Racial Disparities Differ for African Americans and Hispanics in the Diagnosis and Treatment of Penile Cancer

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OBJECTIVE To evaluate racial disparities in the diagnosis and treatment of penile cancer among a contemporary series of men from a large diverse national data base.

MATERIALS AND METHODS Using the 1998-2012 National Cancer Data Base, all men with squamous cell carcinoma (SCC) were stratified by race and ethnicity. Demographic and disease characteristics were compared between groups. Likelihood of undergoing surgery and type of surgery were compared among patients with nonmetastatic disease. Factors influencing disease stage and treatment type were analyzed with univariate and multivariable logistic regressions. Overall survival was examined with Kaplan-Meier and adjusted Cox proportional hazard models.

RESULTS We identified 12,090 men with penile SCC with median age 66 years (range 18-90). Distribution of patients is as follows: 76.8% Caucasian, 10.2% African American (AA), 8.7% Hispanic. On multivariable analysis, Hispanic men are more likely to present with high-risk (≥T1G3) penile SCC (odds ratio [OR] 1.6; confidence interval [CI] 1.20-2.00; $P = .001$) and tend to undergo penectomy rather than penile-sparing surgery (OR 1.46; CI 1.15-1.85; $P = .002$) for equal stage SCC compared to Caucasian patients. Whereas AA men are less likely to undergo surgery of any type (OR 0.67; CI 0.51-0.87; $P = .003$) and have higher mortality rates than Caucasian patients (hazard ratio 1.25; CI 1.10-1.42; $P < .001$).

CONCLUSION Hispanic men with penile SCC are more likely to present with high-risk disease and undergo more aggressive treatment than Caucasian patients but have comparable survival. AA men are less likely to undergo surgical management of their disease and have higher mortality rates. UROLOGY 96: 22–28, 2016. © 2016 Elsevier Inc.

Penile squamous cell carcinoma (SCC) is a rare malignancy that affects 0.81-2.1 per 100,000 men annually in the United States (US) and northern Europe and represents only 0.1% of invasive malignancies in males in the US.[1,2] Surgery is the mainstay of treatment for this aggressive disease, and survival is poor, with a 5-year relative survival rate of 68%.[3]

Patients of minority race and ethnicity are known to experience poorer quality screening and outcomes for most malignancies, including penile cancer. Analysis of patients diagnosed with penile SCC between 1973 and 1998 revealed that African American (AA) men tended to present at a younger age and with a higher stage of disease.[4] This finding was corroborated by more recent data from the National Cancer Data Base (NCDB).[5] In a subsequent study of the Surveillance, Epidemiology, and End Results (SEER) data base, white Hispanic men had the highest incidence of penile cancer from 1993 to 2002.[6]

Whereas the incidence of penile cancer may be associated with race, the epidemiology of treatment modalities has not been well studied. Surgery is the mainstay of curative-intent therapy for this aggressive malignancy, so identification of potential disparities in surgical management or barriers to care is paramount to early, effective treatment. In prostate cancer research, data from the Cancer of the Prostate Strategic Urologic Research Endeavor, among other studies, revealed that AA men are significantly more likely to undergo nonsurgical treatment for prostate cancer of similar risk profile.[7] Given the low incidence of penile cancer, large databases are required to answer many

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clinical questions about this malignancy. The aim of our study is to evaluate the role of race in penile SCC using a large diverse data base (NCDB), specifically offering insight into the treatment choice for penile cancer among various racial and ethnic groups in the US. We hypothesized that minority patients have adverse disease characteristics at diagnosis and are less likely to undergo surgical treatment for penile SCC.

MATERIALS AND METHODS

Data Collection

We used the 1998 to 2012 NCDB for penile cancer to answer our study question. The NCDB, a joint program of the Commission on Cancer (CoC) and the American College of Surgeons, is a clinical oncology data base with data sourced from over 1500 hospital registries accredited by the CoC in the US and Puerto Rico. NCDB data represent approximately 70% of incident cancer nationally. Because the data set is completely deidentified, our study was exempt by the institutional review board.

Study Population

The penile NCDB was queried for patients diagnosed with penile SCC by histologic ICD-O-3 code 807. We included all pathologic subtypes of SCC and all stages of disease. This search resulted in a study cohort of 12,090 men. Patients with metastatic disease were excluded from analysis of surgical management, resulting in a cohort of 11,531 men with American Joint Committee on Cancer (AJCC) clinical M0 disease.

Study Covariates and Outcomes

Variables analyzed included demographic characteristics, hospital-specific factors, disease stage and grade, treatment factors, and survival. Patient-specific covariates were age, Charlson-Deyo comorbidity index (CCI), race and ethnicity, median household income, education level, insurance status, and degree of rurality or urban influence.[8] Race and ethnicity were consolidated into white non-Hispanic, AA, Hispanic, and other categories. Insurance status was categorized as not insured, private insurance, or government payer.

Hospital-specific covariates included facility type and geographic location. Hospital type was categorized as an academic or community facility, comprehensive cancer center, or other, designated by the CoC.[9] Geographic location was based on US Census divisions and further merged into categories of Northeast, South, Midwest, and West.

Primary outcomes included disease severity at diagnosis and treatment modality by race and other potentially confounding factors. Severity of disease was stratified as low and high risk penile cancer, according to the National Comprehensive Cancer Network.[10] In our analysis, low risk encompassed National Comprehensive Cancer Network low or intermediate-risk penile cancer, including T0, Tis, and T1 grades 1 and 2. High-risk disease included T1 grades 3 and 4 and any T2-4. For analysis of surgical management among the M0 cohort, we first compared having any surgical procedure at the primary site with no surgery. For secondary analysis, treatment was stratified into penectomy (simple or partial, total, and radical) and penile-preservation techniques, including wide local excision, excisional biopsy, electrocautery, and laser ablation or excision.

Secondary outcomes included the use of chemotherapy and radiation, and survival. Survival was determined by vital status at last contact or death.

Statistical Analysis

All outcomes were compared between race groups first by univariate chi-square analysis. Variation in median age at diagnosis by race groups was compared with the Mann-Whitney *U* test. Multivariable logistic regression analysis was employed to adjust for patient and hospital factors. Variables that were statistically significant on univariate analysis ($P < .05$) or clinically relevant were included in the adjusted multivariable logistic regression. Overall survival stratified by race was examined unadjusted with Kaplan-Meier and with adjusted Cox proportional hazard models. Statistical analyses were performed using Stata version 11.2 (StataCorp LP, College Station, TX). All tests with $P < .05$ were considered to be statistically significant.

RESULTS

We identified 12,090 men diagnosed with penile SCC from 1998 to 2012. The median patient age was 66 years (range 18 to 90 years). Distribution of patients is as follows: 76.8% Caucasian, 10.2% AA, and 8.7% Hispanic. The majority of men lived in metropolitan areas (80.7%) and had government-provided insurance coverage (57.1%) (Table 1). Non-Caucasian patients were less likely to have insurance, with Hispanic patients significantly less likely to have insurance than AA men (both $P < .001$).

Penile cancers were most commonly diagnosed as pT1 (29.2%) and grade 2 (32.5%). There were 8.5% (1013 of 11,993) of men who had clinically node positive disease and 1.9% (221 of 11,743) had metastases at diagnosis (Table 1). Non-Caucasian men were significantly younger at diagnosis, and Hispanic patients were younger than AA men (median age: Hispanic 56 years, AA 61 years, Caucasian 68 years; all $P < .001$). Hispanic men were also more likely to be diagnosed with high-risk disease (≥T1 grade 3) (57.4% or 427 of 744 men) than both Caucasian (45.4% or 2876 of 6329) and AA men (47.3% or 390 of 825). On multivariable logistic regression, Hispanic ethnicity remained predictive of more advanced disease, with approximately 50% greater odds of high-risk SCC, adjusting for factors including age and insurance type (Hispanic vs Caucasian: odds ratio [OR] 1.60; confidence interval [CI] 1.33-2.00; $P < .001$; and Hispanic vs AA: OR 1.51; CI 1.20-1.93; $P = .002$) (Table 2). On multivariable analysis, there was no significant difference in disease risk at presentation between Caucasian and AA patients ($P = .558$).

Overall, 91.5% (10,561 of 11,543) of patients with nonmetastatic disease underwent surgery of any type. Penile-sparing techniques were performed in 40.2% (4153 of 10,321), and penectomy was performed in 59.8% of patients (6168 of 10,321). Regional lymph node dissection was performed in 17.0% of men (1634 of 9597). On multivariable analysis, AA men were less likely to undergo penile surgery of any type (90.0% or 1029 of 1144) than Caucasian patients (92.8% or 8125 of 8759), adjusting for patient and hospital factors including age, CCI, insurance status, AJCC T classification, and facility type (OR 0.70; CI 0.51-0.87; $P = .003$) (Table 3).

Factors associated with penectomy rather than penile-sparing techniques on multivariable analysis include