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Factors associated with the omission of androgen deprivation therapy in radiation-managed high-risk prostate cancer

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ABSTRACT

PURPOSE: Androgen deprivation therapy (ADT) has been shown to improve survival for men with unfavorable-risk prostate cancer (PCa). We investigated the utilization and factors associated with the omission of ADT in radiation-managed high-risk PCa.

METHODS AND MATERIALS: We used the National Cancer Database to identify men with National Comprehensive Cancer Network high-risk PCa treated with external beam radiation therapy (EBRT) with or without brachytherapy boost from 2004 to 2012. Multivariable logistic regression adjusting for clinical and sociodemographic factors was used to identify independent predictors for ADT use.

RESULTS: A total of 57,968 radiation-treated high-risk PCa men were included in our analysis. There were 49,363 patients (85.2%) treated with EBRT alone and 8605 patients (14.8%) treated with EBRT plus brachytherapy boost. Overall, 77% of men received ADT. In multivariable regression analysis, the use of brachytherapy boost was associated with a significantly lower utilization of ADT (70% vs. 78%; adjusted odds ratio [AOR]: 0.65; 95% CI: 0.62−0.69; p-Value <0.0001), as was treatment at an academic vs. nonacademic center (AOR: 0.90; 95% CI: 0.86−0.95; p-Value <0.0001) and treatment in 2010−2012 compared to 2004−2006 (AOR: 0.85; 95% CI: 0.81−0.90; p-Value <0.0001). Conversely, greater ADT use was seen with higher Gleason scores, PSA, and T-category (all p-Values <0.001).

CONCLUSIONS: Approximately one in four men with radiation-managed high-risk PCa do not receive ADT, which may reflect concerns about its toxicity profile despite known improvements in overall survival. Practice patterns suggest that some providers believe dose escalation through brachytherapy boost may obviate the need for ADT in some high-risk patients, but this hypothesis requires further testing. © 2016 Published by Elsevier Inc. on behalf of American Brachytherapy Society.

Keywords: Brachytherapy boost; Androgen deprivation therapy; High-risk prostate cancer; Prostate neoplasm

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Introduction

Although not in all, androgen deprivation therapy (ADT) in combination with external beam radiation therapy (EBRT) has been shown to improve overall survival for men with high-risk prostate cancer (PCa) in several studies (1−3). However, the potential adverse effects (4) of ADT are considerable and might deter clinicians from prescribing ADT and patients from receiving it (5). In this study, we aim to investigate the trends of ADT use in radiation-treated high-risk PCa in the contemporary US population using the US National Cancer Database (NCDB) (6). We also aim to identify the factors associated with the omission of ADT.

Methods and materials

Data source and study population

We used the NCDB, a joint program of the Commission on Cancer and the American Cancer Society, to select our study population. NCDB is the largest cancer registry worldwide (6), and it captures 70% of the newly diagnosed cases in the United States. Men diagnosed with National Comprehensive Cancer Network's nonmetastatic high-risk (7) PCa (PSA >20 ng/mL or Gleason ≥ 8 or clinical tumor stage ≥ T3) in 2004−2012 were identified, and men who received EBRT with or without brachytherapy boost as the definitive treatment were included in our study. Of note, we restricted our study population to patients with only PCa diagnosis and excluded patients with multiple cancers. We also excluded patients with unavailable prostate-specific antigen (PSA), Gleason score, or tumor stage to ensure precisely defined National Comprehensive Cancer Network's high-risk disease. Figure 1 summarized the study cohort selection process.

Primary end point and determinants

The primary end point was to identify factors associated with the omission of ADT. Clinical factors in this study included PSA (<10, 10−20, >20 ng/mL), Gleason score (≤6, 7, 8−10), tumor stage, and Charlson comorbidity score (0, 1, ≥2). Consistent with a recent prior publication, "favorable high-risk disease" (8) was defined as stage T1c with Gleason score 4 + 4 = 8 and PSA <10 ng/mL or stage T1c with Gleason 6 and PSA >20 ng/mL. Sociodemographic factors included age (<65, ≥65 years), race (non-Hispanic White, Hispanic white, Black, others, unknown), year of diagnosis (2004−2006, 2007−2009, 2010−2012), insurance status (none, private, Medicaid, Medicare, other), residence type (rural, urban, metropolitan), household income, and the percent of education level less than high school for each patient's area of residence. As provided by the NCDB, the patients' household income (9) and education level (10) were quartiles among all US zip codes based on the 2012 American Community Survey and the residence type (11) was determined with the 2003 United States Department of Agriculture Economic Research Service.

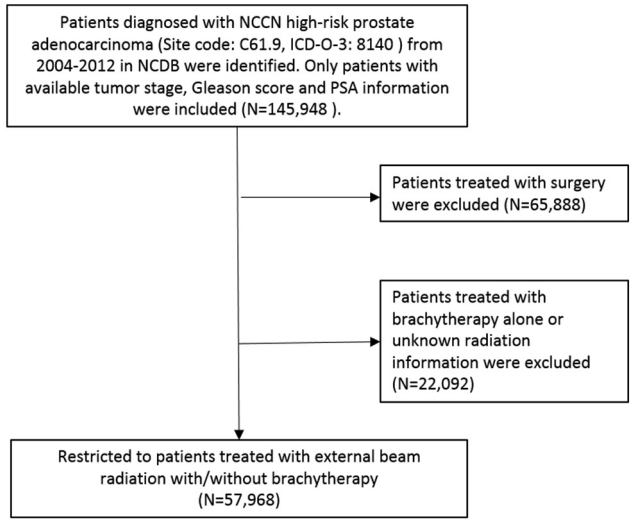

Fig. 1. Study population selection process. NCCN = National Comprehensive Cancer Network; NCDB = National Cancer Database; PSA = prostate-specific antigen.

Statistical analysis

Descriptive statistics were used to present the baseline characteristics. Categorical variables were compared with χ^2 test, and continuous variables were compared by Wilcoxon rank-sum test. Mantel−Haenszel χ^2 analysis for trend was used to examine ADT use over the study period. A multivariable logistic regression model was used to identify independent predictors for omission of ADT. All statistical analyses were performed using SAS version 9.4 (SAS Institute Inc., Cary, NC). We used a two-sided p-Value <0.05 in all analyses as criteria for statistical significance.

Results

Patient baseline characteristics

Our study population consisted of 57,968 radiation-treated men with high-risk PCa. There were 49,363 (85.2%) treated with EBRT alone and 8605 (14.8%) treated with EBRT with brachytherapy boost. Men who received brachytherapy boost were younger (median age: 68 vs. 71 years for men who received EBRT alone, p-Value < 0.0001). There were 18,096 (31.2%) men treated in academic centers, and 39,872 (68.8%) were treated at nonacademic centers. Table 1 summarizes the patient baseline characteristics.

Utilization and independent predictors of omission of ADT

In total, 44,461 (77%) men received ADT and 13,507 (23%) men did not. Overall, a lower rate of ADT use was