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Original articles

A prospective study of health-related quality-of-life outcomes for patients with low-risk prostate cancer managed by active surveillance or radiation therapy

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Abstract

Introduction: Patients with low-risk prostate cancer (PCa) often have excellent oncologic outcomes. However, treatment with curative intent can lead to decrements in health-related quality of life (HRQoL). Patients treated with radical prostatectomy have been shown to suffer declines in urinary and sexual HRQoL as compared to those managed with active surveillance (AS). Similarly, patients treated with external-beam radiation therapy (EBRT) are hypothesized to experience greater declines in bowel HRQoL. As health-related quality-of-life (HRQoL) concerns are paramount when selecting among treatment options for low-risk PCa, this study examined HRQoL outcomes in men undergoing EBRT as compared to AS in a prospective, racially diverse cohort.

Methods: A prospective study of HRQoL in patients with PCa enrolled in the Center for Prostate Disease Research (CPDR) Multicenter National Database was initiated in 2007. The current study included patients diagnosed through April 2014. HRQoL was assessed with the Expanded Prostate Cancer Index Composite (EPIC) and the Medical Outcomes Study Short Form (SF-36). Temporal changes in HRQoL were compared for patients with low-risk PCa managed on AS vs. EBRT at baseline, 1-, 2-, and 3 years post-PCa diagnosis. Longitudinal patterns were modeled using linear regression models fitted with generalized estimating equations (GEE), adjusting for baseline HRQoL, demographic, and clinical patient characteristics.

Results: Of the 499 eligible patients with low-risk PCa, 103 (21%) selected AS and 60 (12%) were treated with EBRT. Demographic characteristics of the treatment groups were similar, though a greater proportion of patients in the EBRT group were African American ($P = 0.0003$). At baseline, both treatment groups reported comparable HRQoL. EBRT patients experienced significantly worse bowel function and bother at 1 year (adjusted mean score: 87 vs. 95, $P = 0.001$ and 89 vs. 95, $P = 0.008$, respectively) and 2 years (87 vs. 93, $P = 0.007$ and 87 vs. 96, $P = 0.002$, respectively) compared to patients managed on AS. In contrast to those on AS, more than half the number of patients who received EBRT experienced a decline in bowel function (52% vs. 17%, $p = 0.003$) and bother (52% vs. 15%, $P = 0.002$) from

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baseline to 1 year. Patients who received EBRT were significantly more likely to experience a decrease in more than one functional domain (urinary, sexual, bowel, or hormonal) at 1 year when compared with those on AS (60% vs. 28%, $P = 0.004$).

Conclusions: Patients receiving EBRT for low-risk prostate cancer suffer declines in bowel HRQoL. These declines are not experienced by patients on AS, suggesting that management of low-risk prostate cancer with AS may offer a means for preserving HRQoL following prostate cancer diagnosis.

Keywords: Active surveillance; Quality of life; Radiotherapy; Prostate cancer; Treatment

1. Introduction

Patients with low-risk prostate cancer (PCa) have multiple treatment options, including active surveillance (AS), external-beam radiation therapy (EBRT), and radical prostatectomy (RP). Each of these treatment modalities confers 5-year survival in excess of 95% [1–4]. However, each treatment option also poses the risk of serious side effects that affect health-related quality of life (HRQOL) [5,6].

Studies demonstrating the safety of long-term AS have resulted in its increased use for patients with low-risk PCa [4,7–13], from 21% to 32% from 2004 to 2010 [14]. Mounting data support the safety of AS [15–17]. However, data are lacking on the effect of AS on HRQoL parameters.

This study examined HRQoL in a prospective, racially diverse cohort of patients with PCa enrolled in the Center for Prostate Disease Research (CPDR) multicanter national database, composed of medical centers offering equal-access health care facilities. A previous study of this cohort found that patients undergoing RP experienced worse urinary and sexual function as compared to patients on AS [18]. EBRT is also thought to adversely affect HRQoL, and specifically bowel function, in comparison to AS, yet studies comparing HRQoL outcomes of these groups are lacking. Thus, this study aimed to determine whether patients with low-risk PCa who undergo EBRT report poorer HRQoL outcomes compared to those managed on AS over a 3-year period.

2. Methods

2.1. Study subjects and setting

The study population was identified from the CPDR Multicenter National Database. Participating medical centers include Walter Reed National Military Medical Center (Bethesda, MD), Madigan Army Medical Center (Tacoma, WA), Naval Medical Center (San Diego, CA), Tripler Army Medical Center (Honolulu, HI), and Virginia Mason (Seattle, WA). Each institution has Institutional Review Board approval to consent and follow patients along the continuum of care for prostate disease, with second-tier Institutional Review Board approval by the Uniformed Services University of the Health Sciences. All subjects enrolled in this database have detailed demographic, clinical, treatment, outcomes, and comorbidity data, including lung disease/chronic obstructive pulmonary disease, heart disease/ coronary artery disease, hypertension, cerebral vascular accident, diabetes, elevated cholesterol, prostatitis, and renal insufficiency.

2.2. HRQoL survey instruments

HRQoL data were collected using 2 validated questionnaires, the Expanded Prostate Cancer Index Composite (EPIC) [19] and the 36-item Medical Outcomes Study Short Form (SF-36) survey [20]. EPIC is designed to evaluate urinary, bowel, sexual, and hormonal function and bother experienced within the past 4 weeks. Higher scores indicate better HRQoL (range: 0–100). The SF-36 measures general physical and mental health through 8 subscales (range: 0–100) that can be combined into a physical component summary and a mental component summary score (standardized mean $= 50$ and standard deviation $= 10$).

Both surveys were administered at baseline (defined as pretreatment and within 3 months of diagnosis), at 3-month intervals for the first year, and 6-month intervals for years 2 and 3. Only survey time points with $\geq 50\%$ completion rates were included.

The study inclusion criteria included a biopsy-confirmed diagnosis of PCa in patients aged 75 years or younger, completion of a baseline HRQoL survey, at least 1 completed follow-up survey, and ≥ 12 months follow-up. The study sample was further restricted to patients diagnosed with "low-risk" PCa, using NCCN criteria: clinical stage T1-T2a, biopsy Gleason score ≤ 6, and prostate-specific antigen (PSA) < 10 ng/mL [21]. AS was defined as no definitive treatment within 12 months of diagnosis, and ≥ 1 PSA or repeat biopsy within 18 months of diagnosis. Intensity-modulated radiotherapy (IMRT), 3-dimensional-conformal RT, and proton-beam therapy within 6 months of diagnosis were combined to represent the EBRT group.

2.3. Statistical analysis

Demographic, clinical, and baseline HRQoL characteristics were compared between treatment groups (EBRT vs. AS) using the Student's *t*-test for continuous variables (unequal variances) and chi-square tests for categorical variables.