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Ethnic differences in bladder cancer survival

David S. Yee^a, Nicole M. Ishill^b, William T. Lowrance^a, Harry W. Herr^a, and Elena B. Elkin^b

^aUrology Service, Department of Surgery, Memorial Sloan-Kettering Cancer Center, New York, New York, USA

^bDepartment of Epidemiology and Biostatistics, Memorial Sloan-Kettering Cancer Center, New York, New York, USA

Abstract

Objectives—Racial disparities in bladder cancer outcomes have been documented with poorer survival observed among blacks. Bladder cancer outcomes in other ethnic minority groups are less well described. We examined trends in bladder cancer survival among whites, blacks, Hispanics, and Asian/Pacific Islanders in the US over a 30-year period.

Methods—From the Surveillance, Epidemiology and End Results cancer registry data, we identified patients diagnosed with transitional cell carcinoma of the bladder between 1975 and 2005. This cohort included 163,973 white, 7,731 black, 7,364 Hispanic and 5,934 Asian/Pacific Islander patients. We assessed the relationship between ethnicity and patient characteristics. Disease-specific 5-year survival was estimated for each ethnic group and for subgroups of stage and grade.

Results—Blacks presented with higher stage disease than whites, Hispanics and Asian/Pacific Islanders, although a trend toward earlier stage presentation was observed in all groups over time. Five-year disease-specific survival was consistently worse for blacks than for other ethnic groups, even when stratified by stage and grade. Five-year disease-specific survival was 82.8% in whites compared with 70.2% in blacks, 80.7% in Hispanics and 81.9% in Asian/Pacific Islanders. There was a persistent disease-specific survival disadvantage in black patients over time which was not seen in the other ethnic groups.

Conclusions—Ethnic disparities in bladder cancer survival persist between whites and blacks, while survival in other ethnic minority groups appears similar to that of whites. Further study of access to care, quality of care and treatment decision making among black patients is needed to better understand these disparities.

Keywords

ethnic groups; healthcare disparities; survival; urinary bladder; urinary bladder neoplasms

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Corresponding Author: David S. Yee, MD, MPH, Urology Service, Department of Surgery, Memorial Sloan-Kettering Cancer Center, 1275 York Avenue, Box 27, New York, NY 10065, United States, Phone: +1-714-767-7227, Fax: +1-646-735-0032, yeed1@mskcc.org.

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INTRODUCTION

Bladder cancer incidence and survival vary among ethnic groups.^{1–3} Prior studies demonstrate lower incidence and poorer survival in blacks compared with whites.^{4–6} Although much of the difference in survival has been attributed to higher stage at presentation in blacks,^{5,6} this disparity persists between whites and blacks with similar stage, grade and treatment.⁷ Research regarding bladder cancer outcomes in other ethnic groups, such as Hispanics and Asian/Pacific Islanders (APIs), is limited.

The objective of this study was to evaluate trends in bladder cancer presentation and disease-specific survival (DSS) in whites, blacks, Hispanics and APIs between 1975 and 2005. Given increased health care awareness, improved socioeconomic conditions and improved access to health care during this time period, we hypothesized that ethnic disparities in bladder cancer outcomes would decrease over time.

MATERIALS AND METHODS

Data Source

We used data from the Surveillance, Epidemiology and End Results (SEER) program, a consortium of population-based cancer registries sponsored by the National Cancer Institute. SEER collects information on patient and disease characteristics and first course of treatment, with active follow-up for vital status and cause of death (<http://seer.cancer.gov>).⁸ In 1975, SEER included the states of Connecticut, Iowa, New Mexico, Utah and Hawaii, the 13-county Seattle-Puget Sound area and the metropolitan areas of Atlanta, Detroit and San Francisco-Oakland. By 2001, the SEER Program had gradually expanded coverage to include California, New Jersey, Kentucky and Louisiana, as well as American Indians residing in Arizona, the Alaskan Native populations residing in Alaska and ten predominantly black rural counties in Georgia.⁸

The SEER areas currently cover more than 25% of the US population and include 23% of blacks, 40% of Hispanics, 42% of American Indians and Alaska Natives, 53% of Asians and 70% of Hawaiian/Pacific Islanders.⁸ The SEER standard for case ascertainment is 98%. To review the trends in bladder cancer over time, 5-year intervals were established beginning in 1975. The most recent interval, 2000–2005, included 6 years of review.

Study Cohort

We identified all patients in SEER diagnosed with transitional cell carcinoma of the bladder (8120.2, 8120.3, 8121.2, 8122.3, 8130.2, 8130.3, 8131.2, 8131.3) between 1975 and 2005 whose race and stage at diagnosis were known. In SEER, race/ethnicity is determined from medical records and registration information for each individual.

Disease-Specific Survival

DSS was defined as the time from initial diagnosis to the time of death attributed to bladder cancer. SEER collects information on underlying cause of death from the state death certificate.⁸

Covariates

In addition to race/ethnicity, we examined a number of patient and disease characteristics. In the absence of individual level data on socioeconomic status, we used the median household income in the census tract of residence. Urban vs rural residence was based on U.S. Census Bureau designations for these areas. Tumor stage was defined as localized for organ-confined tumors, regional for tumors with extravesical extension or regional lymph nodes

and distant for patients with visceral metastases or nodal involvement above the pelvic brim. Advanced stage was defined as regional- or distant-stage disease at presentation. Primary treatment, ascertained from SEER data on the first course of cancer-directed therapy, was categorized as surgery only, radiation therapy only, both or other. 'Other' treatment included strategies that did not involve surgery or radiation therapy, such as observation or systemic chemotherapy.

Statistical Analysis

Chi-square tests were used to evaluate unadjusted associations between race/ethnicity and other demographic and clinical characteristics. We used Poisson regression to determine whether there were differences across racial groups in the proportion of advanced-stage cases over the course of the study. Proportional hazards regression models were used to examine the relationship between disease-specific death and race/ethnicity, adjusting for sociodemographic and disease characteristics. Two-way interactions between ethnicity and other covariates were explored. All *P*-values were two-sided, and *P* < .05 was considered statistically significant. Statistical analyses were performed in SAS (version 9.1, Cary, NC).

RESULTS

Cohort Characteristics

We identified 163,973 white, 7,731 black, 7,364 Hispanic and 5,934 API patients diagnosed with bladder cancer in 1975–2005 (Table 1). There were 1,329 patients of other (*n* = 381) or unknown (*n* = 948) race/ethnicity who were excluded. Of the 185,002 patients in the study cohort, 55,964 (30%) were younger than 65 years of age at the time of diagnosis. Black patients were less likely to be married (47%) at the time of bladder cancer diagnosis compared with whites (65%), Hispanics (62%) and APIs (70%).

Surgery was the predominant treatment modality among all ethnic groups. Radiation was used infrequently and when given, it was usually used in conjunction with surgical therapy. Although a trend toward increasing use of surgery alone was observed in all racial/ethnic groups over time, blacks were less likely to have surgery alone and more likely to receive radiotherapy than whites, Hispanics and APIs in each time period.

Blacks were more likely to present with advanced-stage disease (31%) than whites (21%), Hispanics (24%) and APIs (23%) (*P* < .001 for comparisons of black vs white, black vs Hispanic and black vs API difference between 1975–1979 and 2000–2005).

Higher rates of poorly differentiated and undifferentiated grades at tumor presentation were observed in black (47%) and API (46%) patients compared to white (39%) and Hispanic (40%) patients (*P* < .001 for comparison of black vs white and black vs Hispanic in difference between 1975–1979 and 2000–2005). Over time, the percentage of patients with poorly differentiated or undifferentiated disease increased among all ethnic groups, particularly among Hispanics (27% to 43%), APIs (37% to 49%) and whites (33% to 44%).

Survival

With a median followup of 4.2 years (interquartile range 1.7 – 8.6 years), blacks had poorer DSS than other ethnic groups (Fig. 1). DSS was similar for whites, Hispanics and APIs.

The survival disparity for black patients persisted within strata of disease stage and tumor grade (Table 2). The greatest racial disparities were observed among patients with local and regional stage disease and those with poorly differentiated and undifferentiated disease. For example, in those with regional disease, 5-year DSS was 50.3% in whites compared with

41.5% in blacks – an absolute difference of 8.8%. In those with poorly differentiated disease, 5-year DSS was 67.7% in whites compared with 51.9% in blacks – an absolute difference of 15.8%. Examining cohorts of patients by time period of diagnosis, there was a persistent DSS disadvantage in black patients over time which was not seen in the other ethnic groups. However, DSS improved for all ethnic groups, with the greatest improvement for localized stage tumors in black patients (from 76.2% in 1975–1979 to 85.9% in 2000–2005).

In multivariable analysis, black patients had a higher likelihood of disease-specific death, adjusting for age, gender, marital status, census tract median household income, urban residence, year of diagnosis, geographic area, pathologic stage and grade and treatment (Table 3). With the exception of urban residence, these covariates were also themselves significantly associated with disease-specific mortality. Cancer stage (hazard ratio [HR] 15.97; 95% CI, 15.30 – 16.67; $P < .0001$) and grade (HR 5.90; 95% CI: 5.49 – 6.33, $P < .001$) were strong predictors of cancer-specific death.

COMMENT

Our study provides an initial description and highlights important differences in bladder cancer survival among multiple ethnic groups. In particular, Hispanics and APIs had similar DSS compared to whites. Historically research specific to the health of other minorities has been limited.⁹ A 2003 study showed that the federal government has scant data on the health of APIs and only 0.2% of federal grants from 1986 to 2000, involved API health directly or tangentially.¹⁰

Despite a modest improvement over time in DSS, we observed a persistent disparity for black patients with bladder cancer. Five-year DSS was consistently worse for blacks than for patients of other race/ethnicity, even when stratified by stage and grade and adjusted for other patient characteristics and primary therapy. These findings support a recent SEER study that reported an excess hazard of death from bladder cancer among blacks despite adjusting for age, stage and grade.¹¹

Tumor stage at diagnosis is an independent predictor of bladder cancer survival.^{12,13} Although a stage disparity persists between blacks and other ethnic groups, the gap has narrowed somewhat over the last 30 years. Black patients today are more likely to present with localized disease than their historical counterparts. However, even in the most recent time period we evaluated, the 70% rate of localized disease in blacks was still less than the rate of 79% observed in whites.

A disparity in tumor grade was also observed in this cohort. In each time period, black and API patients presented with higher grade tumors than white patients. We also observed a trend toward increasing rates of poorly differentiated and undifferentiated disease among all ethnic groups. The etiology of this trend is unclear since the percentage of patients with unknown grade remained relatively stable and thus may not be attributable to improved pathology reporting.

A disparity between blacks and whites in 5-year DSS persisted even when comparing patients of similar stage and grade. The disparity was more marked in patients with localized and regional stage disease; poorer survival in these disease stages may reflect treatment delay during a critical period where curative therapy is possible.⁴ The smaller survival disparity between black and white patients with distant-stage bladder cancer likely reflects the poorer prognosis associated with metastatic bladder cancer.

Marital status was also an independent predictor of DSS. Gore et al demonstrated that marriage was associated with improved survival in 7,262 patients treated with radical cystectomy for bladder cancer.¹⁴ Marital status has also been associated with cancer survival in other settings.¹⁵ The nearly 20% higher marriage rate in whites, Hispanics and APIs compared to blacks might contribute to improved survival through several mechanisms. A spouse may encourage more prompt evaluation of symptoms leading to an earlier diagnosis, provide psychosocial support, promote smoking cessation and advocate for care in higher-quality facilities.¹⁴

Currently, no clear genetic differences or tumors with poor prognostic molecular markers have been identified that correlate with more aggressive bladder cancer in blacks. However, ethnic differences in tobacco use have been observed, which are associated with disparities in bladder cancer incidence and possibly survival. According to the 1999 – 2001 National Survey on Drug Use and Health, cigarette smoking was approximately 40% less common in adult APIs than in adult whites and blacks.¹⁶

Hispanics also had an approximately 50% lower average annual prevalence of cigarette smoking than whites in the 1994 – 1996 National Health Interview Survey.¹⁷ A systematic review showed that smoking significantly alters patient prognosis after treatment for bladder carcinoma.¹⁸ Thus, lower smoking rates among Hispanics and APIs compared with blacks may in part explain their higher DSS.

Disproportionate application of treatments may also contribute to survival disparities between black and white patients. Previous studies have reported that blacks are more likely to receive radiation,¹⁹ radiation and chemotherapy²⁰ or no treatment²¹ for bladder cancer compared to whites. We did not detect any ethnic disparities in the use of chemotherapy. Recently, Hollenbeck et al reported racial differences in initial treatment of early stage bladder cancer using SEER-Medicare data from 1992 through 2002.²² However, after the authors adjusted for these differences in initial treatment intensity and in the provider responsible for the bladder cancer care, the differences failed to account for the greater risk of death in black patients compared to white patients.²²

In a cohort of Medicare beneficiaries, Schrag et al also demonstrated that a higher socioeconomic status was associated with a greater likelihood of cystectomy in patients with muscle-invasive bladder cancer.²³ Recently, investigators have established an association between ethnicity and surgical outcomes after cystectomy, where black patients had greater mortality and longer hospitalization than did white patients undergoing cystectomy.^{24,25} These differences in outcomes may be associated with differences in hospital volume, as several studies have demonstrated lower mortality after cystectomy in high-volume hospitals.^{26,27} In a recent study, blacks were less likely to undergo cystectomy at a high-volume hospital, thereby placing them at a higher risk of postoperative complications.²⁴ Race may also be a predictor of adherence to surveillance among patients with superficial bladder cancer.²⁸ Compared with 17% of white patients, almost 30% of black patients and patients of other races had substandard follow-up.

Several limitations in our study should be acknowledged. The SEER program expanded in both size and geography during the study period, thus the racial/ethnic disparities we observed may reflect sociodemographic changes over time in the SEER registries. Race-specific bladder cancer incidence estimates have been stable over time in SEER. Use of SEER historic staging is a less precise alternative to tumor-node-metastasis pathological staging used in clinical decision making. However, the latter was not available for cases diagnosed prior to 1988 and the former sufficiently distinguished organ-confined from non-organ-confined disease. Also, while we assessed variation in primary treatment and its

relationship to both ethnicity and DSS, we had no information on subsequent cancer-directed therapy and the incidence and treatment of recurrent disease. Other potential confounders, such as surveillance after primary therapy, were not available for analysis.

An important limitation of the SEER database is the lack of information on patient comorbidity and hospital volume, factors that are associated with adverse outcomes following radical cystectomy and which may influence diagnosis and treatment.^{26,27,29} While this information may be supplemented by analyzing cases in the linked SEER-Medicare database, that data source is limited to patients aged 65 years or older. Although bladder cancer is primarily considered a disease of the elderly, with the median age at diagnosis of transitional cell carcinoma being 69 years in males and 71 years in females,³ 30% of bladder cancer patients in our study were under age 65.

A final limitation is the lack of patient-level measures of socioeconomic status, an important potential confounder because ethnicity may be a surrogate for socioeconomic status.³⁰ In our analysis, the bottom two quartiles of census tract median income were associated with a higher risk of cancer-specific death, suggesting that lower socioeconomic status also has a deleterious effect on survival outcomes.

CONCLUSIONS

In conclusion, the rate of bladder cancer survival in Hispanics and APIs appears similar to that of whites. However, DSS disparities persist between whites and blacks and are not fully explained by differences in disease presentation and receipt of treatment. Although stage at diagnosis and DSS improved over time in all racial/ethnic groups, blacks were consistently more likely to die from their disease. Factors that may explain survival disparities include variation in quality and timing of primary therapy, surveillance after primary therapy, treatment of recurrent disease, comorbidity and tumor biology. Further investigation of the role of these factors is needed to better understand and eliminate the persistent disparities in bladder cancer outcomes.

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FIG. 1. Disease-specific survival by ethnicity for Surveillance, Epidemiology and End Results (SEER) bladder cancer patients diagnosed 1975 – 2005.

TABLE 1

Patient characteristics stratified by ethnicity for SEER bladder cancer patients diagnosed 1975–2005

	White n=163,973	Black n=7,731	Hispanic n=7,364	API n=5,934
	n (%)	n (%)	n (%)	n (%)
Age at diagnosis, years				
< 50	9,522 (6)	624 (8)	727 (10)	387 (6)
50 – 59	20,888 (13)	1,202 (16)	1,074 (15)	723 (12)
60 – 69	41,343 (25)	2,030 (26)	1,933 (26)	1,423 (24)
70 – 79	54,771 (33)	2,416 (31)	2,235 (30)	2,047 (34)
80	37,449 (23)	1,459 (19)	1,395 (19)	1,354 (23)
Gender				
Male	123,727 (75)	5,149 (67)	5,456 (74)	4,472 (75)
Female	40,246 (25)	2,582 (33)	1,908 (26)	1,462 (25)
Marital status				
Married	107,565 (65)	3,591 (47)	4,581 (62)	4,166 (70)
Not married	50,388 (31)	3,800 (49)	2,537 (34)	1,601 (27)
Unknown	6,020 (4)	340 (4)	246 (3)	167 (3)
Median income (quartiles)				
Highest quartile	42,011 (26)	1,379 (18)	1,772 (24)	1,193 (20)
3 rd quartile	42,398 (26)	1,691 (22)	1,042 (14)	2,930 (49)
2 nd quartile	38,017 (23)	1,793 (23)	2,994 (41)	1,584 (27)
Lowest quartile	41,541 (25)	2,868 (37)	1,555 (21)	226 (4)
Urban residence				
Metro	142,572 (87)	7,491 (97)	6,853 (93)	5,761 (97)
Non-metro	21,395 (13)	240 (3)	510 (7)	172 (3)
Year of diagnosis				
1975–1979	12,734 (8)	479 (6)	251 (3)	257 (4)
1980–1989	32,373 (20)	1,314 (17)	743 (10)	838 (14)
1990–1999	48,722 (30)	2,372 (31)	2,208 (30)	2,142 (36)
2000–2005	70,144 (43)	3,566 (46)	4,162 (57)	2,697 (45)
Geographic area				
Northeast	33,028 (20)	1,030 (13)	1,004 (14)	200 (3)
South	14,480 (9)	1,623 (21)	162 (2)	75 (1)
Midwest	38,465 (23)	2,262 (29)	222 (3)	88 (1)
West	78,000 (48)	2,816 (37)	5,976 (81)	5,571 (94)
Pathologic stage				
Localized	129,933 (79)	5,329 (69)	5,629 (76)	4,567 (77)

	White n=163,973	Black n=7,731	Hispanic n=7,364	API n=5,934
	n (%)	n (%)	n (%)	n (%)
Regional	29,703 (18)	1,947 (25)	1,444 (20)	1,147 (19)
Distant	4,337 (3)	455 (6)	291 (4)	220 (4)
Pathologic grade				
Well differentiated	28,484 (17)	1,062 (14)	1,224 (16)	833 (14)
Moderately differentiated	60,445 (37)	2,396 (31)	2,705 (37)	1,981 (33)
Poorly differentiated	44,531 (27)	2,482 (32)	1,960 (27)	1,812 (31)
Undifferentiated	18,932 (12)	1,132 (15)	987 (13)	880 (15)
Unknown	11,581 (7)	659 (8)	488 (7)	428 (7)
Primary treatment				
Surgery only	146,785 (91)	6,363 (84)	6,643 (91)	5,277 (89)
Radiation only	640 (1)	99 (1)	31 (1)	48 (1)
Surgery + radiation	8,738 (5)	626 (8)	314 (4)	351 (6)
Other	5,614 (3)	505 (7)	326 (4)	224 (4)

P-values are < .001 for all characteristics.

SEER: Surveillance, Epidemiology and End Results cancer registry; API: Asian/Pacific Islander.

'Other' treatment included strategies that did not involve surgery or radiation therapy, such as observation or systemic chemotherapy.

TABLE 2

5-Year disease-specific survival in SEER bladder cancer patients diagnosed 1975–2005

	% 5-Year Disease-Specific Survival			
	White	Black	Hispanic	API
All	82.8	70.2	80.7	81.9
Pathologic stage				
Localized	92.1	85.9	91.6	92.7
Regional	50.3	41.5	49.7	51.3
Distant	8.4	7.4	7.5	8.2
Pathologic grade				
Well differentiated	97.3	94.2	97.6	97.7
Moderately differentiated	92.7	86.7	92.2	93.0
Poorly differentiated	67.7	51.9	62.4	70.6
Undifferentiated	58.1	48.2	57.6	60.4

SEER: Surveillance, Epidemiology and End Results cancer registry; API: Asian/Pacific Islander.

TABLE 3

Multivariable analysis of cancer-specific death for SEER bladder cancer patients diagnosed 1975 – 2005

Variable	HR (95% CI)	P-value
Age at diagnosis, years		<0.0001
< 50	Referent	
50 – 59	1.36 (1.25 – 1.47)	
60 – 69	1.75 (1.63 – 1.89)	
70 – 79	2.34 (2.17 – 2.51)	
80	3.78 (3.51 – 4.07)	
Ethnicity		<0.0001
White	Referent	
Black	1.29 (1.24 – 1.36)	
Hispanic	1.03 (0.97 – 1.10)	
API	0.95 (0.89 – 1.02)	
Gender		<0.0001
Male	Referent	
Female	1.06 (1.03 – 1.09)	
Marital status		<0.0001
Married	Referent	
Not married	1.26 (1.23 – 1.29)	
Median income		<0.0001
Highest quartile	Referent	
3 rd quartile	1.02 (0.98 – 1.05)	
2 nd quartile	1.10 (1.06 – 1.14)	
Lowest quartile	1.10 (1.05 – 1.14)	
Urban residence		0.02
Metro	Referent	
Non-Metro	0.95 (0.91 – 0.99)	
Geographic area		<0.0001
Northeast	Referent	
South	1.02 (0.97 – 1.07)	
Midwest	1.01 (0.96 – 1.05)	
West	0.95 (0.91 – 0.98)	
Pathologic stage		<0.0001
Localized	Referent	
Regional	4.07 (3.95 – 4.19)	
Distant	15.97 (15.30 – 16.67)	
Pathologic grade		<0.0001

Variable	HR (95% CI)	P-value
Well differentiated	Referent	
Moderately differentiated	2.24 (2.09 – 2.40)	
Poorly differentiated	5.21 (4.87 – 5.58)	
Undifferentiated	5.90 (5.49 – 6.33)	
Unknown	3.59 (3.32 – 3.88)	
Year of diagnosis		<0.0001
1975 – 1979	Referent	
1980 – 1989	0.83 (0.80 – 0.87)	
1990 – 1999	0.74 (0.71 – 0.77)	
2000 – 2005	0.73 (0.70 – 0.77)	
Primary treatment		<0.0001
Surgery	Referent	
Surgery + radiation	1.37 (1.32 – 1.41)	
Radiation only	2.06 (1.89 – 2.24)	
Other	2.11 (1.99 – 2.22)	

SEER: Surveillance, Epidemiology, and End Results cancer registry; API: Asian/Pacific Islander.