

Late Side Effects Unchanged 4–8 Years after Radiotherapy for Prostate Carcinoma

A Comparison with Age-Matched Controls

Per Fransson, R.N.
Anders Widmark, M.D., Ph.D.

Department of Oncology, Umeå University, Umeå, Sweden.

BACKGROUND. The authors of this study previously evaluated pelvic irradiation-induced late side effects in patients with localized prostatic carcinoma 4 years after external irradiation by administering a validated self-assessment questionnaire (QUFW94), and compared the results with those of age-matched controls. The current study was designed to evaluate prospectively the patients' problems 8 years after radiotherapy and to compare them with those reported by the same controls.

METHODS. The questionnaire was sent out at a mean of 8 years (range, 72–104 months) after irradiation to 120 patients and 125 controls. For analysis of sexual function, the patient group was divided into two subgroups, one treated with radiotherapy only (RT) and one group treated with radiotherapy plus castration (RT+A). A value of >1 on a 0–10 scale indicated that the patient was having a problem.

RESULTS. The mean age was 73 years for both patients and controls. No changes in urinary problems were seen between the 4-year and the 8-year follow-up in the 2 groups. Sixty percent and 54% of the patients ($P = 0.096$) and 24% and 31% of the controls ($P = 0.988$) reported urinary problems at the 4-year and 8-year follow-ups, respectively. No changes in gastrointestinal late side effects in the patient group were seen between the 4-year (65%) and the 8-year (62%) follow-ups ($P = 0.490$). However, there was a decrease in intestinal problems in the control group between the 4-year (12%) and the 8-year (9%) follow-ups ($P = 0.001$). The sexual problems did not change during the two periods, in the patient groups or in the control groups. Fifty-six percent and 65% of the RT group ($P = 0.052$), 67% and 54% of the RT + A group ($P = 0.555$), and 27% and 33% of the control group ($P = 0.243$) indicated some kind of sexual problem at the 4-year and 8-year follow-ups, respectively.

CONCLUSIONS. The amount of pelvic irradiation-induced urinary late side effects, intestinal late side effects, and sexual function, evaluated with a self-assessment questionnaire, did not change between 4 and 8 years after RT. The age-matched controls reported no change in urinary or sexual problems despite advanced age, but there was a reported decrease in intestinal problems. *Cancer* 1999;85:678–88. © 1999 American Cancer Society.

KEYWORDS: prostate carcinoma, irradiation, complications, self-assessment, questionnaire, control group, sexual function.

During pelvic radiotherapy (RT) against prostate carcinoma (PC) administered by the conventional four-field box technique, many patients experience acute side effects that last several months. Late side effects are less common and mainly involve urinary and gastrointestinal problems. Only a small percentage of irradiated patients

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Address for reprints: Anders Widmark, M.D., Ph.D., Department of Oncology, Umeå University, S-901 85 Umeå, Sweden.

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TABLE 1
Patients and Controls Included in the Study at the 4-Year and 8-Year Follow-Ups

	Patients		Controls	
	Excluded	Included	Excluded	Included
4-yr follow-up study ^a				
Treated with radiotherapy for prostate carcinoma (1986–1989)		284		
Alive according to the Swedish population register (April 1, 1991) and treated with curative intention and a total dose >60 Gy	89	195		
Questionnaires sent out		195		200
Questionnaires completed	14	181	59	141
Total ^b	103	181	59	141
8-yr follow-up study				
Dead according to the Swedish population register (June 1, 1995)	61		16	
Death caused by prostate carcinoma	(40)		(1 ^c)	
Death caused by other disease	(21)		(15)	
Questionnaires sent out		120		125
Answer frequency	16	104 (87%)	26	99 (79%)
Total	77	104	42	99
Excluded from the 8-yr follow-up study because of:				
Disease progression between 4-yr and 8-yr and treatment with castration	18			
Death caused by prostate carcinoma within 6 mos after answering the questionnaire	3			
Diagnosed with cancer ^d between 4-yr and 8-yr			2	
Diagnosed with prostate carcinoma within 3 mos after the 8-yr follow-up			2	
Total ^e	21	83	4	95

^a *Cancer* 1996;78:1066–78.

^b Ten patients had another cancer beside their prostate carcinoma before the first questionnaire. Seven of the controls had cancer before the first questionnaire.

^c Prostate carcinoma was diagnosed after the first questionnaire (1991).

^d Cancer diagnoses: rectal carcinoma (n = 1), prostate carcinoma (n = 1).

^e One of the controls developed laryngeal carcinoma between the two questionnaires.

have serious side effects after conventional RT, such as small bladder or colostomy, but most of the studies have been based on physicians' estimations of major side effects.^{1–11}

External beam radiotherapy also influences sexual function in PC patients, and different studies report various frequencies of preserved potency (52–86%) in this patient group after conventional radiotherapy.^{12–18} With implantation/interstitial techniques, a somewhat higher percentage of potency is reported (85–93%).^{19–23}

Late urinary and intestinal side effects and sexual function were evaluated 4 years after external irradiation with a self-assessment questionnaire (QUFW94) and compared with an age-matched control population.^{24,25} To our knowledge, no study using a validated self-assessment questionnaire evaluation of side effects after RT for PC has been performed comparing late (4-year) and very late (8-year) side-effects. The current study was designed to evaluate urinary, intestinal, and sexual function more than 8 years after radiotherapy and to compare prospectively the changes between 4 and 8 years after treatment using

the same self-administrated questionnaire. Another aim was to compare the changes in urinary problems, intestinal problems, and sexual function in the treated PC patients with the same prospectively followed group of age-matched men (controls).

METHODS

Patient and Control Populations

Between 1986 and the middle of 1989, 284 patients received external radiotherapy to the pelvis with curative intent for localized PC. The treatment was given at the Department of Oncology, Radiotherapy Unit, University of Umeå, Umeå, Sweden. From the primary group of 284 patients, we excluded 89 patients who had died (according to the Swedish population register) at the date of the submission of the questionnaire, patients with distant metastases, and patients who received a total dose of less than 60 gray (Gy) (Table 1). The first self-assessed questionnaire (given at 4-year follow-up) was sent out between April 1991 (when it was sent to the patient group) and November 1991 (when it was sent to controls), giving a mean follow-up

time from the start of radiotherapy of 4 years (range, 24–56 months)^{24,25}

The current study is an 8-year prospective follow-up of the same patient and control groups. The second questionnaire was sent out in May 1995, resulting in a mean follow-up of 8 years from the start of radiotherapy (range 6–9 years). The patient group was also compared with an age-matched control group of men from the same region as the population of treated patients with PC (Table 1).^{24,25}

For analysis of sexual problems, the patient group was divided into two subgroups, one treated with radiotherapy only (RT) and one treated with radiotherapy plus castration (RT + A). Castration was performed by orchiectomy, estramustine phosphate administration, or gonadotropin-releasing hormone administration.

Treatment Technique

Computed tomography (CT)-planned radiotherapy was given with the conventional 4-field box technique, 5 days a week, 2 Gy per fraction, to an average total dose of 65.3 Gy. The total dose of treatment was based on a CRE value of 18.5 (mean, 18.29; range, 17.5–18.8). One hundred four patients were given a split course with a 2- to 3-week pause after the first 35 Gy had been administered. Large treatment volume was cranially extended to the sacral promontory, caudally to the ischial tuberosity, laterally to the medial walls of the pelvis, and ventrally to the symphysis. This setup gave an approximate anterior-posterior field size of 12 · 16 cm and lateral 10 · 16 cm.

Two treatment techniques were given: one with shrinkage field (Type A), and one in which a large treatment volume was given up to full dose (Type B).

Type A

For treatment of localized PC (mostly classified as T0diff–T2), large treatment volume receiving 50 Gy, thereafter a reduction only including prostate with 2 cm marginal. The shrinkage field size was 9 · 9 · 9 cm (anterior-posterior-lateral). This treatment was given to 115 patients, 63 of whom had a split course.

Type B

For treatment of locally advanced PC (mostly positive lymph nodes and/or T3, T4, and all Grade 3), including large treatment volume up to full dose. This treatment was given to 66 patients, 41 of whom had a split course after 35 Gy.

Questionnaire

The validated self-assessment questionnaire, QUFW94 (Table 2), was designed, in Swedish, to evaluate the

side effects after pelvic radiotherapy in patients treated for their PC (Fransson et al., unpublished data). The questionnaire was subdivided into four main categories:

1. General section, including questions about physical ability, life situation, marital status, bowel medicine, and eating habits;
2. Urinary problems;
3. Intestinal problems;
4. Sexual function.

The questions were simple and straightforward, covering the topics listed above. The questionnaire contained 38 questions with modified linear-analogue scales (L-A scales) containing values between 0 and 10; 0 = “no problem/very good” and 10 = “many problem/very bad.” Some questions gave only the choice of answering “yes” or “no.” The patients were encouraged to evaluate their symptoms and life situations during the previous week. Some questions requested only a written answer or comment (those questions are not summarized and reported in the current study). The same questionnaire was used in the 4- and 8 year follow-ups with a few modifications: boxes were used instead of marking on a line in the 8-year follow-up. The questions about existence (Question Number 2; q2), desire (q34), erection (q35), and life situation (q38) were inverted so that a value of 10 meant “many problems/very bad function” and 0 meant “no problems/very good function.” Some new questions were added: frequency of urination (q7 and q8, this was a split of the question about urination frequency during 24 hours, from the old questionnaire), pain while urinating (q9), nausea (q23), gases/bowel movements (q24), and erection quality (q36). Some questions were also excluded from the older version of the questionnaire: use of medicines other than bowel medicines, operations in the urinary tract, the ureter stoma, and one question about sexual life. These modifications of the questionnaire were performed after the validation of the questionnaire (Fransson et al., unpublished data).

Statistical Methods

The statistical analyses were performed by using the SPSS version 6.1.3 software package. To evaluate the differences between patient and control groups, the nonparametric Wilcoxon's rank sum test was used. Correlation coefficients were calculated according to Pearson and considered significant when $P < 0.05$. Boxplots represented the following: 25th percentile, median, and 75th percentile, and 50% of the values lay within the box. The largest and smallest values that were not outliers were also represented at the ends of

the boxes: Outliers indicated values more than 1.5 box-lengths from the 75th percentile, and extremes indicated values more than 3 box-lengths from the 75th percentile.

Permission to perform the study was given from both the Ethical Board at the Umea University of Sweden and the National Computer Inspection Board in Sweden.

RESULTS

Patients and Controls

Sixty-one of 181 patients (34%) and 16 of 141 of the controls (11%) died between the 4-year and 8-year follow-up (Table 1). The questionnaire answer frequency was 87% ($n = 104$ of 120 patients) in the patient group and 79% ($n = 99$ of 125 controls) in the age-matched control group (Table 1). As seen in Table 1, 18 patients with progressive disease were treated with castration between the two questionnaires and were excluded from the study. Three patients died of their PC within 6 months after completion of the second questionnaire (December 1995), and were therefore excluded from the current study. Four controls were excluded because a new cancer was diagnosed between the two follow-up periods. With these exclusion criteria observed, 83 patients and 95 controls were included in the current analysis (Table 1).

The tumor characteristics at the time of diagnosis of the 83 patients who were included in the 8-year follow-up study were as follows: T0 = 9, T1 = 8, T2 = 44, T3 = 21, and T4 = 1.

The mean age of both patients and controls at the time the 8-yr follow-up questionnaire was answered was 73 years (range, 55-85 years). The mean age of those in the two groups who did not answer at the 8-year follow-up questionnaire was higher (77 years; difference not significant, ns).

General Part

The patients' "life situation in general" did not improve significantly between the 4-year (mean = 4.6) and 8-year (mean = 3.4) follow-ups after radiotherapy (the lower the value, the better the life situation on a scale ranging from 0 to 10). The reported life situation for the controls improved significantly, from 4.9 to 2.1, during the follow-up period ($P < 0.000$). The limitations of the daily activity because of the patients' PC did not change significantly between the two follow-up periods (mean values, 2.4 at the 4-year and 2.5 at the 8-year; $P = 0.9383$). Forty-three percent and 46% of the patients reported "no" limitations (0-1 on scale) at the 4-year and 8-year follow-ups, respectively.

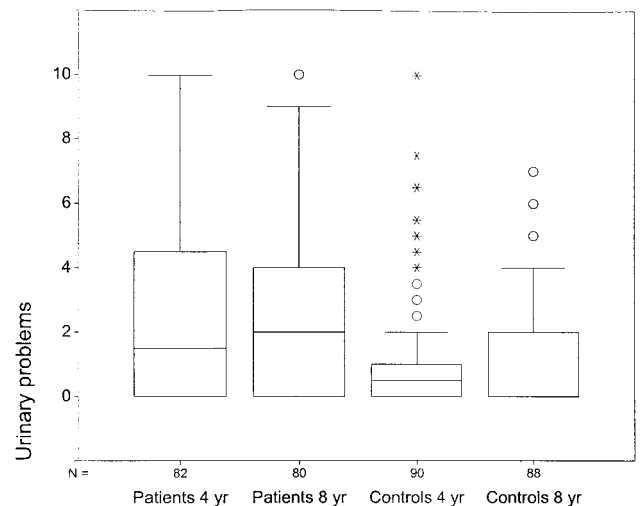


FIGURE 1. Answers to the question "Do you have urinary problems?" from patient and control groups at 4 years (4 yr) and 8 years (8 yr) after radiotherapy are given. Boxplots indicate 25th percentile, median, 75th percentile, outliers (○: values more than 1.5 box-lengths from the 75th percentile) and extremes (*: values more than 3 box-lengths from the 75th percentile).

Urinary Problems

No increase in late side effects were seen between the 4-year and 8-year follow-up periods regarding urinary problems in general in the patient group ($P = 0.096$) and in the control group ($P = 0.988$; Fig. 1). Sixty percent and 54% of the patients and 24%/31% of the controls reported urinary problems in general (>1 on scale) at the 4-year and 8-year follow-ups, respectively. The urinary frequency during 24 hours decreased significantly in both the patient group (mean = 6.9/5.6 at 4-year/8-year; $P = 0.000$) and the control group (mean = 6.2/5.1; $P = 0.000$; Table 3). In the patient group, the most frequently reported urinary problem both at the 4-year and 8-year follow-ups was urgency (46%/42%; >1 on scale). Starting problems ($P = 0.017$) and hematuria ($P = 0.001$) decreased in the patient group between the two follow-ups (Table 3).

In the control group, starting problems were the most frequently reported problem at both the 4-year and the 8-year follow-up (20%/23%; >1 on scale). Hematuria ($P < 0.000$) and urinary problems that interfered with daily activities ($P = 0.004$) decreased in the controls between the 2 follow-up periods (Table 3).

In the patient group, high correlations were seen between urinary problems in general and both urgency ($r = 0.684$, $P = 0.000$) and interference with daily activity ($r = 0.697$, $P = 0.000$) at the 4-year follow-up. Also, interference with daily activity had a

TABLE 3
Patient and Control Groups Reported Mean and *P* Values to the Questions about Urinary Problems at the 4-Year and 8-Year Follow-Ups

Problem	Patients			Controls		
	4-yr mean ^a	<i>P</i>	8-yr mean ^a	4-yr mean ^a	<i>P</i>	8-yr mean ^a
Urinary frequency (in 24 hrs)	6.9	0.000	5.6	6.2	0.000	5.1
Incontinence	1.4	0.624	1.6	0.4	0.530	0.5
Pain	^b	^b	0.8	^b	^b	0.1
Starting problems	2.0	0.017	1.3	0.8	0.646	0.9
Urgency	2.1	0.098	1.7	0.7	0.704	0.7
Interference with daily activity	1.5	0.669	1.7	0.4	0.004	0.3
Hematuria	0.7	0.001	0.3	0.2	0.000	0.0

^a Mean values on a 0–10 scale in which 0 = “No problem” and 10 = “Many problems,” except for the question about frequency, for which values refer to the mean urinary frequency in 24 hrs.

^b This question was not included in the 4-yr follow-up questionnaire.

high correlation with urgency ($r = 0.756$, $P = 0.000$) at that time. At the 8-year follow-up, high correlations were seen between the patients' urinary problems in general and both incontinence ($r = 0.699$, $P = 0.000$) and interference with daily activity ($r = 0.742$, $P = 0.000$). Urgency had a lower correlation with interference with daily activity ($r = 0.550$, $P = 0.000$) compared with the 4-year follow-up.

The strongest correlations in the control group at the 4-year follow-up were seen between urinary problems in general and both urgency ($r = 0.464$, $P = 0.000$) and interference with daily activity ($r = 0.564$, $P = 0.000$). At the 8-year follow-up in the control group, the highest correlations were seen between urinary problems in general and both interference with daily activity ($r = 0.523$, $P = 0.000$) and starting problems ($r = 0.425$, $P = 0.000$). Incontinence had the highest correlation with interference with daily activity ($r = 0.421$, $P = 0.000$) at the 8-year follow-up.

Intestinal Problems

In the patient group, no increase in late side effects were seen between the 4-year and 8-year follow-up periods regarding intestinal problems in general ($P = 0.490$; Fig. 2). However, the control group reported a decrease ($P = 0.001$) regarding intestinal problems in general between the two follow-ups (Fig. 2). Sixty-five%/62% of the patient group and 12%/9% of the control group reported gastrointestinal problems in general (>1 on scale) 4-year/8-years after treatment, respectively. The mean number of the daily stools decreased (ns) between the 4-year/8-year follow-ups in patient (mean = 2.9/2.7), and control (mean = 1.5/1.4) groups, respectively (Table 4). No significant changes were seen in the patient group between the 4-year and

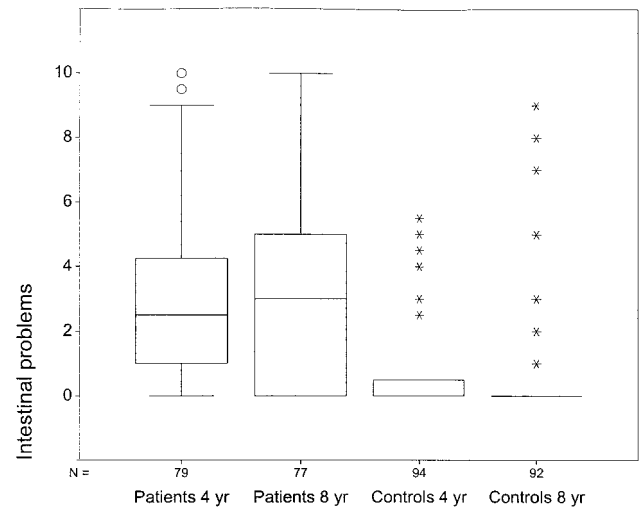


FIGURE 2. Answers to the question “Do you have intestinal problems?” from patient and control groups 4 years (4 yr) and 8 years (8 yr) after radiotherapy are given. Boxplots indicate 25th percentile, median, 75th percentile, outliers (○: values more than 1.5 box-lengths from the 75th percentile), and extremes (*: values more than 3 box-lengths from the 75th percentile).

8-year follow-ups regarding other questions about bowel function (Table 4).

Bowel movements were the most frequently reported intestinal problem (>1 on the scale) at the 8-year follow-up both in the patient (61%) and control groups (26%). That question was not included in the 4-year follow-up questionnaire. However, in the control group there were significant decreases (improvements) in all questions about bowel function between the 4-year and 8-year follow-ups (Table 4).

In the patient group, intestinal problems in

TABLE 4
Patient and Control Groups Reported Mean and *P* Values to the Questions about Intestinal Problems at the 4-Year and 8-Year Follow-Ups

Problem	Patients			Controls		
	4-yr mean ^a	<i>P</i>	8-yr mean ^a	4-yr mean ^a	<i>P</i>	8-yr mean ^a
No. of daily stools	2.9	0.062	2.7	1.5	0.075	1.4
Interference with daily activity	2.2	0.986	2.2	0.2	0.000	0.0
Intestinal blood	1.7	0.104	1.3	0.2	0.000	0.1
Leakage	1.5	0.886	1.6	0.3	0.000	0.1
Bowel movements (gases)	b	b	2.7	b	b	0.9
Nausea	b	b	1.2	b	b	0.2
Mucus	1.9	0.079	1.6	0.3	0.000	0.2
Cramp	1.3	0.055	0.8	0.3	0.000	0.1
Planning	2.0	0.374	2.4	0.3	0.000	0.0

^a Mean values on a 0-10 scale in which 0 = "No problem" and 10 = "Many problems," except on the question about frequency, for which the values refer to the mean stool frequency in 24 hours.

^b This question was not included in the 4-yr follow-up questionnaire.

general correlated mostly highly to leakage ($r = 0.520, P = 0.000 / r = 0.530, P = 0.000$) at both the 4-year and the 8-year follow-ups. Planning of toilet visits had the highest correlation with interference with daily activity ($r = 0.759, P = 0.000 / r = 0.882, P = 0.000$) at both the 4-year and the 8-year follow-ups.

In the control group, intestinal problems in general correlated most highly with cramping ($r = 0.578, P = 0.000$), whereas mucus correlated most highly with the interference of daily activity ($r = 0.733, P = 0.000$) at the 4-year follow-up. In the 8-year follow-up of the controls, leakage was the problem with the highest correlation to the question about intestinal problems in general ($r = 0.471, P = 0.000$). However, leakage also showed the highest correlation to interference with the daily activity ($r = 0.705, P = 0.000$) at the 8-year follow-up.

Sexual Function

On the question about sexual problems in general, 56%/65% of the RT group, 67%/54% of the RT + A group, and 27%/33% of the controls indicated problems (>1 on the scale) at the 4-year and 8-year follow-ups, respectively. There was an increase (ns) in the median score value in sexual problems for patients treated with radiotherapy only (RT) when the 4-year (median = 4.3) and 8-year (median = 7.0) follow-ups were compared ($P = 0.052$; Fig. 3). However, a decrease (ns) in sexual problems were seen in the RT + A ($P = 0.555$) and control groups ($P = 0.243$) when 4-year and 8-year were compared after treatment (Fig. 3).

Thirty-seven percent/36% in the RT group and 76%/70% in the RT + A group reported lack of sexual

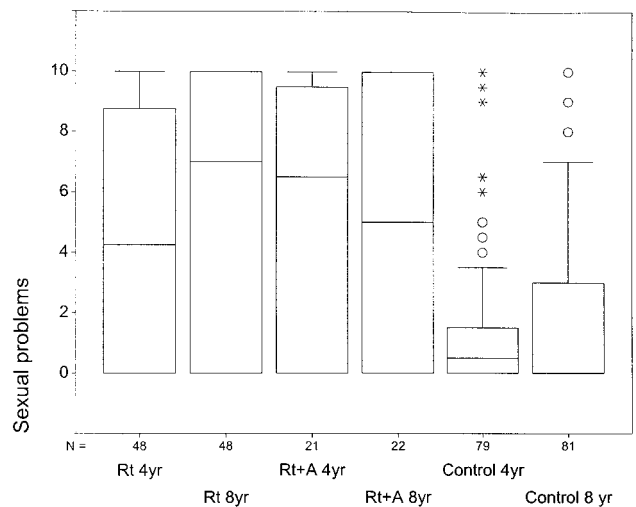


FIGURE 3. Answers to the question "Do you have sexual problems?" from controls and patients treated with radiotherapy (RT) and radiotherapy plus castration (RT + A) 4 years (4 yr) and 8 years (8 yr) after radiotherapy are given. Boxplots indicate 25th percentile, median, 75th percentile, outliers (○: values more than 1.5 box-lengths from the 75th percentile), and extremes (*: values more than 3 box-lengths from the 75th percentile).

desire (≥ 9 on scale) compared with 17%/16% in the control group at the 4-year/8-year follow-ups, respectively. However, none of these changes between the two follow-ups were significant (Table 5).

Fifty-seven percent/65% of the RT group, 84%/89% of the RT + A group, and 15%/19% of the controls reported lack of erection (≥ 9 on scale) at the 4-year/8-year follow-ups. The reported decrease of erection

TABLE 5
Patient and Control Groups Reported Mean and *P* Values to the Questions about Sexual Function at the 4-Year and 8-Year Follow-Ups

Problem	RT			RT + A			Controls		
	4-yr mean	<i>P</i>	8-yr mean	4-yr mean	<i>P</i>	8-yr mean	4-yr mean	<i>P</i>	8-yr mean
Sexual problems in general	4.4	0.052	5.7	5.6	0.555	4.4	1.5	0.243	2.0
Desire	6.9	0.426	6.1	8.2	0.241	8.2	5.9	0.069	5.2
Erection	7.7	0.161	7.8	9.2	0.149	9.2	5.7	0.092	4.8

RT: patients treated with radiotherapy only; RT + A: patients treated with radiotherapy plus castration.

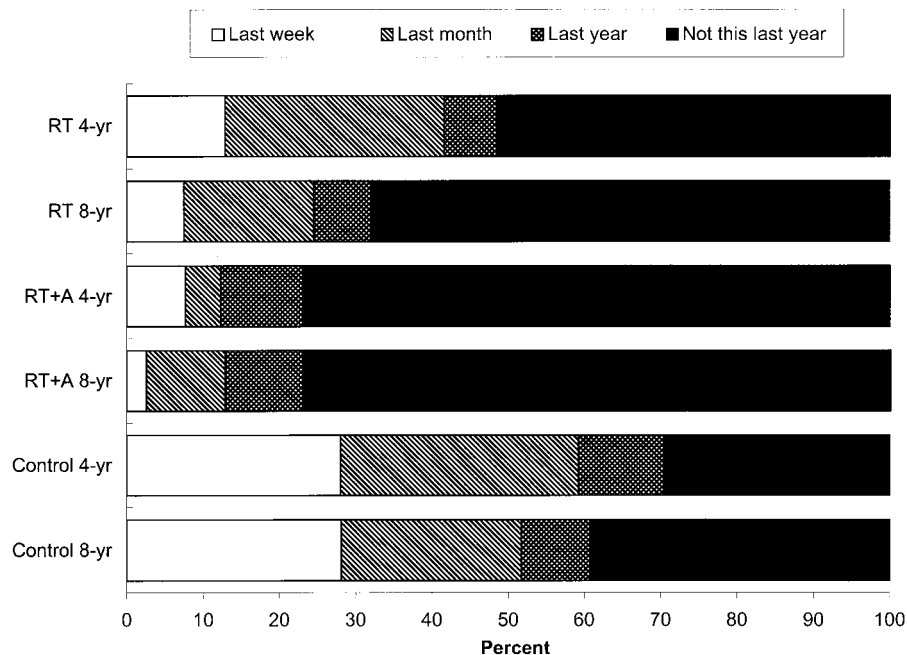


FIGURE 4. Relative frequency of intercourse or fondling, reported in answer to the question "Have you had sexual intercourse or fondling this last week, last month, last year, or not during the last year?" by controls, patients treated with radiotherapy (RT), and patients treated with radiotherapy plus castration (RT + A) 4 years (4 yr) and 8 years (8 yr), is cited.

function between the two periods was not significant in any of the three groups (Table 5).

The "intercourse or sexual fondling" activity decreased in the RT patients between the two follow-ups ($P = 0.005$), whereas there was no change in the RT + A group ($P = 0.236$; Fig. 4). During the previous month, 42%/25% of the RT patients and 12%/13% of the RT + A patients reported sexual activity at the 4-year/8-year follow-ups, respectively (Fig. 4). The RT patients who reported no sexual activity "this last year" increased from 52% to 68% between the 4-year and 8-year follow-ups ($P = 0.0051$).

The control group reported decreased sexual activity between the two periods ($P = 0.040$), whereas 59%/55% reported sexual activity during the last month at the 4-year and 8-year follow-ups, respectively (Fig. 4).

No correlations were seen regarding sexual function in either 4-year or the 8-year follow-up periods.

DISCUSSION

The results of the current study show that evaluation of urinary, intestinal, and sexual function 4 years after RT (Fransson et al., unpublished data, and^{24,25}) effectively predicts symptoms that will be present 8 years after RT. No obvious changes in symptoms or side effects could be detected. However, there was a trend toward increased sexual problems in the RT group. It is difficult to compare various definitions and results of side effects from previous definitions according to different scales, i.e., the criteria of the Radiation Therapy Oncology Group (RTOG).²⁶⁻³¹ Despite the fact that the same validated and sensitive questionnaire (Fransson et al., unpublished data) was used at both

follow-ups in the current study, we could not see any significant changes during the two investigations. To our knowledge, a longitudinal study of this type has not previously been performed. The previously reported difference in the age-matched control population is repeated with longer follow-up, because the same controls were prospectively followed for 4 more years.

The answer frequency was very high in both groups, despite the increased age. However, there was a trend in both groups (ns) that the men of the most advanced age did not answer the questionnaire.

Urinary Problems

Because we strictly defined problems as >1 on the 0–10 scale, there was a fairly high percentage (60%) of patients who had experienced mild (>1 on scale) urinary tract problems 4 years after radiotherapy. Those problems did not change during the follow-up period. If the cutoff of having a problem had been set at ≥ 2.5 on the scale, the percentage of patients reporting problems would have been 45%/34% at the 4-year/8-year follow-ups, respectively. These proportions of patients having mild or more pronounced problems correspond well with other reported results of late side effects.^{3,28}

Within the patient group at the 4-year follow-up, urgency showed the strongest correlation to urinary problems in general, whereas incontinence appeared to be the symptom that was most strongly correlated with the experience of urinary problems in general at the 8-year follow-up. This might be explained either by a real decrease in urgency or an adaptation to this problem, whereas the leakage problem increased and is more difficult to adapt to. However, incontinence and urgency correlated most strongly to the influence on daily activity at both the 4-year and the 8-year follow-up periods. This is probably explained by the pain that occurred with urgency and by the patients' feeling that their daily activities were being disturbed.

Questions about incontinence, and urgency seem to pinpoint accurately patients who experience urinary problems in general and for whom their daily activities were affected. They seem to be very important symptoms to consider in evaluating side effects after pelvic radiotherapy against PC.

Intestinal Problems

Problems in the intestinal tract were the most commonly reported problem in the patient group (62% reported >1 on scale). In contrast, the control group had very few problems with their intestines (less than 9%, >1 on scale). No significant change was seen in the patient group between the two follow-ups. How-

ever, in the control group a marked decrease in intestinal problems was detected: the numbers of controls reporting "no" problems (0 on scale) were 49%/86% at the 4-year/8-year follow-ups.

Intestinal problems were carefully recorded in the RTOG trials (75-07, 77-06)¹⁰ in which some kind of problem was reported for more than 50% of the patients (Grades 1–5). Our data from a self-administered questionnaire detected a similar frequency of problems.^{24,25}

Pilepich et al.³ reported an increased incidence of problems during the second and third year. Our study showed that intestinal problems seemed to have stabilized at 4 years and 8 years. According to classical irradiation damage, late effects are believed to be slowly progressive, but this could not be verified in the current study.

In comparison with an age-matched control population, the patient group undoubtedly had more problems. This difference was more pronounced regarding intestinal problems, probably because men at this age normally have some urinary problems. Furthermore, with the conventional four-field box technique used at that time, a large part of the intestine, the whole rectum, and the bladder received at least 50 Gy, and many patients received >65 Gy to the whole rectum.

This shows that even small problems could be detected in consultation with a physician if the right questions were asked systematically. Other studies have detected a lower frequency of small (minor or mild) problems, approximately 10–20%.^{4,5,32} However, these minor problems are probably of less importance for the patients' daily activity, and over the long term patients have to adapt to symptoms. The current study showed that with our questionnaire (QUFW94 and a newer version), we could still detect symptoms 8 years after RT against localized PC.

Sexual Function

Patients treated with RT only showed a trend toward a progressive decrease in sexual function between 4 and 8 years. A combination of radiotherapy-induced effects on nerves, seminal vesicles, and age may explain the decreased function. However, no decrease could be seen in the age-matched control population, which more or less seemed to maintain sexual function despite an increase in the mean age from 69 to 73 years. The RT + A group had already lost most of their sexual function at 4 years after treatment, so no further decrease could be detected. This was in agreement with a recently published Swedish study on sexual activity in elderly men.³³

CONCLUSIONS

The amount of pelvic irradiation-induced late urinary, intestinal, and sexual function side effects, evaluated with a self-assessment questionnaire, did not change between 4 and 8 years. However, a trend toward a progressive decrease in sexual function was found in the patients treated with radiotherapy only (RT) between the 4-year and 8-year follow-ups. Our results indicate key questions that should be asked in the future. The age-matched controls showed similar values of no increasing urinary and intestinal problems despite more advanced age, but also no progressive decrease in sexual function between the 4-year and 8-year follow-ups. These results showed that evaluation of radiotherapy-induced urinary and intestinal side effects as well as sexual function with a validated self-assessment questionnaire (QUFW94) 4 years after treatment predicted the level of very late side effects.

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