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Original article

15 Years of penile cancer management in the United States: An analysis of the use of partial penectomy for localized disease and chemotherapy in the metastatic setting

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Abstract

Background: Penile cancer remains a rare disease in the United States, and its understanding may be limited by the uncommon nature of the malignancy. We sought to describe recent penile cancer treatment patterns using the National Cancer Data Base.

Methods: A retrospective review of data obtained from the National Cancer Data Base from 1998 to 2012 was performed. We obtained demographic information and therapeutic approaches within the following2 clinical scenarios: performance of partial penectomy for early stage disease (clinical Ta–T2) and the use of chemotherapy for metastatic disease. Multivariate logistic analysis was performed.

Results: A total of 2,677 patients presented with early stage penile carcinoma. The proportion receiving partial penectomy increased from 74% in 1998 to 2000 to 80% in 2010 to 2012 ($P < 0.001$). Partial penectomy was more common in the elderly (age > 80, odd ratios [OR] $= 1.53$, 95% CI: 1.05–2.23), young (age < 50, OR $= 1.46$, 95% CI: 1.02–2.07), and in African Americans (OR $= 1.45$, 95% CI: 1.00–2.12). Increasing tumor size was significantly associated with decreased likelihood of receiving partial penectomy. Of those presenting with metastatic disease ($n = 819$), use of chemotherapy increased over the time period from 39% receiving chemotherapy in 1998 to 2000 to 49% in 2010 to 2012 ($P < 0.03$). Patients least likely to receive chemotherapy were older and with higher Comorbidity score (both $P < 0.05$), African American (OR $= 0.46$, 95% CI: 0.30–0.73), and living ≥ 50 miles from the nearest treatment hospital (OR $= 0.37$, 95% CI: 0.25–0.55).

Conclusions: Penile-sparing surgery for early stage disease and the use of chemotherapy for metastatic disease are becoming more commonly utilized over the past several years. Further work is needed to define clinical and nonclinical factors associated with the treatment.

Keywords: Penile cancer; National Cancer Data Base; Chemotherapy; Partial penectomy; United States

1. Introduction

Penile carcinoma (PC) is a rare disease in the United States with approximately 1,500 new diagnoses and over 300 deaths annually [1]. PC often displays a propensity for locoregional spread to lymph nodes and metastatic deposition to distant sites [2]. In fact, for those with advanced disease already involving the pelvic lymph nodes, 5-year survival may be as low as 10% [3]. Owing to the clinical rarity of the disease, the ability to comprehensively study PC in the United States is limited and most of the available literature is based on small-sized, single-institution retrospective reviews. Thus, the aggressive clinical nature combined with the rarity of the condition may contribute, in part, to a lack of available data to study the disease.

Multiple management strategies are available for men with PC. Increasingly, the surgical approach to the primary tumor has focused on penile preservation advocating for broader use of partial penectomy as opposed to radical penectomy [4]. There are now increasing options for management of metastatic disease with the use of various

Data provided by American College of Surgeons: National Cancer Data Base.

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chemotherapy regimens resulting in improved response rates and survival [5]. Whether these strategies have been adopted by the general urology practice in the United States is unknown. To better understand the use of partial penectomy and chemotherapy in PC, we used the data provided by the National Cancer Data Base (NCDB).

2. Methods

2.1. Study sample

This is a retrospective review based on a cohort created from the Commission on Cancer's NCDB from 1998 to 2012. The sample is de-identified patient level data that are Health Insurance Portability and Accountability Act compliant, thus qualified for a waiver of institutional review board approval.

We analyzed patient characteristics, demographic information, and therapeutic approaches within 2 clinical scenarios —(1) use of partial penectomy for early stage (clinical Ta–T2 disease) and (2) use of chemotherapy for metastatic disease. For Scenario 1, the inclusion criteria were cTa–T2 PC cases with either partial or total penectomy ($n = 2{,}677$). Patients treated with no surgery ($n = 362$), ablation ($n = 1{,}551$), or unknown surgery ($n = 65$) were excluded, as were those with no clinical stage reported. For Scenario 2, examining metastatic PC cases, 37 cases with unknown chemotherapy treatment data were excluded for a total of 817 cases in the analysis.

2.2. Outcome measures

For Scenario 1, the dependent variable was surgery type (partial vs. total penectomy) with the primary independent variable being year of diagnosis in categorical 3-year increments (1998–2000, 2001–2003, 2004–2006, 2007–2009, and 2010–2012). For Scenario 2, the dependent variable was receipt of chemotherapy (yes vs. no) with the primary independent variable being year of diagnosis in same categorical format. Secondary independent variables considered included age, race, insurance type, Charlson Comorbidity score, stage (Ta/T1 vs. T2 for first part of analysis only), clinical nodes, distance traveled to hospital (<50 vs. 50+ miles), median income of patient's area of residence, number of high school graduates in patient's area of residence, if facility was academic center, regional location of facility, and urban/rural status of facility. Income and education variables were estimated by matching the zip code of the patient recorded at the time of diagnosis against files derived from year 2000 US Census data. Tumor size was included in the Scenario 1, but not for Scenario 2. Tumor size was grouped into quartiles.

2.3. Statistical analysis

Descriptive statistics were calculated with univariate associations between dependent variable (surgery type or chemotherapy status) and patient characteristics assessed by chi-square. In Scenario 1, multivariate logistic regression models were constructed to identify factors independently associated with partial penectomy. Only variables that were significantly associated with the outcome in the univariate setting were included in the multivariate model. Variables included in the model were year of diagnosis, age, race, academic center, insurance type, clinical T stage, and clinical node status. Variables considered but not found to appreciably alter risk estimates included distance, hospital location variables, socioeconomic status (SES) variables, and comorbidity scores. Stratified logistic models were created by clinical T stage (Ta–T1 vs. T2). A propensity score–adjusted model was also created for likelihood of partial penectomy. Propensity scores were estimated using a probit model with secondary covariates (age, race, Charlson score, SES measures, facility type, insurance type, distance, and urban/rural status) to predict a subject having partial penectomy. The propensity score satisfied the balancing property. Year of diagnosis, clinical stage, and nodal status covariates were not included in the propensity score so that we could independently assess their association with partial penectomy. The estimates of the logistic model using the propensity score as a covariate along with year of diagnosis and clinical covariates did not substantially differ from the logistic model containing all secondary covariates, thus the nonpropensity score–matched model is presented to illustrate risk estimates across all covariates. In Scenario 2, multivariate logistic regression models were constructed to identify factors independently associated with chemotherapy for patients with metastatic disease. Variables included in the model were year of diagnosis, age, race, and distance in miles between the patient's residence and the hospital that reported the case, Charlson Comorbidity score, and clinical node status. Variables considered but not found to appreciably alter risk estimates included hospital location variables, SES variables, and comorbidity scores. All statistical analyses were conducted using Stata, version 13 (Stata, Inc., College Station, TX).

3. Results

Table 1 shows demographic, clinical, and facility characteristics stratified by the treatment parameters of the 2 analysis cohorts. From 1998 to 2010, a total of 2,677 patients who underwent surgery for early stage disease were identified. The proportion receiving partial penectomy increased from 74% in 1998 to 2000 to 80% in 2010 to 2012 ($P < 0.001$). Compared to those aged 50 to 59, partial penectomy was more common in the old (age > 80, odd ratios [OR] = 1.53, 95% CI: 1.05–2.23) and young (age < 50, OR = 1.46, 95% CI: 1.02–2.07). Treatment at academic centers and those without insurance were less likely to receive partial penectomy (both $P < 0.01$), as were patients with cT2 and node-positive disease