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Overall and recurrence-free survival among black and white bladder cancer patients in an equal-access health system

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Abstract

Background—While the incidence of bladder cancer is twice as high among whites than among blacks, mortality is higher among blacks than whites. Unequal access to medical care may be an important factor. Insufficient access to care could delay cancer detection and treatment, which can result in worse survival. The purpose of this study was to evaluate whether survival differed between black and white bladder cancer patients in the Department of Defense (DoD), which provides universal healthcare to all beneficiaries regardless of racial background.

Methods—This study was based on data from the U.S. DoD Automated Central Tumor Registry (ACTUR). White and black patients histologically diagnosed with bladder cancer between 1990 and 2004 were included in the study and followed to the end of 2007. The outcomes were all-cause mortality and recurrence. We assessed the relationship between race and outcomes of interest using Cox proportional hazard ratios (HRs) for all, non-muscle invasive (NMIBC), and muscle invasive (MIBC) bladder cancers, separately.

Results—The survival of black and white individuals did not differ statistically. No significant racial differences in survival (HR: 0.96, 95% CI: 0.76–1.22) or recurrence-free survival (HR: 0.94, 95% CI: 0.69–1.30) were observed after adjustment for demographic variables, tumor characteristics, and treatment. Similar findings were observed for NMIBC and MIBC patients, respectively.

Conclusion—Black patients were more likely to present with MIBC than white patients. However, white and black patients with bladder cancer were not significantly different in overall

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Conflicts of interest

The authors declare that they have no conflict of interest.

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and recurrence-free survival regardless of muscle invasion. Our study suggests the importance of equal access to healthcare in reducing racial disparities in bladder cancer survival.

Keywords

bladder cancer; race; survival

Introduction

Bladder cancer is the sixth most common malignancy in the U.S. It is estimated that 74,000 new cases and 16,000 deaths will occur in 2015 [1]. There are, however, racial/ethnic differences in incidence and mortality rates [2-5]. Bladder cancer incidence is twice as high among whites than among blacks [6], but mortality is higher among blacks than whites [7, 8]. From 2004 to 2010, five-year survival among black patients was significantly lower than among white patients (64% and 80%, respectively) [1], which may be attributed to later stage at diagnosis [3, 9]. However, disparities persist within given tumor stages, grades, and treatments [9-12]. In a study conducted using the SEER database, the five-year cause-specific survival was significantly worse for blacks than whites even among patients with localized tumors (88% vs. 93%) [10]. Another study, which also used SEER data, found that black patients had worse survival compared to white patients regardless of stage and grade of bladder cancer while other racial/ethnic minority groups had survival similar to that of whites [3].

Racial differences in bladder cancer survival are likely multifactorial. Less access to medical care due to insufficient health insurance could delay cancer detection and treatment, which may lead to worse survival. In the United States, black persons are less likely to have medical insurance compared to white persons [13]. Therefore, black patients with bladder cancer may be less likely to receive timely and sufficient diagnosis and treatment, which can result in worse survival [9, 14, 15]. Research in an equal access medical care system can examine whether racial differences in survival continue to exist when all racial groups are granted equal access to healthcare. If a difference exists within an equal access system, it may suggest the effects of factors beyond access to care.

However, research on racial differences in bladder cancer survival in equal access systems is limited. To the best of our knowledge, only one study on racial disparities utilizing the U.S. Veterans Administration (VA) system has been conducted in a large equal access system [16]. This study found that black patients with localized bladder cancer had significantly worse survival than their white counterparts. Given the limited research available on racial differences in bladder cancer survival in equal access health systems, the purpose of this study was to evaluate whether bladder cancer survival differed between black and white bladder cancer patients in the Department of Defense (DoD), which provides healthcare to all beneficiaries regardless of racial background.

Methods

Data Source

This study was based on data from the U.S. DoD Automated Central Tumor Registry (ACTUR). Initiated in 1986, ACTUR collects medical data on DoD beneficiaries who are diagnosed with cancer or receive cancer treatment at military treatment facilities. DoD beneficiaries include active-duty members, retirees, and their dependents. Local cancer registrars review and confirm all cases reported to ACTUR and follow all cases until death. The ACTUR database contains information on age at diagnosis, gender, race, primary site, tumor stage, tumor grade, histology, diagnosis date, diagnostic confirmation, cancer treatment, recurrence, follow up, and vital status. This research was based on de-identified data approved by the institutional review boards of the U.S. Military Cancer Institute, the Armed Forces Institute of Pathology, Walter Reed National Military Medical Center, and the National Institutes of Health Office of Human Subjects Research.

Study Subjects

White and black patients histologically diagnosed with bladder cancer between 1990 and 2004 were eligible for the study. Other racial groups were not included due to a relatively small number of patients. Bladder cancer was identified using ICD-O-3 topography code C67. Tumor stage was defined based on AJCC TNM stage group information (Stage 0-IV). Tumors were further categorized into non-muscle invasive bladder cancer (NMIBC: Stage 0-I) and muscle invasive bladder cancer (MIBC: Stage II-IV) because of differences in risk factors, management, recurrence, and survival [17, 18]. Persons who had a previous or current diagnosis of another cancer were excluded from the analysis. The final number of individuals included in the analysis was 2,467.

Statistical Analysis

Survival time was calculated as the time between cancer diagnosis and date of death due to any cause. Although the registry does have cause of death, the information is not complete; thus all-cause death was used. Follow up was conducted through December 31, 2007 and was based on the period from the date at diagnosis to the date of last contact. Similarly, recurrence time was calculated as the time between cancer diagnosis and date of first documented recurrence with a follow-up through the end of 2007. As the first step of data analysis, we presented the distribution of demographic and tumor characteristics by race. Unadjusted and adjusted cox proportional hazard ratios (HRs) and corresponding 95% confidence intervals (CIs) were then calculated to estimate the relationship between race/ethnicity and survival or recurrence-free survival. To assess the effects of each category of variables, models were first adjusted for demographic variables (age, sex, marital status, and active-duty status at diagnosis) and then adjusted for tumor characteristics (tumor stage, grade, and histology), and receipt of treatment (any bladder surgery, chemotherapy, radiation, and immunotherapy) in addition to demographic variables. Missing and unknown values were retained in analysis and categorized as unknown when appropriate. Analyses were conducted for all, NMIBC, and MIBC types, separately. Time-dependent variables for immunotherapy and surgery, were adjusted for in survival analyses because of non-proportional hazards.

Results

The study subjects consisted of 2,313 white and 154 black patients diagnosed with urinary bladder carcinoma between 1990 and 2004 (Table 1). The average age at diagnosis for white and black patients was 64 and 62 years of age, respectively. While the two groups were not statistically significant in demographic or tumor characteristics, black patients tended to be younger and more likely to be active duty than whites. In terms of tumor-related characteristics, black patients tended to have a higher proportion of tumors that were muscle invasive or stages T2–T4, grade III, and non-urothelial at diagnosis compared to white patients and were less likely to have surgery.

Survival and recurrence-free survival of black and white individuals did not significantly differ, regardless of muscle invasion. In overall survival, no racial differences were observed (HR: 0.96, 95% CI 0.76-1.22) after adjustment for demographic variables, tumor characteristics, and treatment (Table 2). The HRs were 0.85 (95%CI, 0.58-1.24) and 1.04 (95%CI, 0.76-1.41) for NMIBC and MIBC, respectively. Similarly, when recurrence was the outcome, no racial differences were observed (HR: 0.94, 95%CI 0.69-1.30 for all; HR: 1.00, 95%CI 0.69-1.46 for NMIBC; and HR: 0.86, 95%CI 0.47-1.60 for MIBC) (Table 3).

Discussion

In the present study, we found that black bladder cancer patients were more likely to present with MIBC compared with white patients. However, white and black patients were not significantly different in overall survival and recurrence-free survival. After adjusting for covariates, bladder cancer survival was similar between black and white patients despite muscle invasion status.

Previous studies in the general population tended to find racial differences in bladder cancer survival [3, 9, 10, 12, 19]. In SEER data from 1975 to 2005, black bladder cancer patients had an HR of 1.29 (95% CI: 1.24-1.36) when compared with white patients [3]. In a population-based cohort identified from Atlanta, New Orleans, and San Francisco/Oakland cancer registries [9], the researchers also found that black patients as a whole had a worse all-cause survival compared with white patients (p -value<0.003). Further analysis showed that the racial difference existed among MIBC (T2, T3) patients only (p -value<0.05) [9]. In contrast, other studies found significant racial differences in survival among NMIBC [19, 20] and MIBC [21] patients.

Fewer studies have investigated racial differences in recurrence-free survival of bladder cancer. In a SEER-Medicare-linked study, the 10-year recurrence was 74.3% and 75.9% for white and black patients, respectively; and recurrence-free survival was not significantly different between the two groups [20]. Another study conducted at the University of Alabama reported an adjusted HR of 2.48 (95% CI: 0.98-6.29) where 25% of black and 12.8% of white patients had a recurrence with a median follow up of 17.6 months [22].

Unequal access to medical care may play a role in the racial disparities observed [11]. Research showed that insufficient insurance coverage is related to later tumor stages at diagnosis and worse outcomes [23-25]. Black persons are less likely to have sufficient

healthcare insurance and therefore have less access to cancer care [13]. As a result, they are more likely to have late-stage tumors and worse prognosis [9, 11]. However, a previous study conducted in the VA system, which provides equal access to care, found that black persons had shorter survival than white persons [16] despite the groups' equal access to care. While the VA study did not account for tumor grade, the study included a larger number of study subjects and stratified results by stage.

Our finding of no difference in survival by race/ethnicity differs from that of the VA [16]. Our study suggests that black and white patients diagnosed with NMIBC or MIBC tumors within the DoD health system have similar survival and recurrence. While the reasons for the difference between our study and the VA study are not clear, the VA study did not adjust for the potential effects of age at diagnosis and receipt of treatment [16]. Also, the VA and MHS populations may be different in demographic features, e.g. a very high proportion of low-income patients in the VA system [26]. We do not exclude the possibility that the VA and MHS systems differ in the actual utilization of care between the two racial groups as a result of the differences between the two populations. Previous research in cancer screening showed no racial differences in mammography screening within the MHS system [27], but there were racial differences in colon cancer screening within the VA system [28]. Racial differences in lung cancer treatment have also been observed. In the VA, blacks were less likely to receive recommended stage-appropriate treatment compared to whites [29], but there were no racial differences in lung cancer treatment within the MHS [30].

Since there are no screening programs for bladder cancer conducted among the general population, survival time depends mainly on cancer stage at diagnosis and access to quality cancer care and treatment after diagnosis. All individuals in our study were DoD beneficiaries and were entitled to equal access to medical care. Our study suggests the importance of equal access to healthcare in reducing racial disparities in bladder cancer survival.

This study had some limitations. First, all-cause death rather than bladder cancer-specific death was used in data analysis. Because this study observed no racial differences in all-cause death, if the higher bladder cancer-specific death rate among black persons observed in the general population had been true in our population, black persons would have been less likely to die of other causes in our population. While the data for this study prevent us from assessing this possibility, this conjecture seems unlikely. Second, capture of recurrence might not be complete, and thus, we do not exclude the possible effects of the incompleteness on the results. However, we do not have evidence showing that the incompleteness was differential between whites and blacks, which might bias the racial differences in recurrence. Third, there were limited details on type of surgery, such as transurethral resection (TUR) and cystectomy, in the ACTUR database. TUR is often curative for NMI, but diagnostic for MI tumors. Thus, it was not distinguished whether a surgical procedure was curative or diagnostic. Finally, the study power might be insufficient due to the small sample size of black patients, specifically for stratified analysis by muscle invasion status.

In conclusion, racial disparities in localized bladder cancer survival or recurrence were not observed among DoD beneficiaries. More studies are needed in equal-access health care systems to confirm these findings.

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Table 1

Distribution of characteristics by race among patients diagnosed with bladder cancer, 1990-2004, the U.S. military Department of Defense Cancer Registry

Characteristic N (%)	White N=2,313	Black N=154	p-value
Age^a			0.064 ^b
20-44	159 (6.87)	14 (9.09)	
45-54	260 (11.24)	23 (14.94)	
55-64	726 (31.39)	58 (37.66)	
65-74	712 (30.78)	35 (22.73)	
75+	456 (19.71)	24 (15.58)	
Sex^a			0.406 ^b
Male	1880 (81.28)	121 (78.57)	
Female	433 (18.72)	33 (21.43)	
Marital status^a			0.422 ^b
Married	1770 (76.52)	111 (72.08)	
Not Married	405 (17.51)	31 (20.13)	
Unknown	138 (5.97)	12 (7.79)	
Active duty status^a			0.134 ^b
Non-active duty	2148 (92.87)	138 (89.61)	
Active duty	165 (7.13)	16 (10.39)	
Tumor grade^a			0.324 ^b
Grade I	430 (18.59)	24 (15.58)	
Grade II	537 (23.22)	36 (23.38)	
Grade III	754 (32.60)	62 (40.26)	
Grade IV	123 (5.32)	6 (3.90)	
Unknown	469 (20.28)	26 (16.88)	
Tumor stage^a			0.326 ^b
0	687 (29.70)	45 (29.22)	
I	912 (39.43)	50 (32.47)	
II	295 (12.75)	23 (14.94)	
III	186 (8.04)	17 (11.04)	
IV	233 (10.07)	19 (12.34)	
Muscle invasion^a			0.054 ^b
No	1599 (69.13)	95 (61.69)	
Yes	714 (30.87)	59 (38.31)	
Histology^a			0.247 ^b
Urothelial	2197 (94.98)	143 (92.86)	
Non-Urothelial	116 (5.02)	11 (7.14)	
Surgery			0.087 ^c
No	139 (6.01)	16 (10.39)	

Characteristic N (%)	White	Black	<i>p</i> -value
	N=2,313	N=154	
Yes	2163 (93.51)	138 (89.61)	
Unknown	11 (0.48)	0	
Radiation			0.260 ^c
No	2140 (92.52)	138 (89.61)	
Yes	130 (5.62)	11 (7.14)	
Unknown	43 (1.86)	5 (3.25)	
Chemotherapy			0.918 ^c
No	1961 (84.78)	130 (84.42)	
Yes	297 (12.84)	20 (12.99)	
Unknown	55 (2.38)	4 (2.60)	
Immunotherapy			0.662 ^c
No	1930 (83.44)	125 (81.17)	
Yes	349 (15.09)	27 (17.53)	
Unknown	34 (1.47)	2 (1.30)	

^aAt diagnosis;

^bChi-square *p*-value;

^cFisher's Exact *p*-value

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Table 2

Multivariate analysis assessing racial variations in overall survival among patients diagnosed with bladder cancer, 1990-2004, the U.S. Department of Defense Cancer Registry

	Event/Total	HR ¹ (95% CI)	HR ² (95% CI)	HR ³ (95% CI)
All				
White	1189/2313	Reference	Reference	Reference
Black	74/154	1.02 (0.81-1.29)	1.16 (0.92-1.47)	0.96 (0.76-1.22)
Non-muscle invasive				
White	660/1599	Reference	Reference	Reference
Black	28/95	0.76 (0.52-1.11)	0.89 (0.61-1.31)	0.85 (0.58-1.24)
Muscle invasive				
White	529/714	Reference	Reference	Reference
Black	46/59	1.11 (0.82-1.50)	1.18 (0.87-1.60)	1.04 (0.76-1.41)

¹Unadjusted

²Adjusted for age (continuous), sex, marital status, and active duty status

³Adjusted for age (continuous), sex, marital status, active duty status, tumor stage, histology, grade, receipt of surgery, chemotherapy, radiation, and immunotherapy.

Table 3

Multivariate analysis assessing racial variations in recurrence-free survival among patients diagnosed with bladder cancer, 1990-2004, the U.S. Department of Defense Cancer Registry

	Event/Total	HR ¹ (95% CI)	HR ² (95% CI)	HR ³ (95% CI)
All				
White	663/2292	Reference	Reference	Reference
Black	40/149	0.93 (0.68-1.28)	0.98 (0.71-1.35)	0.94 (0.69-1.30)
Non-muscle invasive				
White	498/1587	Reference	Reference	Reference
Black	29/92	1.00 (0.69-1.46)	1.09 (0.75-1.58)	1.00 (0.69-1.46)
Muscle invasive				
White	165/705	Reference	Reference	Reference
Black	11/57	0.79 (0.43-1.46)	0.81 (0.44-1.48)	0.86 (0.47-1.60)

¹Unadjusted

²Adjusted for age (continuous), sex, marital status, and active duty status

³Adjusted for age (continuous), sex, marital status, active duty status, tumor stage, histology, grade, receipt of surgery, chemotherapy, radiation, and immunotherapy.