Gender and Racial Disparities and All-Cause Mortality in Bladder Cancer Patients in the U.S.

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BACKGROUND

- Sociodemographic characteristics i.e. gender, race, and age at diagnosis affect bladder cancer mortality, plausibly through differences in tumor stage at bladder cancer diagnosis.[1,2,3]
- While bladder cancer incidence is higher in Caucasian Americans compared to African Americans, African American race may predict poor survival irrespective of age, marital status, tumor grade and stage, and treatment received.[2,3]
- More advanced disease at bladder cancer diagnosis and higher bladder cancer mortality is noted in female vs male patients.[3] African American women are more prone to being diagnosed at late stage of bladder cancer and possibly higher mortality.[4]
- Most evidence evaluating differences in mortality across racial/ethnic groups, gender and age at bladder cancer diagnosis is outdated. A gap exists in terms of current evidence regarding any differences in mortality across racial/ethnic groups, gender as well as age at diagnosis of bladder cancer.

OBJECTIVE

- To examine recent data for sociodemographic differences in all-cause mortality among bladder cancer patients.
  - Assess for differences in all-cause mortality among bladder cancer patients in the US across racial/ethnic groups and by gender
  - Determine if age at cancer diagnosis, tumor type or Medicare region influence the association of all-cause mortality with race/ethnicity and gender

METHODS

Design and data source

- This was a retrospective database analysis of U.S. bladder cancer patients treated in the community urology setting
- Data from 31 community urology practices collected in the Precision Point Specialty Bladder Cancer database* were used for this study. The data were de-identified and this study was exempted from an IRB review

Study sample

Inclusion Criteria:

- Diagnosis of bladder cancer between January 01, 2006 to January 31, 2022
- Patients were followed until death, end of clinical activity in the database or data cutoff date of January 31, 2022

Exclusion Criteria

- Patients were excluded for a missing initial bladder cancer diagnosis date or having an initial diagnosis date before January 01, 2006, unidentified gender, missing data on tumor type and missing death date for deceased patients
- Demographic and clinical variables abstracted for the study were gender, race, Medicare ID, and tumor type

Study sample selection

Patients with a Bladder Cancer Diagnosis N=6,265

↓

BC patients diagnosed between Jan 01, 2006 - Jan 31, 2022 N=5,941 (94.8%)

↓

BC Patients who identified as either Male or Female diagnosed between Jan 01, 2006 - Jan 31, 2022 N=5,934 (99.8%)

↓

Male or Female BC patients with complete data on tumor type N=5,922 (99.8%)

↓

Male or Female BC patients with complete data on tumor type and date of death N=5,844 (98.7%)

Outcomes

- The main outcome variable was all-cause survival time. Patients who were diagnosed with bladder cancer and died of all causes were considered 'events'.
- 'Time to event' was the time from the date of initial bladder cancer diagnosis to the time of death
- Bladder cancer patients who had not died during the observation period were considered as 'censored'
- Key explanatory variables: Gender and race. Main covariates: Age at diagnosis, tumor type and Medicare Region
  - Gender was categorized as Male or Female.
  - Race was categorized as Caucasian American, African American, Asian and Other. 'Asian' race was grouped with 'Other'.
  - Age at diagnosis (DxAge) was categorized into <50 years and ≥50 years for statistical analysis
  - Tumor type was grouped into High Risk and Low Risk categories based on the tumor value (t). Tumor values Tis, T0 and T1 were categorized as Low risk while Tumor values of T2, T3, and T4 were categorized as High Risk.
  - Medicare Region referred to associated CMS regional offices and the patients belonged to one of the states covered by that office and were defined as Medicare Regions 2,3,4,5,6, and 10[5]

Statistical analyses

- Descriptive statistics (Mean, median, standard deviation) were used to summarize continuous variables; N, frequency, or % were used to summarized categorical variables.
- Log Ranks Odds of survival test was conducted to study the univariate association of categorical variables with 5-, 10- and 15-year survival of bladder cancer patients
- Chi-square test was used to study bivariate associations between categorical variables
- Cox regression model was used to assess the multivariate relationship between all-cause survival and key outcomes of gender and race adjusting for main covariates i.e. age at diagnosis, tumor risk and Medicare region
- The analysis was performed using SAS system version 9.4 M7 at 5% significance level

BLADDER CANCER

RESULTS

Demographics are shown in Table 1

- A total of 5844 patients were identified; 4486 (76.8%) patients were male and 1358 (23.2%) were females
- The mean age at diagnosis was 51.6 years, median was 51 years
- 4801 (82.2%) patients were Caucasian American, 299 (5.1%) African American, and 744 (12.7%) Other
- Most patients received care in New York (N=3477; 59.5%), followed by Chicago (N=1176; 20.1%), Dallas (N=652 ;11.2%), Seattle (N=302; 5.2%), Atlanta (N=206; 3.5%) and Philadelphia (N=31; 0.5%)
- Bladder cancer was more prevalent in patients 50 years old or older 4171 (71.4%) compared to those younger than 50 years old 1673 (28.6%).
- Diagnosis of low-risk tumor 4491 (76.8%) was more common than of high-risk tumor 1353 (23.2%).
- 460 (7.9%) patients diagnosed with Bladder Cancer died of all-cause mortality. Mean survival was 13.23 years

TABLE 1: Characteristics of patients diagnosed with bladder cancer from 2006 - 2022 (N= 5844)

Gender, n (%)	
Male	4486 (76.8)
Female	1358 (23.2)
Race, n (%)	
Caucasian American	4801 (82.2)
African American	299 (5.1)
Other	744 (12.7)
Medicare Region, n (%)	
2 - New York	3477 (59.5)
3 - Philadelphia	31 (0.5)
4 - Atlanta	206 (3.5)
5 - Chicago	1176 (20.1)
6 - Dallas	652 (11.2)
10 - Seattle	302 (5.2)
Age at diagnosis (yrs.)	
Mean	51.6
Median	51
Mode	53
Age at diagnosis, n (%)	
< 50 years	1673 (28.6)
≥50 years	4171 (71.4)
Tumor Type, n (%)	
Low risk	4491 (76.8)
High risk	1353 (23.2)

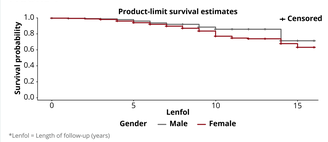
Survival in bladder cancer patients

- 5, 10 and 15-year survival rates in females were better than in males (p=0.0004) as shown in **Figure 1**

TABLE 2: Log rank odds of all-cause survival in bladder cancer patients stratified by gender p=0.0004

All cause survival	Male %	Female %
5-year	94.2	96.2
10-year	77.3	85.9
15-year	63.3	71.6

FIGURE 1



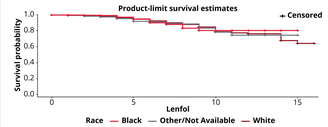
*Lenfol = Length of follow-up (years)

- 5, 10 and 15-year survival did not differ amongst Caucasian American, African American and Other races (p=0.4616) as shown in **Figure 2**

TABLE 3: Log rank odds of all-cause survival in bladder cancer patients stratified by race p=0.4616

All cause survival	Caucasian American	African/Black American	Other
5-year	94.9	94.7	92.2
10-year	79.3	80.7	78.7
15-year	64.7	-	75.0

FIGURE 2



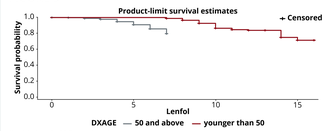
*Lenfol = Length of follow-up (years)

- Bladder cancer patients with age at diagnosis younger than 50 years had better 5, 10 and 15-years survival rates than their older counterparts (p<0.0001) as shown in **Figure 3**

TABLE 4: Log rank odds of all-cause survival in bladder cancer patients stratified by age at diagnosis p<0.0001

All cause survival	younger than 50	50 and above
5-year	98.7	91.1
10-year	86.6	79.8
15-year	71.8	-

FIGURE 3



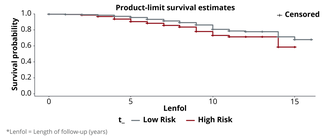
*Lenfol = Length of follow-up (years)

- Patients diagnosed with low-risk tumors had statistically better 5, 10 and 15-year survival rates than patients diagnosed with high-risk tumors (p<0.0001) as shown in **Figure 4**

TABLE 5: Log rank odds of all-cause survival in bladder cancer patients stratified by tumor risk p<0.0001

All cause survival	High risk	Low risk
5-year	90.5	95.8
10-year	73.5	81
15-year	58.8	68.2

FIGURE 4



*Lenfol = Length of follow-up (years)

Stratification by gender is shown in Table 6

- Differences in race were observed between males and females (p-value = 0.0156).
- Both male and female patients were equally likely to develop bladder cancer at ages 50 years or above (p-value = 0.155). Male and female patients had similar distribution in tumor risk categories with more patients being diagnosed with low-risk tumors (p-value = 0.7917).

TABLE 6: Bivariate analysis stratified by gender

	Male N=4486	Female N=1358	p-value
Race, n (%)			**0.0156**
Caucasian American	3718 (82.9)	1083 (79.7)	
African American	213 (4.7)	86 (6.3)	
Other	555 (12.4)	189 (14)	
Medicare Region, n (%)			**0.0992**
2 - New York	2669 (59.5)	808 (59.5)	
3 - Philadelphia	21 (0.5)	10 (0.70)	
4 - Atlanta	169 (3.8)	37 (2.7)	
5 - Chicago	918 (20.4)	258 (19)	
6 - Dallas	488 (10.9)	164 (12.1)	
10 - Seattle	221 (4.9)	81 (6)	
Age at diagnosis, n (%)			**0.155**
Younger than 50	1305 (29.1)	368 (27.1)	
50 and above	3181 (70.9)	990 (72.9)	
Tumor Type, n (%)			
Low risk	3451 (76.9)	1040 (76.6)	0.7917
High risk	1035 (23.1)	318 (23.4)	

Stratification by race is shown in Table 7

- Differences in racial distribution within Medicare regions were observed (p<0.0001).
- Likewise, differences in the proportion of patients diagnosed before age 50 vs after age 50 were observed (p<0.0001). In all race designations, age at diagnosis of 50 years or above was more prevalent than age at diagnosis < 50 years.

TABLE 7: Bivariate analysis stratified by race

	Caucasian American N=4801	Black American N=299	Other N=744	p-value
Medicare Region, n (%)				**p<0.0001**
2 - New York	2706 (56.4)	202 (67.6)	569 (76.5)	
3 - Philadelphia	19 (0.4)	9 (3)	3 (0.4)	
4 - Atlanta	195 (4.1)	4 (1.3)	7 (0.9)	
5 - Chicago	1068 (22.2)	65 (21.7)	43 (5.8)	
6 - Dallas	538 (11.2)	19 (6.4)	95 (12.8)	
10 - Seattle	275 (5.7)	0	27 (3.6)	
Age at diagnosis, n (%)				**p<0.0001**
Younger than 50	1469 (30.6)	68 (22.7)	136 (18.3)	
50 and above	3332 (69.4)	231 (77.3)	608 (81.7)	
Tumor Type, n (%)				**0.067**
Low risk	3718 (77.4)	220 (73.6)	553 (74.3)	
High risk	1083 (22.6)	79 (26.4)	191 (25.7)	

Risk of all-cause bladder cancer mortality is shown in Table 8

- Females diagnosed with bladder cancer had a lower risk of all-cause mortality when compared to their male counterparts (HR=0.649; p=0.0007).
- Risk of all-cause mortality was similar in African Americans as compared to Caucasians (HR=1.022; p=0.9193) and in Other races as compared to Caucasian (HR=1.084; p=0.5806)
- Patients diagnosed with bladder cancer at 50 years old or older had a significantly higher risk of all-cause mortality than their younger counterparts (HR=18.808; p<0.0001).
- Bladder cancer patients diagnosed with high-risk tumor had a higher risk of all-cause mortality than those diagnosed with a low-risk tumor (HR=1.731; p<0.0001).
- Patients diagnosed with bladder cancer in different Medicare regions had similar risk of all-cause mortality

TABLE 8: Cox proportional hazard model for risk of all-cause bladder cancer mortality

Variables	Hazard Ratio	p-value
Gender		
(Reference group, Males)		
Females	0.649	0.0007
Race		
(Reference group, Caucasian Americans)		
Black	1.022	0.9193
Other/Not Available	1.084	0.5806
Age at diagnosis		
More than 50	18.808	p<0.0001
Tumor Type		
(Reference group, Low risk)		
High risk	1.731	p<0.0001
Medicare Region		
(Reference group, 10 - Seattle)		
2 - New York	0.755	0.1364
3 - Philadelphia	0.317	0.2596
4 - Atlanta	1.071	0.8056
5 - Chicago	0.926	0.7096
6 - Dallas	0.297	0.764

LIMITATIONS

- The data provided all-cause mortality and not bladder cancer specific mortality; there was no way to ascertain bladder cancer specific mortality
- Data represent the community urology perspective and may not be representative of other settings
- Information to TNM was not captured, preventing analysis of mortality in relation to tumor grade.

CONCLUSIONS

- This study provides an updated assessment of all–cause mortality in US bladder cancer patients treated in the community urology setting. All-cause survival rates in this population were shown to differ by gender, age at diagnosis, and high vs low tumor risk and suggest that treatment guidelines should consider males, younger age, and high risk tumors at diagnosis.
- There is a need for further investigation into patient journey, socioeconomic status, insurance type, treatment patterns, healthcare patterns and tumor grade, and their association with bladder cancer specific mortality to fully understand the true picture of bladder cancer specific mortality in the US

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FOOTNOTES

* Precision Point Specialty (PPS) Analytics database aggregates data from Electronic Medical Records (EMR), practice management, imaging, and in-office dispensing from a number of US community urology practices.

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