Original Study

Changing Trends for Suicidal Death in Patients With Bladder Cancer: A 40+ Year Population-level Analysis

Zachary Klaassen,[1,2] Hanan Goldberg,[1] Thenappan Chandrasekar,[1] Karan Arora,[3] Rashid K. Sayyid,[1] Robert J. Hamilton,[1] Neil E. Fleshner,[1] Stephen B. Williams,[4] Christopher J.D. Wallis,[1] Girish S. Kulkarni[1,2]

Abstract

To identify the demographic and clinical factors associated with suicidal death among patients with bladder urothelial carcinoma, patients diagnosed from 1973 to 2013 were identified in the Surveillance, Epidemiology, and End Results database. Using a competing risks model, factors associated with suicidal death included older age, unmarried status, white race, male gender, regional disease, living in the Southeast United States, and not undergoing a radical cystectomy.

Background: Previous studies suggest that patients with bladder cancer (BCa) are at increased risk of suicide compared with the general population. The objective of this study is to improve our understanding of patients at high risk for suicidal death and to better characterize patients at risk of delayed suicide years after diagnosis. **Patients and Methods:** Patients with bladder urothelial carcinoma were identified between 1973 and 2013 using the Surveillance, Epidemiology, and End Results (SEER) database (n = 333,679). Competing risks models were performed to generate hazard ratios (HRs) to identify variables associated with suicidal death. Among patients dying of suicide, logistic regression modelling was used to generate odds ratios (ORs) for factors associated with suicide > 36 months after diagnosis. **Results:** There were 794 patients (0.24%) that died of suicide, 190,734 patients (57.2%) that died from other causes, and 142,151 patients (42.6%) that were alive. Significant factors associated with suicide included diagnosis between 1973 and 1983 (HR, 2.22), unmarried (HR, 1.74), white race (HR, 2.22), male (HR, 6.91), regional disease (HR, 2.49), living in the Southeast United States (HR, 2.43), and not undergoing a radical cystectomy (HR, 1.42). Older age was associated with suicide, whereas younger age was protective. No radical cystectomy (OR, 0.45), older age (OR, 0.32), unmarried status (OR, 0.65), and regional disease (OR, 0.19) were significantly associated with decreased odds of suicidal death > 36 months after diagnosis. **Conclusions:** Those at highest risk for suicidal death include male gender, the elderly, white, unmarried, and patients with nonlocalized disease. These patients may benefit from targeted survivorship care plans.

Clinical Genitourinary Cancer, Vol. ■, No. ■, 1-7
Keywords: Competing risks, Radical cystectomy, SEER, Suicide, Survivorship

Introduction

The majority of patients diagnosed with bladder cancer (BCa) have nonmuscle-invasive bladder cancer (NMIBC), which carries a high risk of recurrence (up to 78% within 5 years of initial resection) and a risk of progression (up to 45% at 5 years from diagnosis).[1] A substantial subset of patients with BCa are thus long-term survivors requiring significant follow-up regimens that are both physically strenuous for the patient and caregivers and also economically challenging. Patients with localized muscle-invasive disease, on the other hand, often undergo a radical cystectomy

[1]Department of Surgery, Division of Urology, University Health Network, Princess Margaret Cancer Centre, Toronto, Ontario, Canada
[2]Institute of Health Policy, Management and Evaluation, University of Toronto, Toronto, Ontario, Canada
[3]St George's University School of Medicine, St George's, Grenada, West Indies
[4]Division of Urology, The University of Texas Medical Branch at Galveston, Galveston, TX

Submitted: Sep 30, 2017; Revised: Dec 27, 2017; Accepted: Dec 29, 2017

Address for correspondence: Zachary Klaassen, MD, Division of Urology, University Health Network, Princess Margaret Cancer Centre, 700 University Ave, 6th Fl, Toronto, Ontario, Canada M5G 1Z5
E-mail contact: zklaassen19@gmail.com

1558-7673/$ - see frontmatter
https://doi.org/10.1016/j.clgc.2017.12.016

(RC) with urinary diversion, a potentially morbid and body dysmorphic procedure in an already comorbid and elderly population.

All groups of patients with nonmetastatic BCa thus experience significant treatment burdens that can be emotionally and psychologically taxing. In fact, previous studies have suggested that patients with genitourinary malignancies,[2,3] specifically patients with BCa,[4,5] are at increased risk of suicide compared with the general population. In a Surveillance, Epidemiology, and End Results (SEER) database study, patients with BCa had a suicide rate nearly 3 times that of the general population (standardized mortality ratio [SMR] for suicide = 2.71 [95% confidence interval (CI), 2.02-3.62]).[4]

Although it is clear that patients with BCa are at higher risk for suicide compared with the general population, the specific factors associated with suicidal death in this highly comorbid population with a potentially aggressive malignancy remain relatively unknown. Furthermore, temporal trends and potential geographic differences in suicide have not been explored. Finally, identification of patients that are at high risk for 'late suicide' after diagnosis, who may benefit the most from a long-term relationship with a psychologist/psychiatrist[6] has not been performed. This study aimed to address these issues.

Materials and Methods

Study Population and Outcome

All patients diagnosed with bladder urothelial carcinoma were identified using the SEER database (1973-2013). The SEER database reports cancer-specific outcomes from specific geographic areas representing 28% of the United States (US) population.[7] Patients were identified utilizing the bladder cancer site code (C67.0-C67.9) and International Classification of Diseases for Oncology codes (8120, 8122, 8123, 8130, 8131) for urothelial carcinoma. Patients were excluded from the sample if they were < 18 years of age (n = 100), had an unknown vital status (n = 247), or insufficient socioeconomic status (SES) information (n = 50), for a final sample size of 333,679. The primary outcome of interest was suicidal death.

Variables of Interest

Demographic variables of interest included age at diagnosis (by decade), gender, race (black vs. white vs. other), marital status (married vs. unmarried), and US geographical region (South vs. West vs. Midwest vs. Northeast). Geographical region was delineated by SEER registry and is provided in the Supplemental Appendix 1 (in the online version). Patients that were single, divorced, widowed, and separated were classified as unmarried. Year of diagnosis was classified as 1973 to 1983, 1984 to 1993, 1994 to 2003, and 2004 to 2013. SES score was calculated as previously described,[8,9] operationalized as quartiles of county-level data (high school education, poverty level, and median family household income [score range 3-12; 3 = highest, 12 = lowest score]), and reported as a median value. Clinicopathologic variables included SEER stage (localized vs. regional vs. distant), RC (yes vs. no), and survival (suicidal death vs. nonsuicidal death vs. alive). Patients were considered to have died of suicide as previously described.[3] Briefly, patients were considered to have died of suicide if the cause of death variable was "Suicide and Self-Inflicted Injury."

Statistical Analysis

Temporal trends in suicidal death were calculated for each decade increment (1973-1983, 1984-1993, 1994-2003, and 2004-2013) and reported as suicide rates per 100,000 person-years of follow-up. A Fine and Gray's sub-distribution competing risks model was performed to generate HRs for variables associated with suicidal death using the covariates described above. The competing risk was mortality, and the model variable selection was exploratory in nature.

Several secondary analyses were performed. Among patients dying of suicide, χ^2 analysis for categorical variables and the Kruskal-Wallis test for continuous variables were used to compare demographic and clinicopathologic variables between patients dying of suicide ≤ 36 months compared with > 36 months after diagnosis. The cut-point of 36 months was selected a priori for 2 reasons: (1) the likelihood of surviving more than 5 years, regardless of disease stage, is 77.5%,[10] thus identifying a meaningful time period for which to classify long-term survivors; (2) older community-dwelling (nononcology) adults participating in programs linked with psychiatric care/support for more than 2 years had a decrease in suicide rate of 48%.[6] To allow for adequate follow-up in this subset analysis (at least 36 months from diagnosis until suicidal death [ie, a landmark analysis with left censoring]), this cohort only included patients diagnosed from 1973 to 2010. Subsequently, logistic regression modelling was used to generate ORs for identification of variables associated with suicide > 36 months after diagnosis, adjusting for the covariates discussed above.

A competing risks model was performed on a subset of patients with SEER regional stage disease (cancer beyond the bladder to nearby lymph nodes or adjacent organs) to assess the impact of RC on patients who were theoretically candidates for RC based on SEER stage. All models were tested for variable multicollinearity, with all variables having a variance inflation factor < 4, thus not collinear. Statistical analyses were performed using SAS 9.4 (SAS Institute, Cary, NC). All tests were 2-sided and with a statistical significance set at $P < .05$.

Results

Factors Associated With Suicidal Death

There were 794 patients (0.24%) that died of suicide, 190,734 patients (57.2%) that died from other causes, and 142,151 patients (42.6%) that were alive (Table 1). Patients aged 60 to 69 and 70 to 79 years comprised more than one-half (65.1%) of the patients dying of suicide, and the majority (94.6%) were men. There was a general decline in suicide rate over the first 3 decades of the study; however, the suicide rate for 2004 to 2013 increased to 39 suicidal deaths per 100,000 person-years of follow-up (Figure 1). Among patients dying of suicide, median time to suicide was 43 months (interquartile range [IQR], 14-93 months).

Competing risk modeling for suicidal death identified diagnosis between 1973 and 1983 as the decade with the strongest likelihood of suicide (vs. 2004-2013: HR, 2.22) (Table 2). Other factors associated with the risk of suicide included: unmarried status (HR, 1.74), white race (vs. black: HR, 2.22), male gender (HR, 6.91),