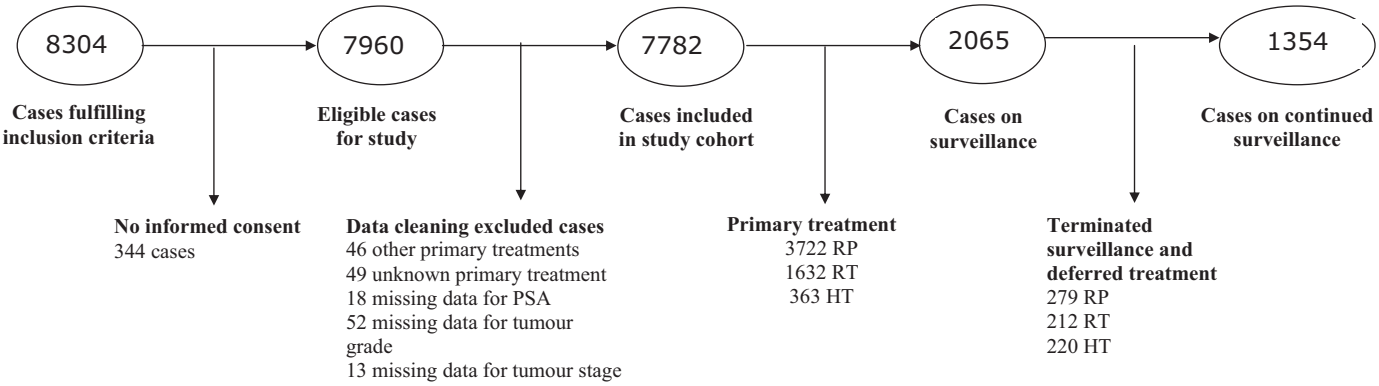

FIG. 1. Flow chart for primary treatment and deferred treatment in NPCR of Sweden in men younger than 70 years with clinical local stage T1 or T2 prostate cancer, no signs of metastatic disease (Nx or N0 and M0 or Mx) and serum PSA less than 20 ng/ml.

reported without any further subclassification into T2a, b or c. We identified all men with an incident prostate cancer diagnosis in NPCR between 1997 and 2002 in 5 of 6 regions in Sweden and in 1 region for men diagnosed between 1998 and 2002, who were 70 years or younger at diagnosis, with clinical local stage T1a, b, c or T2, without signs of lymph node metastasis (Nx or N0) or bone metastasis (Mx or M0) and with serum PSA 20 ng/ml or less. We defined low risk cases as stage T1a, b or c, with tumor differentiation Gleason score 2-6 or WHO I–II and serum PSA less than 10 ng/ml. Intermediate risk cases were defined as T2 tumors, or tumor differentiation of Gleason score 7, or PSA greater than 10 ng/ml. High risk tumors were defined as tumors with Gleason score 8-10 or WHO III, irrespective of PSA or local stage, ie T1a, b, c or T2.

Data Extraction in Followup Study

Data on observations made more than 6 months after the date of diagnosis of prostate cancer were extracted from medical records by cancer registry nurses under supervision by a urologist in each region. The retrospectively extracted data from the charts included date of last followup, date of termination of surveillance which was defined as the date of start of deferred treatment, reason for termination of surveillance and type of deferred treatment. As this was a retrospective observational study, followup and initiation of deferred treatment was made at the discretion of the physician and the patient, and there was no protocol for followup or criteria for termination of surveillance. The study was approved by the Research ethical committee of Gothenburg University and consent was obtained from all study subjects by the use of an opt-out protocol.

Statistical Methods

Chi-square tests were used to test for difference in distribution of surveillance vs active treatment and vs termination of surveillance according to tumor characteristics and age. A nonparametric test for trend across ordered groups was used

TABLE 1. *Primary treatment in the NPCR*

	Surveillance		RP		RT		HT*		All	
No. pts	2,065		3,722		1,632		363		7,782	
No. T stage (%):†										
T1a	337	(81)	57	(14)	17	(4)	3	(<1)	414	(100)
T1b	97	(49)	51	(25)	34	(17)	15	(8)	197	(100)
T1c	1,032	(27)	1,930	(51)	686	(18)	113	(3)	3,761	(100)
T2	599	(18)	1,684	(49)	895	(26)	232	(7)	3,410	(100)
No. Gleason score (%):†,‡										
2–6	1,444	(29)	2,424	(49)	925	(19)	131	(3)	4,924	(100)
7	100	(8)	716	(57)	343	(27)	104	(8)	1,263	(100)
8–10	19	(6)	150	(46)	110	(34)	48	(15)	327	(100)
Missing	502	(40)	432	(34)	254	(20)	80	(6)	1,268	(100)
No. WHO grade (%):										
I	375	(51)	218	(30)	111	(15)	26	(4)	730	(100)
II	110	(24)	177	(39)	123	(27)	41	(9)	451	(100)
III	17	(20)	37	(43)	20	(23)	13	(15)	87	(100)
No. ng/ml PSA (%):†										
0–4	429	(46)	367	(40)	117	(13)	17	(2)	930	(100)
4–10	1,066	(25)	2,217	(52)	869	(20)	150	(3)	4,302	(100)
10–20	570	(22)	1,138	(44)	646	(25)	196	(8)	2,550	(100)
Median ng/ml PSA (25–75 percentile)	6.7 (4.1–10.0)		7.5 (5.0–11.0)		8.8 (6.0–12.0)		10.0 (7.7–14.0)		7.8 (5.0–11.0)	
No. pt age (%):†										
Younger than 60	301	(15)	1,314	(66)	349	(17)	31	(2)	1,995	(100)
60–64	525	(23)	1,196	(53)	469	(21)	79	(3)	2,269	(100)
65–70	1,239	(35)	1,212	(34)	814	(23)	253	(7)	3,518	(100)
Mean pt age (SD)	64.7	(4.6)	61.4	(5.3)	63.5	(4.9)	65.8	(4.2)	62.9	(5.2)

* Included monotherapy with per oral antiandrogen blockade in 83 men, castration therapy in 212 and hormonal treatment not specified in 68.
† p_{diff} <0.001 between surveillance vs active primary treatment.
‡ Gleason score and WHO combined GS 2–6 + WHO I, II, GS 7, and GS 8–10 + WHO III.