

ORIGINAL ARTICLE

Partnership status affects the association between gastrointestinal symptoms and quality of life after radiation therapy for prostate cancer

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Abstract

Purpose. To study if partnership modifies the effect of gastrointestinal symptoms on quality of life after radiation therapy for prostate cancer. **Material and methods.** Using a study-specific questionnaire we conducted a cross-sectional follow-up of the occurrence gastrointestinal symptoms and quality of life after radiation therapy for prostate cancer. We obtained information from 874 prostate cancer survivors treated with radiation therapy at the Sahlgrenska University Hospital, Sweden between 1994 and 2006. In this paper we describe how partnership status affects the association between gastrointestinal symptoms and quality of life. **Results.** We found that unpartnered men with gastrointestinal symptoms reported a lower quality of life than unpartnered men without such symptoms. Unpartnered men with symptoms had an excess risk of low quality of life compared with unpartnered men without symptoms for those experiencing altered composition of stools, prevalence ratio 3.8 (95% CI 1.1–13.1), leakage, 3.6 (1.3–10.1), sensory bowel symptoms, 4.5 (1.6–12.8), and for urgency, 4.2 (1.2–15.1). We also found that unpartnered men with symptoms had an excess risk of low quality of life compared with partnered men with symptoms for those experiencing altered composition of stools, prevalence ratio 2.9 (95% CI 1.4–5.8), leakage 2.8 (1.2–6.4), sensory bowel symptoms 3.4 (1.5–7.4), urgency 2.6 (1.2–5.8), and for any gastrointestinal symptom 2.5 (1.3–4.9). **Conclusion.** Unpartnered men may represent a group that is specifically vulnerable to the distressful effects of gastrointestinal symptoms after radiation therapy for prostate cancer.

Pelvic radiation therapy increases overall survival in men with advanced localized prostate cancer [1]. However, for some prostate cancer survivors cure comes at a cost: radiation-induced gastrointestinal symptoms [2]. Fifty percent of prostate cancer survivors treated with radiation therapy report that such gastrointestinal symptoms affect quality of life and for 20–40% this effect is moderate to severe [3].

Lack of support can reduce quality of life for men diagnosed with prostate cancer [4,5]. Unpartnered men are less content with their life and report a poorer psychological and overall well-being compared with partnered men when facing a prostate

cancer diagnosis [4–7]. However, it is not known if unpartnered men are more vulnerable to the late side effects after prostate cancer treatment.

In a cross-sectional follow-up in 2008, we sent a study-specific questionnaire to all men who received radiation therapy for prostate cancer at the Sahlgrenska University Hospital, Gothenburg, Sweden, between 1994 and 2006. The questionnaire assessed gastrointestinal symptoms and quality of life after radiation therapy for prostate cancer. In this paper we report the results on partnership status as an effect-modifier for the association between gastrointestinal symptoms (exposure) and quality of life (outcome).

Material and methods

Study population

In 2008, using information from the Swedish Total Population Register and computerized hospital medical records, we identified 985 living prostate cancer survivors consecutively treated with radiation therapy between 1994 and 2006 at the Sahlgrenska University Hospital, Gothenburg, Sweden. Eligible men were 80 years old or younger, had no diagnosed distant metastases, and were resident in Sweden at the time of follow-up. The Regional Ethical Review Board in Gothenburg approved the project.

Radiation therapy

External beam radiation therapy was based on computerized tomography with the patient in supine position. The planning target volume consisted of the prostate or the post-operative prostatic region with 20 mm margin except for the rectal margin, which was 15 mm or, at most, half the cross-sectional rectal area. The patient was treated using a conformal three-field technique with one anterior and two lateral wedged fields with 11 or 15 MV photon energy. Brachytherapy was planned and delivered under the guidance of transrectal ultrasound with the patient in lithotomy position. The dose distribution was optimized to cover the prostate plus 2 mm margin with the prescribed dose while keeping the absorbed dose to the anterior rectal wall below a 6 Gy per fraction.

The questionnaire

The study-specific questionnaire was in Swedish and has been described in detail elsewhere [2]. It was designed to survey patient-reported symptoms after radiation therapy for prostate cancer, several of which have not been reported previously. It was developed according to the well-founded method established at the Division of Clinical Cancer Epidemiology at the University of Gothenburg in Göteborg and the Karolinska Institutet in Stockholm, Sweden, documented in more than 100 published articles [7–11]. Briefly, we started out by making structural assessments of four previously validated questionnaires from other projects at our division concerning pelvic symptoms after radiation therapy and/or surgery for prostate cancer [9–12]. From these, we conceptualized clear-cut atomized definitions of relevant symptoms, which we used to construct single-item questions in the questionnaire. In addition, we conducted four semi-structured interviews with irradiated prostate cancer survivors to certify that we did not miss any common symptoms. Face-validity

was assured by having 15 men (10 prostate cancer survivors) complete the questionnaire separately with one investigator (DA) present. During and after this procedure, the investigator discussed the questionnaire with each man noting any issues regarding confusion, misinterpretation, negative apprehension or lack of understandability of specific questions. After each completed questionnaire the investigator edited all questions that were misinterpreted or not directly understood. We repeated this procedure until no further changes were suggested. We also consulted external experts in clinical radiation oncology and urology to review the questionnaire. Finally, we conducted an unpublished preparatory study including 30 prostate cancer survivors to test for logistics and participation rate. Omerov et al. give a thorough description of a similar process from our division for a questionnaire concerning suicide-bereaved parents in Sweden [13].

Data collection

We sent out the questionnaire between February and November 2008. It included 165 questions on pelvic symptoms, demographic data, co-morbid diseases, other treatments, quality of life, and physical health. In the questionnaire responders assessed 34 questions that specifically reflected the occurrence of gastrointestinal symptoms the previous six months. Responders also assessed one question reflecting quality of life the previous six months on a visual digital scale ranging from 0 to 6, where 0 meant “worst possible” and 6 meant “best possible”. Responders reported their current civil status by stating if they were “Married or cohabiting”, “Living alone, without a partner”, or “Living alone but having a partner (live-apart)”.

Statistical analyses

All calculations were done in SAS 9.2 for Windows (SAS Institute Inc., Cary, NC, USA) and Stata/IC 11.2 for Mac (StataCorp., College Station, TX, USA). We evaluated differences in the characteristics of the study population at follow-up using a non-parametric Kruskal-Wallis test for age and time to follow-up and a χ^2 -test for the remaining variables. We dichotomized outcome variables to get a balance between clinical relevance and background noise (sporadic symptom occurrence) and to reduce the risk of recall bias by reporting more frequently occurring symptoms [8–12]. We considered 0–2 on the visual digital scale as indicating a low quality of life.

We assigned each of the 34 symptom questions to one out of six categories, based on common

Table I. Categories of gastrointestinal symptoms*.

Symptom category	Designated symptoms with cut-off levels
Altered composition	<ul style="list-style-type: none"> • Black blood in stools, <i>at least once a week</i> • Distended bowel because of excess gas, <i>at least once a week</i> • Frequent loose stools, diarrhea, <i>at least once a week</i> • Hard stools, constipation, <i>at least once a week</i> • Mucus in stools, <i>at least once a week</i> • Red blood in stools, <i>at least once a week</i>
Flatulence	<ul style="list-style-type: none"> • Uncontrolled passing of gas, <i>at least once a week</i>.
Leakage	<ul style="list-style-type: none"> • Fecal leakage while awake, <i>at least once a month</i> • Fecal leakage while asleep, <i>at least once a month</i> • Fecal leakage while coughing, laughing or sneezing, <i>at least once a month</i> • Fecal leakage during physical exercise, <i>at least once a month</i> • Leakage of mucus while awake, <i>at least once a week</i> • Leakage of mucus while asleep, <i>at least once a week</i> • Leakage of red blood while awake, <i>at least once a week</i> • Leakage of red blood while asleep, <i>at least once a week</i> • Unexpected total emptying of all stools into clothing, <i>at least once the previous six months</i>
Pain	<ul style="list-style-type: none"> • Abdominal pain, <i>at least once a week</i> • Abdominal cramps, <i>at least once a week</i>
Sensory	<ul style="list-style-type: none"> • Sensation of incomplete evacuation, <i>at least half of the occasions</i> • Sensation of passing gas but in effect passing feces, <i>at least once a week</i>
Urgency	<ul style="list-style-type: none"> • Defecation urgency prompting the immediate need to visit a toilet, <i>at least once a week</i>
Any gastrointestinal symptom	<ul style="list-style-type: none"> • Any of the above mentioned symptoms

*In the questionnaire, responders were asked to assess symptom occurrence the previous six months.

features of clinical presentation (Table I). For each symptom category we divided the responders into the following four groups based on symptom occurrence and stratified for partnership status as an effect modifier: A) symptom/unpartnered, B) no symptom/unpartnered, C) symptom/partnered, and D) no symptom/partnered. To estimate differences between these four groups (A–D) we used a log-binomial model (GENMOD procedure in SAS 9.2 for Windows) to calculate the prevalence ratio of low quality of life. We also calculated the prevalence ratios of gastrointestinal symptoms between partnered and unpartnered men to assure that the combined symptom/partner groups (A–D) were not subjected to bias due to differences in symptom occurrence. We also included the possible confounders' age, comorbid diseases (cardiovascular disease, diabetes, heart failure, neurological disease, psychiatric disease, pulmonary disease, and rheumatic disease), educational level, radiation modality, smoking, and time to follow-up in a multivariable log-binomial model to produce adjusted prevalence ratios. We considered a confidence interval not including 1.0 or a p-value of 0.05 or less as indicating statistical significance.

Results

Altogether 874 (89%) of the 985 eligible prostate cancer survivors returned a filled in questionnaire. We found a significant difference between the four

groups (A–D) for age ($p = 0.009$), comorbid diseases ($p = 0.05$), radiation modality ($p = 0.02$), smoking ($p = 0.022$) and widowers (< 0.001) (Table II). We found no difference in the prevalence of gastrointestinal symptoms among unpartnered men compared with partnered men (Table III).

The men in group A (symptom/unpartnered) reported a lower quality of life compared with the men in group B (no symptom/unpartnered) for the symptom categories: altered composition of stools, prevalence ratio 3.8 (95% CI 1.1–13.1), leakage 3.6 (1.3–10.1), sensory bowel symptoms 4.5 (1.6–12.8), and for urgency 4.2 (1.2–15.1) (Table IV). However, for any gastrointestinal symptom the difference was not statistically significant.

The men in group A (symptom/unpartnered) reported a lower quality of life compared with the men in group C (symptom/partnered) for the symptoms categories: altered composition of stools, prevalence ratio 2.9, (95% CI 1.4–5.8), leakage, 2.8, (1.2–6.4), sensory bowel symptoms, 3.4, (1.5–7.4), and urgency, 2.6, (1.2–5.8). For any gastrointestinal symptom, 14% of the men in group A reported a low quality of life compared with 6% of the men in group C prevalence ratio 2.5, (95% CI 1.3–4.9). For the groups as a whole, more men in group A (14%) reported a low quality of life compared with the men in group B (8%), group C (6%), and group D (1.4%) (Figure 1). Adjusting for the possible confounders age, comorbid disease, educational level, radiation modality, smoking, and time to follow-up,

Table II. Characteristics of the study-population.

	Group A: Symptom/ unpartnered n = 73	Group B: No symptom/ unpartnered n = 27	Group C: Symptom/ partnered n = 496	Group D: No symptom/ partnered n = 263	P-value
Age in years , mean (range)	70.7 (59–80)	73.0 (62–80)	71.3 (53–80)	70.0 (49–80)	0.009
Time to follow-up in years , median (range)	5.8 (2–12)	6.6 (2–14)	6.1 (2–15)	5.8 (2–14)	0.44
Radiation modality , No. (%)					0.02
EBRT	25/73 (34)	10/27 (37)	187/496 (38)	74/263 (28)	
EBRT-BT	34/73 (47)	16/27 (59)	201/496 (41)	115/263 (44)	
Postoperative EBRT	14/73 (19)	1/27 (4)	108/496 (22)	74/263 (28)	
Educational level , No./total No. (%)					0.24
Primary school	28/73 (38)	16/27 (59)	200/493 (41)	104/263 (40)	
High school	23/73 (32)	4/27 (15)	119/493 (24)	54/263 (21)	
College or post-graduate	22/73 (30)	7/27 (26)	174/493 (35)	105/263 (40)	
Widower , No./total No. (%)	21/73 (29)	9/25 (36)	17/475 (4)	9/251 (4)	< 0.0001
Comorbid diseases , No./total No. (%)					0.05
Yes	44/73 (76)	24/27 (62)	285/453 (63)	153/263 (53)	
Smoking , No./total No. (%)					0.022
Yes	13/70 (19)	3/27 (11)	47/487 (10)	17/262 (6)	

BT, brachytherapy; EBRT, external beam radiotherapy; No., number.

in a multivariate analysis did not change the results substantially (Supplementary material Table I, available online at <http://informahealthcare.com/doi/abs/10.3109/0284186X.2013.841988>), nor did analyzing the exposure (gastrointestinal symptoms) without dichotomization and the outcome (quality of life) without trichotomization (data not shown).

Discussion

Being unpartnered, especially if you are a man, can have a large negative impact on your quality of life, as can gastrointestinal symptoms after radiation therapy for prostate cancer. This study shows that unpartnered prostate cancer survivors experiencing these symptoms report a lower quality of life compared with unpartnered survivors without symptoms and partnered survivors with symptoms.

Our results add to current knowledge by suggesting that unpartnered prostate cancer survivors could represent a group of men specifically vulnerable to distress from gastrointestinal symptoms. Zhou and co-workers found an association between high levels of baseline social support and high ratings of “health-related quality of life” two years after surgery or radiotherapy for localized prostate cancer [14]. The authors suggest that this association is partially mediated through lower perception of stress. They also found that a high level of baseline social support predicts a high level of well-being two years after treatment [15]. A Danish study showed that prostate cancer survivors who lived alone had a higher risk of reduced quality of life compared with partnered men [16]. Our data indicate that being afflicted with gastrointestinal symptoms could further aggravate this decline in quality of life.

Table III. Prevalence of gastrointestinal symptoms among prostate cancer survivors with or without partner, who had been treated at the Sahlgrenska University Hospital, Gothenburg, Sweden between 1994 and 2006.

Symptom category*	No. with symptom/ total No. (%)		Prevalence ratio (95% CI)
	Partner N = 764	No partner N = 100	
Altered composition	302/758 (40)	37/100 (37)	0.9 (0.7–1.2)
Flatulence	155/754 (21)	16/98 (16)	0.8 (0.5–1.3)
Leakage	136/757 (18)	21/100 (21)	1.2 (0.8–1.8)
Pain	74/758 (10)	7/99 (7)	0.7 (0.3–1.5)
Sensory	168/763 (22)	25/100 (25)	1.1 (0.8–1.6)
Urgency	217/756 (29)	35/98 (36)	1.2 (0.9–1.7)
Any gastrointestinal symptom	496/759 (65)	73/100 (73)	1.1 (1.0–1.3)

*As displayed in Table I.

Table IV. Prevalence ratio of low* quality of life, among irradiated prostate cancer survivors with or without a partner, who had been treated at the Sahlgrenska University Hospital, Gothenburg, Sweden between 1994 and 2006.

Symptom category [†]	Group A: Symptom/ unpartnered	Group B: No symptom/ unpartnered	Group C: Symptom/ partnered	Group D: No symptom/ partnered
Altered composition				
<i>Low* quality of life, No./total No. (%)</i>	9/43 (21)	3/54 (6)	24/333 (7)	7/415 (2)
<i>Prevalence ratio, (95% CI)</i>	12.4 (4.7–31.7) 2.9 (1.4–5.8) 3.8 (1.1–13.1)	3.3 (0.9–12.4) 0.8 (0.2–2.5) 1.0 (Reference)	4.3 (1.9–9.8) 1.0 (Reference)	1.0 (Reference)
Flatulence				
<i>Low* quality of life, No./total No. (%)</i>	2/16 (13)	9/79 (11)	14/154 (9)	17/591 (3)
<i>Prevalence ratio, (95% CI)</i>	4.3 (1.1–17.2) 1.4 (0.3–5.5) 1.1 (0.3–4.6)	4.0 (1.8–8.9) 1.3 (0.6–2.8) 1.0 (Reference)	3.2 (1.6–17.2) 1.0 (Reference)	1.0 (Reference)
Leakage				
<i>Low* quality of life, No./total No. (%)</i>	6/21 (29)	6/76 (8)	14/135 (10)	17/613 (3)
<i>Prevalence ratio, (95% CI)</i>	10.3 (4.5–23.5) 2.8 (1.2–6.4) 3.6 (1.3–10.1)	2.9 (1.2–7.0) 0.8 (0.3–6.4) 1.0 (Reference)	3.7 (4.5–23.5) 1.0 (Reference)	1.0 (Reference)
Pain				
<i>Low* quality of life, No./total No. (%)</i>	2/7 (29)	9/89 (10)	8/72 (11)	23/677 (3)
<i>Prevalence ratio, (95% CI)</i>	8.4 (2.4–29.0) 2.6 (0.7–9.8) 2.8 (0.8–10.6)	2.9 (1.4–6.2) 0.9 (0.4–2.2) 1.0 (Reference)	3.3 (1.5–7.0) 1.0 (Reference)	1.0 (Reference)
Sensory				
<i>Low* quality of life, No./total No. (%)</i>	7/23 (30)	5/74 (7)	15/167 (9)	16/587 (3)
<i>Prevalence ratio, (95% CI)</i>	11.2 (5.1–24.5) 3.4 (1.5–7.4) 4.5 (1.6–12.8)	2.5 (0.9–6.6) 0.8 (0.3–2.0) 1.0 (Reference)	3.3 (1.7–6.5) 1.0 (Reference)	1.0 (Reference)
Urgency				
<i>Low* quality of life, No./total No. (%)</i>	7/34 (21)	3/61 (5)	17/216 (8)	14/531 (3)
<i>Prevalence ratio, (95% CI)</i>	7.8 (3.4–18.1) 2.6 (1.2–5.8) 4.2 (1.2–15.1)	1.9 (0.6–6.3) 0.6 (0.2–2.1) 1.0 (Reference)	3.0 (1.5–5.9) 1.0 (Reference)	1.0 (Reference)
Any gastrointestinal symptom				
<i>Low* quality of life, No./total No. (%)</i>	10/71 (14)	2/26 (8)	28/491 (6)	3/259 (1)
<i>Prevalence ratio, (95% CI)</i>	12.2 (3.4–38.0) 2.5 (1.3–4.9) 1.8 (0.4–7.8)	6.6 (1.2–38.0) 1.3 (0.3–5.4) 1.0 (Reference)	4.9 (1.5–16.0) 1.0 (Reference)	1.0 (Reference)

*0–2 on a visual digital scale ranging from 0 to 6, where 0 denoted lowest possible and 6 denoted highest possible; [†]As described in Table I.

We hypothesize that the emotional and physical support from a partner may enable partnered men to be more tolerant of gastrointestinal side effects compared to unpartnered men. This hypothesis is supported by data from other previously published studies on cancer patients and survivors. In a study on 1736 patients treated for head and neck cancers, Dilling et al. found that unpartnered males had inferior overall survival rates compared to partnered males, adjusted hazard ratio 1.20 (95% CI 1.09–1.28) [17]. They hypothesize that partnered patients receive more support from their partners, both emotional and physical and therefore tolerate treatment better, leading to less treatment breaks and better outcomes. Wu et al. show that spouse timeline beliefs mediated the association between spouse treatment control beliefs and

patient quality-of-life six months later [18]. They argue that spouses' beliefs likely shaped interactions between the couple, reinforced daily life activities and influenced coping behaviors that bolstered patients' quality-of-life. Data from the Whitehall II study show that a low level of confiding and emotional support from the "closest person" predicts psychiatric morbidity after an "acute life event" [19]. They report that for men, 92% of the "closest persons" were a spouse, a partner or a cohabitee and that the perceived social support from this "closest person" had a larger effect on psychiatric morbidity than tangible or practical aspects of support. Furthermore, investigations of low-income, uninsured men with prostate cancer show that those who are partnered have better health and lower symptom distress than

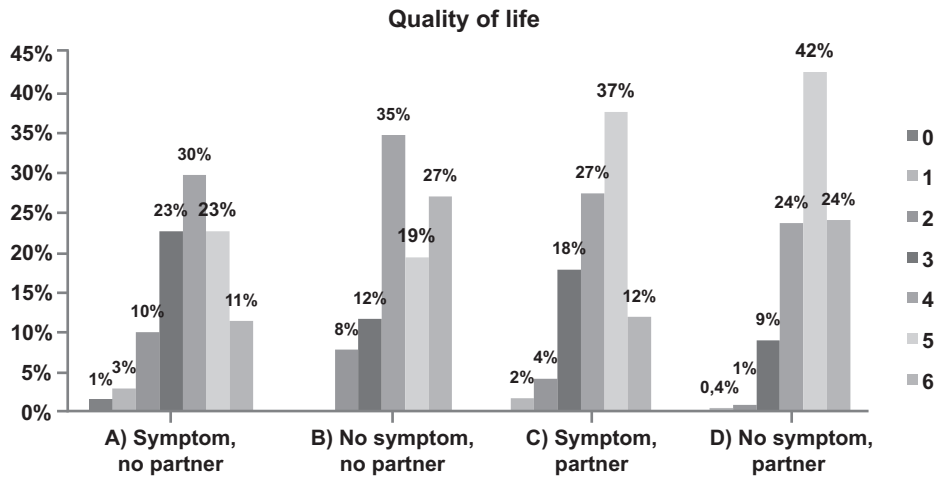


Figure 1. Quality of life among 874 long-term prostate cancer survivors who had been treated with radiation therapy between 1994 and 2006. The results are presented according to partnership status (partnered/unpartnered) and presence of gastrointestinal symptoms (yes/no). Quality of life was assessed on a visual digital scale ranging from 0 to 6, where 0 denotes “worst possible” and 6 denotes “best possible”.

those who are unpartnered, pointing to the alleviating role of a partner for men in a vulnerable position [20].

The strengths of this study include a large study population with a long time to follow-up and information on symptom background rates in a non-irradiated population. We used epidemiological methods adapted to the cancer survivorship field according to the hierarchical step-model for causation of bias [21]. The Swedish Total Population Register enables us to follow-up all eligible survivors and together with a high participation rate and high response rates to individual questions this reduces the risk of selection-induced problems. The use of postal questionnaire minimizes the risk of interviewer-related problems. Although the treatment protocols remained stable over time, there may have been minor adjustments for which we lack data. However, we have no reason to believe that this would alter the overall result of this study.

Nevertheless, this study has limitations that could affect the results. We cannot exclude that there are unmeasured confounding factors associated with both the occurrence of gastrointestinal symptoms (exposure) and quality of life (outcome). It is possible that men with a lower quality of life overestimate the occurrence of gastrointestinal symptoms, thereby introducing a differential misclassification. Speaking against this, however, is the consistent difference we found in quality of life rating between men with or without symptoms among both unpartnered and partnered men. Moreover, we found no difference in reported symptom occurrence between unpartnered and partnered men.

Gastrointestinal symptoms can cause considerable psychosocial distress among men irradiated for

prostate cancer [3]. Our results indicate that, in a clinical situation with limited resources, we may consider prioritizing unpartnered men as having the largest benefit from interventions aimed at distressful consequences of gastrointestinal symptoms after prostate irradiation.

Declaration of interest: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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Supplementary material available online

Supplementary material Table I.