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Prostate Cancer

Impact of Age on Quality-of-life Outcomes After Treatment for Localized Prostate Cancer

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Abstract

Background: Men aged >65 yr are less likely to receive local therapy for prostate cancer (PCa), perhaps because of concerns about quality-of-life (QOL) outcomes.
Objective: To describe QOL before and after PCa treatment in men of varying ages.
Design, setting, and participants: Participants enrolled in CaPSURE who underwent radical prostatectomy, brachytherapy, external beam radiation, androgen deprivation therapy, or active surveillance for localized PCa.
Outcome measurements and statistical analysis: QOL changes over time were assessed among age groups using repeated-measures mixed models adjusted for race, year, clinical risk, treatment, comorbidities, and an age-time interaction term. Differences are reported as adjusted least-square means and percentage decline. Secondary analyses evaluated age and QOL for local (prostatectomy, radiation) compared to nonlocal treatment (hormonal, surveillance).
Results and limitations: Older men had lower mean unadjusted pre- and post-treatment QOL scores for nearly all domains. Of the domains evaluated, adjusted mean sexual function, sexual bother, and urinary function showed greater declines from baseline to 2 yr. At 2 yr, more men <60 yr than those >70 yr experienced declines in urinary function (14% vs 9%) and sexual bother (39% vs 17%). Declines in these domains were also greater for local than for nonlocal treatment.
Conclusions: Definitive treatment for localized disease should not be deferred for older men because of fears regarding QOL declines. Younger men should be counseled about potential post-treatment declines in QOL despite higher absolute QOL scores. Communicating these differences to patients will facilitate more appropriate treatment decision-making in men of all ages.
Patient summary: In this study we evaluated quality of life before and after treatment for localized prostate cancer in a diverse patient population. Declines in quality of life after treatment varied according to age and treatment. We conclude that counseling about quality of life will help patients of all ages to make more appropriate treatment decisions.

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1. Introduction

Prostate cancer is the most common malignancy diagnosed in men of all ages in the USA, with 57.5% of new cases diagnosed in men aged ≥65 yr and a median age at diagnosis of 66 yr [1–3] At the time of diagnosis, considerable emphasis is placed on integrating health-related quality-of-life (QOL) considerations into treatment decisions, which may be even

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more important in older patients who may have lower baseline QOL [4,5]. Knowledge about the varied effects of prostate cancer treatment modality on QOL domains can help to inform patients about the potential impact of a given treatment type and may improve treatment decision-making by allowing the physician to uniquely personalize counseling to reflect each patient's treatment preferences and objectives [6–9].

It is known that patient age also strongly influences treatment decision-making. Studies have shown that older men are less likely to receive potentially curative local therapy at any level of disease risk, perhaps in part because of fears about QOL outcomes after treatment for older patients [10–12]. However, older men are more likely to be diagnosed with high-risk disease and these individuals face a higher risk of cancer-specific mortality in the absence of local therapy [13–15]. Despite this, older men have comparable outcomes and cancer control after treatment for localized disease [16,17]. Therefore, the potential impact of treatment on QOL must be measured against the individualized risk of progressive cancer.

The associations between age and QOL outcomes after treatment in contemporary practice are not well defined [10,18,19]. Our objective was to describe QOL in men before and after primary treatment for prostate cancer, examining the impact of age on QOL outcomes. We hypothesized that while older men may have lower absolute function and bother at baseline and follow-up compared to younger men, declines in QOL after treatment would be less meaningful to older men, particularly in regard to their bother scores. To investigate, we performed a retrospective review of a prospectively maintained, nationwide, largely community-based prostate cancer registry with longitudinal QOL follow-up.

2. Patients and methods

Cancer of the Prostate Strategic Urologic Research Endeavor (CaPSURE) is a prospective, longitudinal, observational study of men with biopsy-proven prostate cancer [1,3]. CaPSURE includes data on men treated at 43 community-based, academic, and veterans' practices nationwide. Participating urologists consent and enroll patients consecutively within 6 mo after diagnosis, treat according to their usual practices, and follow the patients until study withdrawal or death. Site urologists report clinical, treatment, and outcome data to the registry. Patients report demographic, comorbidity, and QOL data at diagnosis, and complete QOL questionnaires at regular intervals following treatment. Informed consent and data reporting are coordinated under central institutional review board supervision.

Our cohort included men who were newly diagnosed with prostate cancer during 1999–2013, prospectively enrolled in CaPSURE, underwent primary treatment with radical prostatectomy (RP), brachytherapy (BT), external beam radiation (EBRT), primary androgen deprivation therapy (ADT), or active surveillance/watchful waiting (AS/WW), and completed QOL questionnaires at baseline and/or within 2 yr after treatment. Baseline QOL was reported before treatment for all but the AS/WW group. Men enrolled in AS/WW received no active treatment within 6 mo after diagnosis, so the baseline for this group was set to the diagnosis date plus 6 mo. Localized disease was defined as $\leq$cT3aN0M0 disease. Clinical risk at diagnosis was defined according to the University of California, Los Angeles (UCLA) Cancer of the Prostate Risk Assessment (CAPRA) score (0–10 scale). Validated CAPRA groups are classified as low (0–2), intermediate (3–5), or high (6–10) risk [4]. Age at diagnosis was categorized into three subgroups ($<$60, 60–70, $>$70 yr) for assessment. Prior studies have used similar age groupings to assess the impact of age on QOL [6] and have identified the $\leq$60-yr age group as a population at high risk of treatment-related effects on QOL [10], prompting our evaluation for these age categories.

General QOL outcomes were assessed using the mental health and physical function scales from the RAND 36-item short-form health survey (SF-36), a well-validated, widely used measure of physical and mental well-being [13]. Treatment-specific QOL was reported via the UCLA Prostate Cancer Index (PCI), which measures function and bother for urinary, sexual, and bowel domains [20]. Scores for all SF-36 and PCI domains range from 0 to 100, with higher scores representing better QOL. Outcomes were defined as changes in QOL scores over time from baseline up to 2 yr after treatment.

Demographics, clinical characteristics, and QOL scores were compared between age groups using the Mantel-Haenszel χ^2 test for trends for categorical variables. QOL changes over time between age groups were assessed using repeated-measures mixed models in which the independent variables included race, year of diagnosis, CAPRA score, type of primary treatment, number of comorbidities, age group, time, and time-age interaction. Least-square means for the age-time interaction term were used to assess whether the trajectory of QOL over time differed by age category, indicating whether younger men experienced the same pattern of change over 2 yr as older men. A set of secondary models with the same covariates addressed three-way interactions among age, time, and primary treatment. The five primary treatment types were regrouped as local (RP, BT, EBRT) versus nonlocal treatment (ADT, AS/WW) for these additional models. We performed pairwise comparisons using the Tukey-Kramer method to adjust for multiple statistical testing. Least-square means with confidence intervals from the mixed models were graphed to illustrate adjusted changes over time. We explored both continuous differences and the amount of decline for ease of clinical interpretation. Model covariates were selected a priori and assessed for interitem correlations. A p value <0.01 was considered significant. Analyses were performed using SAS 9.4 for Windows (SAS, Cary, NC, USA) and R statistical software (R Foundation, Vienna, Austria).

3. Results

Among 9945 men newly diagnosed with prostate cancer and enrolled prospectively in CaPSURE during 1999–2013, 8069 were diagnosed with localized disease and treated with RP, BT, EBRT, ADT, or AS/WW. Of those, 6522 (81%) reported QOL data within 2 yr and formed the study cohort (Fig. 1). Among the study cohort, 5362 men had multiple QOL assessments within 2 yr and were included in repeated-measures analyses. Men who were excluded from analysis owing to a lack of QOL data had a similar age distribution, but fewer were Caucasian (76% vs 90%), clinical CAPRA risk was higher (14% vs 10% CAPRA $\geq$6), and fewer underwent RP (56% vs 44%) in comparison to the final analytic group (all $p < 0.01$; Supplementary Table 1).

Patient characteristics are listed in Table 1. Of the patients, 27% were younger than 60 yr, 44% were 60–70 yr, and 29% were older than 70 yr. Older men tended to have higher biopsy Gleason grade, PSA at diagnosis, and clinical CAPRA scores (all $p < 0.01$). Of the cohort, 44% underwent RP (of whom 2% had RP + EBRT), 29% received radiotherapy (of whom 48% had BT, 38% had EBRT, and 14% had BT + EBRT), 18% had primary ADT (of whom 68% were treated