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Prostate Cancer

New Rates of Interventions to Manage Complications of Modern Prostate Cancer Treatment in Older Men

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Abstract

Background: Interventions to treat complications from prostate cancer (PCa) treatment are common and affect the course of a patient's life.
Objective: To examine rates of complications other than urinary incontinence and impotence for older patients treated for PCa.
Design, setting, and participants: Population-based retrospective cohort study of patients aged 65–79 yr receiving radical prostatectomy or radiotherapy (RT) from 2001 to 2008 in the US Surveillance Epidemiology and End Results and Medicare linked databases.
Outcome measures and statistical analysis: Complications were organised in three categories: urologic procedures, rectal–anal procedures, and major surgeries. We analysed the role of primary treatment on the number of complications using negative binomial regression.
Results and limitations: Among 60 476 men, 14 492 underwent primary surgery and 45 984 underwent primary RT; 33 418 (55%) experienced at least one complication (mean: 2.6 complications per patient). For both groups, complications peaked within 2 yr of treatment but continued at a steady rate for 10 yr. Patients treated with radiation had higher rates of urologic procedures (adjusted relative rate [aRR]: 1.25; 95% confidence interval [CI], 1.2–1.3; $p < 0.0001$) and rectal–anal procedures (aRR: 1.4; 95% CI, 1.4–1.5; $p < 0.0001$) but a lower rate of major surgeries (aRR: 0.9; 95% CI, 0.8–0.9; $p < 0.0001$) compared with those having surgery. Because patients treated with RT were older and more comorbid, selection bias limits the strength of conclusions that can be drawn from this data.
Conclusions: Complications are common following PCa cancer treatment and occur many years after treatment. The primary treatment is an important predictor of complication rates that may inform treatment decisions and long-term survivorship plans.
Patient summary: We examined complications after prostate cancer treatment in a large American population. Patients treated with radiotherapy rather than surgery had higher rates of complications requiring urologic procedures and rectal–anal procedures but lower rates of open surgeries. However, we were only able to examine men aged >65 yr, and this, along with the observational study technique, means that these results may not apply to all patients and that factors beyond those that we could measure may have affected these results.

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1. Introduction

The most studied complications of prostate cancer (PCa) treatment are urinary incontinence and erectile dysfunction, with well-established differences between patients who undergo surgery and radiation [1–3]. We recently examined other treatment-related complications resulting in hospital admissions, genitourinary and rectal–anal procedures, open surgeries, and secondary malignancies following open radical prostatectomy and external-beam radiation therapy [4]. Age, comorbidity, and radiotherapy (RT) treatment were significantly associated with time to first complication [4].

Many patients experience multiple complications of the same or different type over time; therefore, survival analysis may not provide optimal information for patients and physicians. Using the US Surveillance Epidemiology and End Results (SEER) cancer registries and Medicare databases, we sought to compare rates of these complications by capturing repeated events in a cohort of 60 476 men treated for clinical localised PCa from 2001 to 2008. We calculated incidence density rates of urologic procedures, rectal–anal procedures, and major surgeries and compared the rates between patients who had surgery or RT.

2. Methods

2.1. Data sources

SEER-Medicare data provide treatment information and outcomes for cancer patients [5–8]. We linked the SEER cancer registry with administrative data on physician billings from the National Claims History database and outpatient procedures from the outpatient claims database. Data from these sources were captured in the 2 yr prior to diagnosis (to calculate comorbidity) and in the years following diagnosis. Local research ethics approval was received.

2.2. Population and covariates

We examined men aged 65–79 yr diagnosed with clinically localised PCa from 2001 to 2008 who had no previous cancer history and were treated with radical prostatectomy or RT within a year of diagnosis. Additional inclusion criteria included standard methodology for SEER studies: not enrolled in an health maintenance organisation (HMO) at diagnosis and full Medicare (parts A and B) coverage during the study time frame. Men were excluded if they lacked eligible follow-up time posttreatment, were treated before the diagnosis date, or were missing data on diagnosis date or rurality. Less than 1% of patients were excluded due to missing data.

Men were followed from the date of treatment until death or December 31, 2010. Medicare data linkage was only available until this date and allowed a minimum of 2 yr of follow-up for each individual.

Race, marital status, rurality, and comorbidity (Klabunde-modified Charlson Comorbidity Index [9]) were collected to control for potential confounding.

2.3. Noncancer control group

We created an age-matched cohort of noncancer patients with the same eligibility criteria using a 5% random sample of Medicare patients with no cancer history. The index date corresponded to the treatment date of their age-matched PCa. The purpose of this cohort was to provide a baseline estimate of these outcomes in an untreated noncancer population. A cohort of untreated, similarly staged PCa patients was not used for this comparison because these patients differ significantly from treated patients in age [10–13], ethnicity [10,12], and overall prognosis [13].

2.4. Primary treatment

Standard SEER-Medicare variables and data sources were used to identify the primary treatment [6,14] using physician billing data [15,16]. Specific codes for open, laparoscopic, and robotic prostatectomy and for brachytherapy, three-dimensional conformal radiotherapy, and intensity-modulated radiotherapy radiation [15–17] were used to categorise treatment assignment. All patients who received adjuvant or salvage treatments were included and classified according to their initial treatment.

2.5. Treatment-related complications

Counts of treatment-related complications were measured for each individual using the Medicare databases. Potentially relevant procedural codes were identified from the literature and a blinded review of the cohort medical procedures (Supplementary Table 1) [15–23]. Both methods were used to ensure comparability with existing literature and to capture all potentially clinically relevant complications. Three categories were defined based on our previous work [4]: minimally invasive urologic procedures, rectal–anal procedures, and major (open or laparoscopic) surgeries. Codes related to erectile dysfunction and incontinence were considered outside the scope of this study. The grouping of these codes was made irrespective of primary treatment, blinded to index treatment. All physician billings and procedures that matched the eligible complication codes were counted. Supplementary Table 2 lists the included complications.

2.6. Statistical analysis

Analyses of complications can measure the first presentation of the complication in an individual or measure the total number of complications the person experiences. Counts of each complication were reported as incidence density rates, using the total count of a complication as the numerator and the number of person-years at risk as the denominator. Rates were stratified by primary treatment. Multivariate negative binomial regression was used to study the association between primary treatment and complication rates. Each treatment rate ratio was adjusted for the effect of age (65–69, 70–74, 75–79 yr), comorbidity (0, 2, 3, 4, $\geq$5), race (white, black, other), marital status (single, married, widowed, separated/divorced, unknown), and rurality (big metropolis [metro], metro, urban, rural) [24,25]. The negative binomial distribution was used rather than Poisson due to the skewed nature of health services data [24,25]. Where the negative binomial model did not converge, a modified Poisson regression with robust error variance was performed [26]. We further compared both groups with the noncancer controls to quantify differences from the baseline event rates for each treatment. To contextualise the results of the multiple event analysis, probabilities of experiencing one or more events at 2 and 8 yr were estimated using Kaplan-Meier methods.

To adjust for potential biases resulting from nonrandom treatment assignment, we performed a sensitivity analysis using propensity score matching. The propensity score represented the probability of receiving a particular treatment using multivariate logistic regression including age category, comorbidity, race, marital status, and year of diagnosis. Pairs were created without replacement in a 1:1 match using the greedy algorithm [27]. Analyses were performed using generalised estimating equations with a negative binomial distribution to account for the