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Original article

Demographic and socioeconomic predictors of treatment delays, pathologic stage, and survival among patients with penile cancer: A report from the National Cancer Database

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Abstract

Objectives: To evaluate whether socioeconomic factors affect pathologic stage, treatment delays, pathologic upstaging, and overall survival (OS) in patients with penile cancer (PC).

Patients and methods: A total of 13,283 eligible patients diagnosed with PC from 1998 to 2012 were identified from the National Cancer Database. Socioeconomic, demographic and pathologic variables were used in multivariable regression models to identify predictors of pathologic T stage ≥2, pathologic lymph node positivity, cT to pT upstaging, treatment delays, and OS.

Results: A 5-year OS was 61.5% with a median follow-up of 41.7 months. Pathologic T stage ≥2 was identified in 3,521 patients (27.2%), 1,173 (9.2%) had ≥pN1 and 388 (7.9%) experienced cT to pT upstaging. Variables associated with a higher likelihood of pathologic T stage ≥2 included no insurance (OR = 1.79, $P < 0.001$), lower higher education based on zip code (OR = 1.13, $P = 0.027$), black race (OR = 1.17, $P = 0.046$) and Hispanic ethnicity (OR = 1.66, $P < 0.001$). Patients with Hispanic ethnicity (OR = 1.46; $P < 0.001$) or living in nonmetropolitan areas were more likely to have ≥pN1 ($P = 0.001$). Lack of insurance was associated with cT to pT upstaging (OR = 2.05, $P = 0.001$) as was living in an urban vs. metropolitan area (OR = 1.35, $P = 0.031$). In addition to TNM stage, black vs. white race (HR = 1.56, $P < 0.001$), living in an urban vs. metropolitan area (hazard ratio [HR] = 1.18, $P = 0.022$), age (HR = 1.04, $P < 0.001$) and Charlson score (HR = 1.49, $P < 0.001$) were associated with lower OS.

Conclusion: Socioeconomic variables including no insurance, lower education, race, Hispanic ethnicity, and nonmetropolitan residence were found to be poor prognostic factors. Increased educational awareness of this rare disease may help reduce delays in diagnosis, improve prognosis and ultimately prevent deaths among socioeconomically disadvantaged men with PC.

Keywords: National Cancer Database; Penile cancer; Socioeconomic status; Disparities; Overall survival

1. Introduction

Penile cancer (PC) is a rare disease that accounts for approximately 0.2% of male related malignancies annually in the United States, and comprises roughly 1% of all cancers limited to the male genital system [1]. Outside of the United States, this incidence varies significantly. The variance in incidence has been linked to differences in religious practices and socioeconomic conditions [2–4]. The overwhelming majority of PCs are classified as squamous cell carcinoma (SCC) [4–7]. Risk factors for PC include smoking, human papilloma virus infection, phimosis, and lack of neonatal circumcision [4,8,9]. Mortality from this disease is primarily driven by tumor stage, grade, and lymph node involvement [1,10,11].

Factors including awareness, access to care and embarrassment are known to influence the decision to seek medical care and, ultimately survival [12,13]; however, few studies have investigated whether socioeconomic

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factors influence survival and the likelihood that a patient will be diagnosed with more aggressive PC. Identification of those most likely to be diagnosed with these adverse features may facilitate earlier identification, earlier treatment, and ultimately improved survival for these patients. A report from the NCDB published in 2016 by Sharma et al. [13] detailed racial and economic disparities in the treatment of penile SCC, ultimately demonstrating that black men presented with a higher disease stage and had worse survival, and men with private insurance and higher median income had better survival. Our study aims to explore whether socioeconomic factors influence survival, treatment delays, and adverse pathologic features including pathologic T stage ≥2, pathologic node positive disease, and cT to pT upstaging among patients diagnosed with PC. It is our hope that, compared to the aforementioned report from the NCDB, our analysis of a significantly larger cohort of a patients allows for both stronger conclusions to be made on the survival disparities in PC, and importantly investigate potential causes for treatment delays and upstaging of disease.

2. Patients and methods

The National Cancer Database was used to identify 14,395 patients with diagnosed PC. Patients with distant metastases ($n = 311$), no data on curative treatment received ($n = 694$) were excluded from analysis. Patients lacking data on all outcomes analyzed ($n = 107$) including pathologic T and N stage, cT to pT upstaging, time to treatment and overall survival (OS) data were also excluded. There were 13,283 patients with pathologically diagnosed PC from 1998 to 2012 for analysis.

Univariable and multivariable binary logistic regression models were used to identify whether demographic and socioeconomic variables independently predicted pathologic T stage ≥2, pathologic lymph node positivity and pathologic upstaging defined as an increase from <cT1 to >pT1, cT2 to >pT2, and cT3 to >pT3. Univariable and multivariable linear regression models were used to identify predictors of treatment delays defined as the number of days between diagnosis and the first treatment received. This value was log 10 transformed due to violations of the linear regression model assumptions before transformation. A univariable and multivariable cox regression model was used to assess the relationship of these demographic and socioeconomic variables in addition to pathologic TN stage and grade with survival.

Variables evaluated in the regression models included year of diagnosis, age, race, (black, white, and other), patient's primary insurance carrier at the time of initial diagnosis (no insurance vs. any insurance), Charlson-Deyo score, income based on zip code (median household income of the patient's zip code), education based on zip code (percent of adults in the patients residing area without a high school diploma), residential area of the patient (metropolitan, urban, and rural), cancer program type reporting the case (i.e., Community and Academic/Research), region of the cancer program in which the patient was treated, distance from the patient's home to the program reporting the case (miles), histology (SCC vs. non-SCC), pathologic TN stage, and pathologic grade.

The covariate (e.g., age, income, and insurance) was included in the final multivariable model for the outcome analyzed (e.g., OS and upstaging) if in univariable analysis, the covariate was associated with the outcome at the $P < 0.15$ level.

Values for the Charlson-Deyo score were 0, 1, 2 (greater than 1) since the NCDB truncates Charlson-Deyo scores of >1 into 1 category (i.e., 2) due to the low number of patients with a Charlson-Deyo score >1. Charlon-Deyo score was not included in multivariable models for pTN stage or upstaging as this field is not available for patients diagnosed from 1998 to 2002 ($n = 4,183$) but was included in the model for OS due to the clinically significant relationship of comorbidities and OS. The lowest quartile of income (<$38,000) was compared to all other quartiles of income (≥$38,000) and the lowest quartile of education based on zip code (≥21% of adults in the patient's zip code without a high school diploma) was compared to all other quartiles of education (<21% of adults in the patient's zip code without a high school diploma) in the analysis.

Because a multivariable model omits patients with missing data on any covariate included in the model, only patients with complete data for covariates included in the regression model were analyzed for pathologic T stage ($n = 8,717$), pathologic lymph node positive disease ($n = 5,724$), upstaging ($n = 4,723$), treatment delays ($n = 3,065$), and survival ($n = 4,316$). All statistical analyses were conducted in R version 3.1.3 using a 2-tailed significance level of 0.05 for all multivariable models.

3. Results

3.1. Demographic and clinical characteristics

Patient demographic, socioeconomic, and clinical data are presented in Table 1. Median age was 66 years. Most patients were white ($n = 11,399$, 87.3%), 9.7% were Hispanic, most lived in a metropolitan area ($n = 10,334$, 80.8%). No insurance was listed for 718 (5.4%) patients, 2,904 (5.4%) patients were in the lowest quartile of income based on zip code (<$38,000), and 2,864 (22.4%) patients had the lowest education based on zip code. The median distance from the patient's home to the facility reporting the case was 10.3 miles. The distribution of patients treated at community vs. academic/research hospitals was 58.3% and 41.7%, respectively. The most common hospital regions included the South Atlantic (21.2%), East North Central (17.8%), and Mid-Atlantic (14.0%) regions with the