Original Study

Female, Black, and Unmarried Patients Are More Likely to Present With Metastatic Bladder Urothelial Carcinoma

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Abstract

To identify the demographic and clinical factors associated with bladder urothelial carcinoma metastasis at diagnosis, patients diagnosed from 2004 to 2010 were identified in the SEER database. Factors associated with metastasis at diagnosis included female gender, black race, unmarried, unemployed, and foreign-born status. Clinicians should be aware of these potential health care disparities in order to improve early care.

Background: Although there are well-established risk factors for the diagnosis of bladder cancer, there is no consensus regarding risk factors for presentation of advanced or metastatic disease at diagnosis. The objective of this study was to identify the demographic and clinical factors associated with metastasis at diagnosis in patients with bladder urothelial carcinoma. **Patients and Methods:** Patients diagnosed with bladder urothelial carcinoma from 2004 to 2010 were identified in the Surveillance, Epidemiology, and End Results (SEER) database (n = 108,417). The primary outcome was metastatic disease at the time of diagnosis. Demographic and socioeconomic variables were analyzed, and multivariable logistic regression models were performed to generate odds ratios (OR) for factors associated with metastasis at diagnosis. **Results:** Of patients with bladder cancer, 3018 (2.8%) had metastasis at diagnosis and 105,399 (97.2%) had nonmetastatic disease. Patients with metastatic disease at diagnosis were more frequently female (29.6% vs. 23.6%, $P < .001$), black (9.4% vs. 5.0%, $P < .001$), and unmarried (44.1% vs. 32.5%, $P < .001$) compared to patients with nonmetastatic disease. On multivariable analysis, the following characteristics were confirmed to be independently associated with metastatic disease at diagnosis: female gender (vs. male, OR 1.21), black race (vs. white, OR 1.71), unmarried (vs. married, OR 1.46), unemployed (OR 1.02), and foreign-born status (OR 1.01). **Conclusion:** Female gender, black race, unmarried, unemployed, and foreign-born status are independently associated with metastasis at diagnosis for bladder urothelial carcinoma. All clinicians should be aware of these potential health care disparities in order to involve social services and other support mechanisms in efforts to improve early care.

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Introduction

Bladder cancer is the ninth most common malignancy worldwide, with an estimated 430,000 new cases diagnosed each year.[1] The majority of cases are diagnosed as non-muscle-invasive disease, with a 5-year survival rate of 88% that decreases to 15% when there is metastatic progression.[2] Furthermore, poor performance status and the presence of visceral metastasis are factors associated with worse prognosis in patients undergoing treatment for metastatic bladder urothelial carcinoma.[3,4] These points emphasize the importance of early detection, stringent surveillance, adequate social work infrastructure, and identification of at-risk patients for metastases.

Although there are well-established risk factors for the diagnosis of bladder cancer,[5] there is no consensus regarding risk factors for presentation of advanced or metastatic disease at diagnosis. Previous studies have demonstrated that black race imparts a higher risk for metastasis at the time of diagnosis.[6] However, other socioeconomic variables have not been investigated. Additionally, health care disparities continue to exist for bladder cancer despite interventions

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aimed at improving these inequalities.[7,8] The objective of this study was to use a population-based cohort to identify demographic and socioeconomic factors associated with metastatic disease at diagnosis in patients with bladder urothelial carcinoma.

Materials and Methods

Study Population

Patients diagnosed with bladder cancer from 2004 to 2010 were identified in the Surveillance, Epidemiology, and End Results (SEER) database. The SEER database reports cancer-specific outcomes from specific geographic areas representing 28% of the US population.[9] Patients ≥ 18 years of age with bladder urothelial carcinoma were identified utilizing the primary site codes C67.0 to C67.9, and International Classification of Diseases for Oncology, 9th edition (ICD-O), codes 8210/3, 8122/3, 8123/3, 8130/3, and 8131/3 (urothelial carcinoma) for a study cohort of 108,417 patients. Patients were divided into those with metastatic disease and those with nonmetastatic disease at the time of diagnosis.

Description of Covariates

Demographic variables of interest included age at diagnosis, gender, race (white vs. black vs. other), and marital status (married vs. single/divorced/widowed [SDW]). Socioeconomic variables included county data for family income, percentage of persons living in poverty, educational attainment (percentage with less than ninth-grade education), percentage unemployment, and percentage foreign-born status. Insurance status (insured vs. any government insurance vs. uninsured) was also investigated for data available from 2007 to 2010.

Statistical Analysis

Descriptive statistics for demographic and socioeconomic variable comparisons were performed by the Student *t* test for continuous variables and the chi-square test for categorical variables. Multivariable logistic regression models were performed to generate odds ratios (OR) for the identification of factors associated with metastasis at diagnosis. The model was constructed and analyses were performed using backward selection, removing all insignificant variables until the best-fit model was achieved. Models were assessed for confounding and interaction. Statistical analyses were performed by SAS 9.4 (SAS Institute, Cary, NC). All tests were 2 sided; statistical significance was defined as $P < .05$.

Results

Population Sociodemographics

There were 3018 patients (2.8%) who had metastasis at diagnosis and 105,399 patients (97.2%) who had nonmetastatic disease. Patients with metastatic disease were more often female (29.6% vs. 23.6%, $P < .001$), black (9.4% vs. 5.0%, $P < .001$), and had SDW marital status (44.1% vs. 32.5%, $P < .001$) compared to patients with nonmetastatic disease at diagnosis (Table 1). Furthermore, patients with metastatic disease at diagnosis were more frequently residing in a county with a higher percentage of people living in poverty ($P = .001$), unemployed ($P < .001$), poorly educated ($P < .001$), and foreign born ($P < .001$) (Table 2). Patients with metastatic disease at diagnosis were also less likely to have medical insurance (81.4 vs. 86.3%) and more likely to have government insurance (12.5 vs. 6.2%) compared to those without metastatic disease ($P < .001$).

Table 1 Demographics of Patients With Bladder Urothelial Carcinoma Stratified by Metastasis at Diagnosis

Variable	Metastasis at Diagnosis (n = 3018)	No Metastasis at Diagnosis (n = 105,399)	*P*
Age, years, median (IQR)	72 (17)	72 (17)	.80
Gender, n (%)			<.001
Female	893 (29.6)	24,906 (23.6)	
Male	2125 (70.4)	80,493 (76.4)	
Race, n (%)			<.001
White	2610 (86.5)	94,668 (89.8)	
Black	283 (9.4)	5268 (5.0)	
Other	122 (4.0)	4010 (3.8)	
Unknown	3 (0.1)	1453 (1.4)	
Marital Status, n (%)			<.001
Married	1576 (52.2)	63,936 (60.7)	
SDW	1332 (44.1)	34,224 (32.5)	
Unknown	110 (3.7)	7239 (6.8)	

Abbreviations: IQR = interquartile range; SDW = single, divorced, widowed.

Factors Associated With Metastatic Disease at Diagnosis

Independent factors associated with metastasis at diagnosis included female gender (vs. male; OR, 1.21; 95% confidence interval [CI], 1.11-1.32; $P < .001$), black race (vs. white; OR 1.71; 95% CI, 1.50-1.95; $P < .001$), SDW status (vs. married; OR, 1.46; 95% CI, 1.35-1.58; $P < .001$), being unemployed (OR, 1.02; 95% CI, 1.00-1.03; $P = .02$) and being foreign born (OR, 1.01; 95% CI, 1.00-1.01; $P < .001$) (Table 3).

Table 2 Socioeconomic Data of Patients With Bladder Urothelial Carcinoma Stratified by Metastasis at Diagnosis

Variable	Metastasis at Diagnosis (n = 3018)	No Metastasis at Diagnosis (n = 105,399)	*P*
Family income, $, median (IQR)	67,450 (22,350)	68,880 (23,420)	.02
% Persons < poverty, median (IQR)	13.01 (5.77)	12.74 (6.38)	<.001
% Unemployed, median (IQR)	9.19 (2.34)	9.02 (2.13)	<.001
Percentage with less than ninth-grade education, median (IQR)	6.13 (5.91)	5.76 (5.19)	<.001
% Foreign born, median (IQR)	16.40 (16.39)	14.38 (16.22)	<.001
Insurance Status, n (%)[a]			<.001
Insured	1479 (81.4)	52,908 (86.3)	
Any government insurance	227 (12.5)	3818 (6.2)	
Uninsured	52 (2.9)	999 (1.6)	
Unknown	58 (3.2)	3612 (5.9)	

Abbreviation: IQR = interquartile range.
[a]Data from 2007-2010 (n = 1816 for metastasis at diagnosis; n = 61,337 for no metastasis at diagnosis).