Original article

Discrepancies in staging, treatment, and delays to treatment may explain disparities in bladder cancer outcomes: An update from the National Cancer Data Base (2004–2013)

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Abstract

Introduction: We sought to characterize national disparities in the diagnosis of advanced stage bladder cancer. Among patients with advanced disease, we explored disparities in overall survival, treatment, and time to treatment.

Methods and materials: We queried the National Cancer Data Base for patients diagnosed with bladder urothelial carcinoma. We used multivariable logistic regression to assess the association between covariates and diagnosis of advanced disease (AJCC stage III–IV). We used Kaplan-Meier, log-rank, and Cox proportional analyses to evaluate disparities in overall survival for patients with advanced disease. Receipt of treatment and delays to treatment were compared between subgroups.

Results: Among our cohort of 328,560 patients, 7.6% were diagnosed with advanced disease. Female sex, black race, Hispanic ethnicity, and living in a region of lower income and education were all associated with increased odds of advanced disease. Female sex (HR = 1.16; 95% CI: 1.12–1.20; $P < 0.001$), black race (HR = 1.10; 95% CI: 1.04–1.18; $P = 0.002$), and lower regional income levels (fourth quartile compared to first: HR = 1.08; 95% CI: 1.02–1.16; $P = 0.016$) portended worse overall survival. Chemotherapy (HR = 0.55, 95% CI: 0.53–0.57; $P < 0.001$) and radical cystectomy (HR = 0.61; 95% CI: 0.59–0.64, $P < 0.001$) improved survival. Females, black patients, and patients from regions of lower income and education were less likely to receive treatment and less likely to receive treatment within 12 weeks of diagnosis.

Conclusion: There are several disparities in the diagnosis and treatment of advanced bladder cancer. Overall survival for certain groups may benefit from earlier diagnosis and improved timely access to potentially life prolonging treatment. © 2018 Elsevier Inc. All rights reserved.

Keywords: United States; Epidemiology; Urinary bladder neoplasms; Healthcare disparities; Therapeutics; Cystectomy; Survival

1. Introduction

Bladder cancer is the fourth most common cancer in men and fifth most common cancer overall. Nearly 80,000 new cases of bladder cancer will be diagnosed in 2017 and over 16,000 will die as a result of the disease [1]. The survival for bladder cancer diagnosed at a distant stage is the fourth worst behind pancreas, lung and bronchus, and liver or bile duct cancer [1]. Estimated 5-year survival for metastatic bladder cancer is approximately 8% with no recent improvements over time in the United States [2].

Historical imbalances in survival between various sociodemographics have been described in bladder cancer [3–9]. Socioeconomic mortality disparities have been documented in both historical [3,4] and more recent [5] data, reflecting the financial toxicity associated with care of bladder cancer from diagnosis to death relative to other malignancies [10]. Race and female sex are considered risk factors for later stage at diagnosis and stage-specific mortality [6–8]. In

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addition, nonprivate insurance coverage is associated with disparities in cancer outcomes, specifically in the United States, resulting in worse survival [9].

In the current study, we used a national, hospital-based cohort of patients with well-described oncologic outcomes to provide a contemporary assessment of disparities in bladder cancer outcomes. Our hypothesis was that disparities in late stage bladder cancer diagnoses, treatment receipt, and delays to treatment may lead to worse overall survival.

2. Methods and materials

2.1. Data source and patients

We queried the National Cancer Data Base (NCDB), a hospital-based cancer registry comprised of over 1,500 healthcare centers approved by the American College of Surgeons' Commission on Cancer (CoC) and the American Cancer Society [11]. In 2013, it captured data on approximately 70% of all bladder cancer cases in the United States [12,13].

We identified all patients diagnosed with urothelial carcinoma of the bladder (International Classification of Diseases for Oncology codes 8120–8139) from 2004 through 2013 (n = 412,428). We included only patients with complete TNM staging information (n = 333,379, 81%) and those who had information on income and education level (n = 328,560, 80%).

2.2. Covariates

Patient race/ethnicity were *patient defined and* coded as non-Hispanic White, non-Hispanic Black, Hispanic, and unknown or other. Insurance status was dichotomized as private or Medicare vs. no insurance or Medicaid. Distance from patients' home to the treating hospital was assessed based on zip codes of the patient and hospitals. Facility type is a variable generated by the NCDB based on cancer patient yearly volume. Comprehensive and academic facilities treat > 500 cancer patients while community facilities treat > 100 patients annually. In addition, academic facilities must have at least four graduate medical education programs. Annual bladder cancer volume per treatment center was recorded as quartiles relative to all facilities within the current study.

Tumor grade was coded as high or low. We used American Joint Committee on Cancer (AJCC) to determine clinical stage at diagnosis [14]. Other covariates included age at diagnosis, sex, year of diagnosis, facility location within a United States region, and patient Charlson-Deyo Comorbidity index [15]. Treatment was recorded as receipt or no receipt of chemotherapy, radical cystectomy, or radiation therapy.

The NCDB generates patient income and acquisition of high school education based on American Community Survey data from 2008 through 2012. Based on ZIP Code Tabulation Areas (ZCTAs), patients are categorized in national quartiles of median household income and percentage of adults who did not graduate high school. In subgroup analyses, we compared patients who lived in zip codes with the fourth quartile (lowest) levels of both education and income to those living in zip codes with first quartile (highest) levels for both education and income.

2.3. Outcome variable and statistical analysis

Our primary outcomes were late clinical stage at diagnosis (stage III or IV) among the cohort of all bladder cancer patients, and overall survival for patients with late stage disease at diagnosis. We provide descriptive statistics of our entire cohort and those diagnosed with late stage cancer. Multivariable logistics regression analysis was performed to assess the association between covariates and late stage bladder cancer. Cox proportional, Kaplan-Meier, and log-rank analyses were used to assess the association between socioeconomic status (SES), sex, race/ethnicity, and other covariates with overall survival. To identify potential mechanisms behind survival disparities, we assessed differences in treatment receipt and delay to treatment between sociodemographic subgroups and compared groups using Pearson's chi-squared analyses. To assess the relationship between treatments and survival for different sociodemographics, we performed interaction analyses with treatment types significantly associated with improved survival. Delay to treatment was defined as greater than 12 weeks following diagnosis based on previous data suggesting worsened mortality with greater delay among radical cystectomy patients with muscle invasive bladder cancer [16]. Stata 13.0 (College Station, TX) was used for all analyses. $P < 0.05$ was considered significant. Our study was considered IRB exempt due to using de-identified, publically available data.

3. Results

3.1. Disparities in the diagnosis of advanced stage bladder cancer

We first identified a cohort of advanced stage bladder cancer (Stage III and IV) from the National Cancer Database. Of the 328,560 patients diagnosed with urothelial carcinoma, 25,046 were advanced stage bladder cancer at diagnosis (7.6%; Table 1). Multivariable analyses were used to determine the association between covariates of diagnosis of late stage disease. Although females comprised fewer bladder cancer patients overall, a higher percentage of females were diagnosed with advanced stage bladder cancer compared to males (8.8% vs. 7.2%; OR = 1.23, 95% CI: