Original Study

National Trends and Predictors of Locally Advanced Penile Cancer in the United States (1998-2012)

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Abstract

Penile squamous cell carcinoma (SCC) is rare in the Western world. We analyzed trends in presentation using the National Cancer Database. Of 5767 patients, cT1 was the most common presentation (40.7%), while 5.9% had locally-advanced disease (cT3-cT4) with increasing proportion over time ($P = .001$). Predictors of advanced presentation were age, comorbidity, and insurance status ($P < .05$ for all). More penile SCC is being diagnosed in the United States with the proportion of those with advanced disease increasing over time. Whether HPV vaccination in the male population will cause correspondent decreases in HPV-related precancerous lesions remains to be seen.

Background: We analyzed the trends in presentation of squamous cell carcinoma (SCC) of the penis and determined the socioeconomic predictors for locally advanced (cT3-cT4) disease in the United States. **Patient and Methods:** The National Cancer Database was queried for patients with clinically nonmetastatic penile SCC and staging available from 1998 to 2012. Temporal trends per tumor stage were evaluated, and a multivariable logistic regression model was used to identify predictors for advanced presentation during the study period. **Results:** A total of 5767 patients with stage $\leq$ T1-T2 (n = 5423) and T3-T4 (n = 344) disease were identified. Increasing trends were noted in all stages of penile SCC with a greater proportion of advanced cases over time ($P = .001$). Significant predictors of advanced presentation were age > 55 years, the presence of comorbidities, and Medicaid or no insurance ($P < .05$ for all). **Conclusion:** More penile SCC is being detected in the United States. Our results have demonstrated older age, presence of comorbidities, and Medicaid or no insurance as potential barriers to early access of care in the male population. Understanding the current socioeconomic gaps could help guide targeted interventions in vulnerable populations.

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Introduction

Squamous cell carcinoma (SCC) of the penis accounts for 95% of penile tumors, with progression and treatment having potentially devastating consequences.[1] It is a highly aggressive malignancy characterized by early locoregional penetration and lymphatic spread.[2] The etiology of penile cancer is multifactorial, with many risk factors recognized to date, including phimosis, smoking, a greater number of sexual partners, chronic inflammatory states, and human papillomavirus (HPV) infection.[3,4]

Until recently, penile cancer had been considered a relatively rare malignancy in the Western world.[5,6] From 1973 to 2002, the overall incidence had been reported to be decreasing in the United

States.[7] However, recent reports of increased rates have been described in other developed nations such as Denmark, the Netherlands, and England.[8-10] Most recently, the first data on high-risk genital HPV prevalence were reported at 23.4% among US males from 2013 to 2014.[11] In the present study, we evaluated contemporary trends in the presentation of clinically localized penile SCC and explored the clinical and socioeconomic factors associated with advanced (T3-T4) presentation using a large nationwide cancer registry.

Patients and Methods

Data Source

The National Cancer Database (NCDB) is a nationwide cancer registry that serves as a comprehensive surveillance resource for cancer care in the United States. The NCDB includes ∼75% of new cancer cases in the United States and collects data from > 1400 hospitals that have cancer treatment programs accredited by the US Commission on Cancer.[12] Institutional review board approval was not required for the present study because no patient, physician, or hospital identifiers were examined.

Study Population

The NCDB was queried for cases of SCC of the penis diagnosed from 1998 to 2012. The histologic type was determined using the International Classification of Diseases for Oncology, 3rd edition. From a population of 9075 men who presented with penile SCC, we identified 6589 men who had presented with clinically localized (cN0M0) disease. After removing those with missing tumor stage (n = 797) and cases coded as T0 (n = 25), the final study population included 5767 evaluable patients (Figure 1).

Definition of Variables

The NCDB reports numerical variables as quartiles. Age was grouped as < 55, 55 to 64, 65 to 74, and ≥ 75 years. Race was

categorized as white, black, other, or unknown. Ethnicity was defined as Spanish/Hispanic origin of any race. Insurance status was defined as the primary insurance carrier at the diagnosis and was categorized as private insurance, Medicaid, Medicare or other government, and uninsured. Facility type was defined as community, comprehensive community, or academic, depending on the case volume and available services. The patients' zip code and 2008 to 2012 American Community Survey data were used to determine the residential area median income quartiles and high school graduation rates, respectively. County residence was categorized as rural, urban, or metropolitan based on population 1 million; respectively. The presence of comorbidities were determined using the Charlson/Deyo score and truncated to 0, 1, or ≥ 2 using the sum of the scores for each of the comorbid conditions listed in the Charlson/Deyo comorbidity score mapping table.[13]
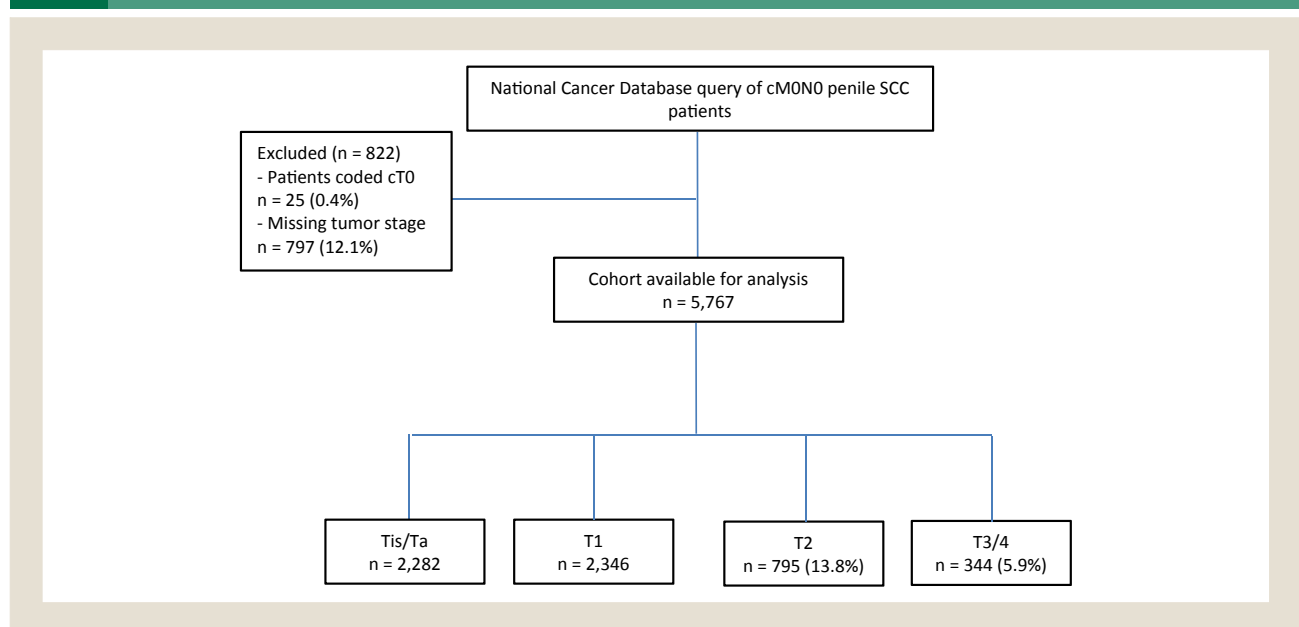
Statistical Analysis

Patient demographic data and clinical characteristics were summarized using descriptive percentages. Univariable analyses were performed using the Pearson χ^2 test for categorical variables. A multivariable logistic regression model was developed to identify predictors of T3-T4 presentation, with an odds ratio (OR) > 1 or < 1 indicating an increasing or decreasing likelihood, respectively. The Cochran-Armitage trend test was used to identify differences in the annual trends. Statistical analyses were performed using the Statistical Package for the Social Sciences software package, version 24 (IBM Corp, Armonk, NY).

Results

Patient and Disease Characteristics

A total of 5767 patients were available for analysis, with the larger groups comprising Tis-Ta and T1 patients (39.6% and 40.7%, respectively) and 344 patients (5.9%) presenting with advanced-stage disease. The median follow-up period from diagnosis to the last

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Figure 1 Flow Diagram Detailing Patient Inclusion and Exclusion for Determining the Analysis Group