Bladder Cancer Mortality in the United States: A Geographic and Temporal Analysis of Socioeconomic and Environmental Factors

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Abbreviation and Acronym

EPA = Environmental Protection Agency

GIS = geographic information systems

NPCR = National Program of Cancer Registries

Accepted for publication July 27, 2015.

No direct or indirect commercial incentive associated with publishing this article.

The corresponding author certifies that, when applicable, a statement(s) has been included in the manuscript documenting institutional review board, ethics committee or ethical review board study approval; principles of Helsinki Declaration were followed in lieu of formal ethics committee approval; institutional animal care and use committee approval; all human subjects provided written informed consent with guarantees of confidentiality; IRB approved protocol number; animal approved project number.

Supported by Pilot Grant UL1 RR024999 through the National Center for Research Resources.

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Purpose: We assessed the association of temporal, socioeconomic and environmental factors with bladder cancer mortality in the United States. Our hypothesis was that bladder cancer mortality is associated with distinct environmental and socioeconomic factors with effects varying by region, race and gender.

Materials and Methods: NCI (National Cancer Institute) age adjusted, county level bladder cancer mortality data from 1950 to 2007 were analyzed to identify clusters of increased bladder cancer death using the Getis-Ord Gi* statistic. Socioeconomic, clinical and environmental data were assessed using geographically weighted spatial regression analysis adjusting for spatial autocorrelation. County level socioeconomic, clinical and environmental data were obtained from national databases, including the United States Census, CDC (Centers for Disease Control and Prevention), NCHS (National Center for Health Statistics) and County Health Rankings.

Results: Bladder cancer mortality hot spots and risk factors for bladder cancer death differed significantly by gender, race and geographic region. From 1996 to 2007 smoking, unemployment, physically unhealthy days, air pollution ozone days, percent of houses with well water, employment in the mining industry and urban residences were associated with increased rates of bladder cancer mortality ($p < 0.05$). Model fit was significantly improved in hot spots compared to all American counties ($R^2 = 0.20$ vs 0.05).

Conclusions: Environmental and socioeconomic factors affect bladder cancer mortality and effects appear to vary by gender and race. Additionally there were temporal trends of bladder cancer hot spots which, when persistent, should be the focus of individual level studies of occupational and environmental factors.

Key Words: urinary bladder neoplasms, geographic information systems, mortality, risk, environmental exposure

In contrast to lung cancer, bladder cancer mortality has not changed in the last 30 years in the United States despite decreased smoking and increased screening guidelines by the AUA (American Urological Association) and National Comprehensive Cancer Network®.[1] The proportion of patients presenting with advanced disease remains static in certain areas.[2] In addition, bladder cancer is rarely diagnosed at autopsy,

0022-5347/16/1952-0290/0
THE JOURNAL OF UROLOGY®

http://dx.doi.org/10.1016/j.juro.2015.07.091
Vol. 195, 290-296, February 2016
Printed in U.S.A.

distinct from many other malignancies.[3] Therefore, mortality likely reflects the natural history of the disease. Further, bladder cancer is the most expensive cancer to treat per patient from diagnosis to death.[4] There have been national efforts to improve outcomes and better characterize racial and gender disparities.[5,6]

While demographics such as gender and race have been associated with bladder cancer mortality,[7] the risk is also influenced by environmental factors. Almost 90% of patients with bladder cancer are older than 55 years, suggesting occupational and environmental exposures have latency periods before the disease manifests.[8] Exposure to tobacco, aromatics, arsenic, hydrocarbons and other environmental factors have been associated with bladder cancer.[9]

Geographic differences in bladder cancer incidence and mortality have long been noted.[10] While smoking is a well-known risk factor,[11] areas of highest bladder cancer mortality do not necessarily correlate with highest tobacco use.[12] Previous studies describing geographic variability in bladder cancer did not link regional data to risk factors in rigorous fashion.[12] This may be due to multiple reasons, including lack of modeling tools capable of layering multiple potential causes of bladder cancer to regional mortality, data processing limitations for large data sets and availability of data. Addressing these limitations may enhance our understanding of bladder cancer at the population level.

We hypothesized that bladder cancer mortality is associated with environmental and socioeconomic factors with effects varying by region, race and gender. We characterized the geographic variability of bladder cancer mortality based on socioeconomic and environmental factors using GIS technology to integrate data collected along different parameters (eg city, county, regional and state levels) over multiple time points.

METHODS

Data Sources

An ecological study design was used with counties as the geographic units of analyses. Data from 3,109 counties in the contiguous United States were used for which bladder cancer mortality data were available online from the NCI SEER (Surveillance, Epidemiology and End Results) program, and CDC NVSS (National Vital Statistics System) and NPCR.[13] Data were pooled at NCI and NPCR into 3 periods (1950 to 1969, 1970 to 1994 and 1996 to 2007) and grouped by gender and race (black and white). Mortality was reported as the age adjusted average annual death rate per 100,000 people and based on the death certificate address from NPCR. Covariates were obtained from the United States Census Bureau, EPA, BRFSS (Behavioral Risk Factor Surveillance System), County Health Rankings, NCHS, ARF (Area Resource File), SAHIE (Small Area Health Insurance Estimates), SAIPE (Small Area Income and Poverty Estimates), departments of public works or health and CDC. Data from USGS (United States Geological Survey) and EPA included the location, condition and behavior of groundwater, aquifers, well water sources and air pollutants.

Analyses

Geographic Information Systems. Spatial analyses were performed during 3 periods for all contiguous American counties. Depending on the race/gender group fewer than 2% of study counties were excluded from study due to unreported statistics. Analyses were performed using ArcGIS Desktop 10 (Esri®).

Using the Getis-Ord Gi* method geographic hot spots were identified for bladder cancer mortality rates.[14] Gi* is calculated by dividing the sum of values in a spatial neighborhood by the sum of values for the entire study area. The spatial neighborhood of a county was defined as its adjacent counties. The statistical significance of a Gi* result is calculated with a Z-score, which is generated by subtracting the expected Gi* for a random distribution of values from the county Gi* and dividing the result by the square root of the variance for all features in the study area.[15] A hot or cold spot indicates a Z-score greater or less than 1.96 (outside the 95% CI) for a county, representing high or low bladder cancer mortality rates, respectively. For each gender and race combination hot spots were identified at a Z-score greater than 2.58 (greater than 99% CI).

Regression. Multivariable logistic regression analyses were performed to assess correlations of age adjusted bladder cancer mortality rates with socioeconomic, demographic and environmental variables chosen a priori. Most variables were reported as a proportion of the adult population of each region. Exceptions included the number of urologists per 10,000 adults and the Gini score, which accounts for income dispersion where 0 corresponds to perfect equality and 1 corresponds to perfect inequality.[16] Physically unhealthy days are reported as the number of mean unhealthy days per month. Air pollution particulate matter days were defined as 24-hour averages of ambient levels of particulate matter less than 2.5 μ. Air pollution ozone days were considered the average daily maximums of ambient ozone levels from 8-hour blocks. The β coefficients are reported to compare the relative strength of predictors. The Box-Cox transformation was performed to stabilize variance in covariates without normal distributions.

RESULTS

Maps were generated displaying bladder cancer mortality rates by race and gender throughout the United States (fig. 1). The distribution of bladder cancer mortality in the most recent interval (1996 to 2007) varied by gender and race with black men and women more likely to die in the South, Southeast and Northwest. Alternatively white women had the