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EUO Priority Article – Prostate Cancer

Quality of Life after Radical Prostatectomy or Watchful Waiting With or Without Androgen Deprivation Therapy: The SPCG-4 Randomized Trial

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Abstract

Background: Men with prostate cancer experience adjuvant androgen deprivation therapy (ADT) differently.

Objective: To evaluate the effect of ADT on quality of life (QoL), patients' experience of clinical check-ups, and differences in cancer information as explanatory factors.

Design, setting, and participants: A study-specific questionnaire was sent to all men randomized in the SPCG-4 trial to radical prostatectomy (RP) or watchful waiting (WW) still alive (400/695) and a control group of 281 men.

Intervention: ADT.

Outcome measurements and statistical analysis: Self-assessed QoL, worry at clinical check-ups, and amount of information received. Estimated relative risks with associated 95% confidence intervals (CI) for risk comparisons between groups using a log-binomial regression.

Results and limitations: The SPCG-4 men had median follow-up of 12.2 yr and median age of 77.0 yr; 26% in the RP group and 40% in the WW group received ADT treatment. High QoL for men without ADT was 36% for the RP group, 44% for the WW group, and 45% for the control group. High QoL for men with ADT was 30% for the RP group and 20% for the WW group. Among men with ADT, those in the WW group received significantly less information about the disease than men in the RP group. Receiving no or little information about prostate cancer was reported by 17% of patients in the RP group and 39% in the WW group among men receiving ADT (relative risk 0.44, 95% CI 0.22–0.89). At clinical check-ups, men treated with ADT had significantly higher levels of worry, regardless of study group, than men without ADT. Limitations include the lack of longitudinal data and a low number of men receiving ADT in the RP group.

Conclusions: Men on WW without ADT reported high QoL comparable to that for men without prostate cancer. ADT treatment in the WW group was associated with the lowest scores for all psychological parameters, and these men reported that they were least informed about prostate cancer and its consequences.

Patient summary: Good communication and information from caregivers are associated with less negative psychological effects at prostate cancer progression.

[†] The participants in the SPCG-4 study are listed in the Supplementary material.

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1. Introduction

Men with prostate cancer progression needing androgen deprivation therapy (ADT) often experience a good clinical response but are at risk of side effects including cardiovascular disease, diabetes, bone loss, loss of libido, and depression [1–5]. ADT decreases the quality of life for men with localized prostate cancer, even when used for a limited time [6]. Information and good physician communication can empower cancer patients and give them better ability to cope with the disease and decrease the occurrence of anxiety and depressive symptoms [7–9].

In the SPCG-4 study, men with localized prostate cancer were randomized to radical prostatectomy (RP) or watchful waiting (WW) and given ADT at disease progression. At mean follow-up of 4 yr, ADT affected men differently, depending on their initial treatment group. Androgen-deprived men allocated to WW were significantly more negatively affected regarding quality of life, depression, and anxiety than those allocated to RP, which indicates that factors other than biological ones have an effect. We hypothesized that the quality and duration of counseling differed between the groups, favoring the RP group, and that as a corollary these men would experience less worry at medical check-ups and at disease progression [10].

In this study with a median of 12.2 yr (range 7–17) of follow-up, we evaluated the effects of ADT in men allocated to RP or WW. We further explored if the amount of information influences a patient's ability to cope with his cancer and how he experienced medical check-ups. For comparison, we enrolled a population-based control group.

2. Patients and methods

2.1. Study design

In the SPCG-4 study, described in detail in a previous publication [11], 695 men aged <75 yr with clinically localized prostate cancer and a life expectancy of >10 yr were randomly assigned to RP or WW between October 1, 1989 and February 28, 1999. Other inclusion criteria were newly diagnosed tumors and prostate-specific antigen (PSA) <50 ng/ml. The protocol is available online at www.roc.se. Figure 1 shows the randomization of the study population and the recruitment of a population-based control group.

Urologists followed the SPCG-4 men every 6 mo for 2 yr and annually thereafter with blood tests, including PSA, and physical and digital rectal examinations. A bone scan was performed annually. ADT was recommended for local histology-verified recurrence in the RP group and for disseminated disease in both groups. Transurethral resection was recommended for urinary obstruction in the WW group. In January 2003, an amendment to the protocol allowed physicians to start ADT in both groups if it appeared beneficial for the patient.

The present study included all 400 living Swedish and Finnish men. Four men from Iceland were excluded for practical reasons. A research assistant contacted all men by letter and telephone.

An age-matched (with an interval of 4 yr) and region-matched control group of 300 Swedish men was sampled from the Swedish Total Population Register. The research assistant contacted them by letter and telephone; 19 were excluded because of a prior diagnosis of prostate cancer or unwillingness to participate.

All men who agreed to participate were posted a study-specific questionnaire, distributed between October 2006 and November 2008. The questionnaire was developed after interviews with men with prostate cancer and tested for face validity on both patients and healthy men. One investigator (E.J.) accompanied them while completing the questionnaire. Questions that were not immediately understood were discussed and changed until interpreted as intended. The questionnaire was further validated in a pilot study. The development of a study-specific questionnaire has been described in previous methodological and empirical articles and is based on a "one concept, one question" method producing patient-reported outcomes [10,12–15]. The study-specific questionnaire contained 141 questions and is included in the Supplementary material. The population-based controls answered 111 questions in a modified version of the questionnaire in which the specific cancer-related questions were excluded. The questionnaires explored psychological symptoms (anxiety, depressed mood), sense of well being, and quality of life using a seven-point visual digital scale: one and two on this scale were assessed as low intensity, three to five as moderate, and six and seven as high intensity. The questionnaire also contained questions on how much information the patient received from his doctor. We specifically explored information received concerning treatment alternatives for cancer, possible negative side effects of the treatment alternatives, and how the different treatments could affect daily life (quality of life). The following alternatives were possible as answers: no information; a little information; quite a lot of information; and very much information. A group of questions explored how the patient experienced outpatient visits for medical checks-ups. Additional information was collected on potential confounders and effect-modifying factors, such as concurrent diseases and treatments.

2.2. Statistical methods

All analyses followed the intention-to-treat principle. Outcome variables were dichotomized using cutoff values previously used by our group. We estimated relative risks for the dichotomized outcomes with associated 95% confidence intervals for risk comparisons between groups using a log-binomial regression [16]. All calculations were carried out using SAS v.9.2 statistical software and all tests were performed at the 5% significance level. Individuals who failed to respond to a question were excluded from the analyses for that specific variable. The study was approved by the Karolinska Institutet ethics committee.

3. Results

In all, 88% (182/208) in the RP group and 87% (167/192) in the WW group answered the questionnaire. The follow-up time varied from 7 to 17 yr (median 12.2 yr). In the age-matched population control group, 214/281 (76%) answered the questionnaire. The median age at randomization was 64.0 yr for the RP group and 65.0 yr for the WW group, and the median age when the questionnaire was completed was 77.0 yr for the RP group and 78.0 yr for the WW group; the age-matched control group had a median age of 71.0 yr. Social status and education level had similar distributions between the randomized groups and the control group (Table 1).

Among responding men assigned to RP, 94% (171/182) had their prostate removed; the remainder were node-positive at the time of surgery or declined surgery. In the WW group, 15% (25/167) ultimately had radical surgery. Men treated with ADT (via surgical castration, injections with a gonadotropin-releasing hormone analog, or