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Original article

Disparity between pre-existing management of penile cancer and NCCN guidelines

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Abstract

Objective: To determine the locoregional management of penile cancer before the introduction of NCCN guidelines and how much shift in practice patterns is required to meet the guidelines.

Methods: The National Cancer Data Base was queried to identify 6,396 patients with squamous cell carcinoma of the penis diagnosed between 2004 and 2013. The cohort was divided into management groups based on the NCCN guidelines: cTa and cTis (cTa/is), pT1 low grade (T1LG), pT1 high grade (T1HG), and pT2 or greater (T234). These groups were analyzed to determine if management of locoregional disease complies with the 2016 NCCN guidelines and logistic regression analyses were performed to determine factors associated with adherence.

Results: Nationwide management of the primary tumor closely follows the NCCN guidelines, with 96.9% adherence for cTa/is, 91.4% for T1LG, and 94.2% for T234. Management of regional lymph nodes (LNs) was inadequate with only 62.9% of patients with clinical N1 or N2 disease undergoing regional LN dissection (LND). The percentage of patients with known LN metastases who received regional LND increased over time (46.2% in 2004 to 69.4% in 2013, $P = 0.034$). Patients treated at community cancer programs (odds ratio [OR] = 0.26, 95% CI: 0.19–0.35), comprehensive community cancer programs (OR = 0.34, 95% CI: 0.29–0.41), and integrated network cancer programs (OR = 0.36, 95% CI: 0.25–0.52) were significantly less likely to receive LND compared with patients treated at academic comprehensive cancer programs.

Conclusions: Before the introduction of NCCN guidelines, national practice patterns for the management of the primary tumor were consistent with the recommendations. However, the management of regional LNs deviated from the guidelines, reflecting an area for improvement.

Keywords: Penile cancer; NCCN guidelines; Penile-sparing surgery; Penectomy; Lymph node dissection

1. Introduction

Penile cancer is a rare malignancy, with an incidence of 0.6 per 100,000 in the United States [1,2], accounting for an estimated 0.2% of malignancies in men [3]. The mortality rate is 0.15 per 100,000 in the United States and is higher in African American men compared with that in whites [1,2,4]. Historically, total or partial penectomy with a 2-cm margin was the gold standard of treatment. Recent studies have shown that conservative surgery and smaller surgical margins are oncologically safe, and that local recurrence does not affect survival [5–10]. Additionally, penile-sparing surgery (PSS) offers better cosmetic results, urinary function, and quality of life than total penile amputation [6,7,9,11,12]. In 2013, the National Comprehensive Cancer Network (NCCN) created guidelines for the management of penile cancer, which have since been updated in 2016 [13,14]. These guidelines include the recommendation of organ-sparing surgery for patients with cTis, cTa, and pT1 disease as defined by the 2010 TNM clinical and pathological classification system [13–15].

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For tumors that are T2 or greater, partial or total penectomy is still the recommended therapy [14]. In addition, radiotherapy is an option for stage T1–T4 tumors and chemoradiotherapy may be used for T1b–T4 tumors [14].

Inguinal lymph node (LN) involvement is the most important prognostic factor in penile cancer [16]. The number of positive LNs, the presence of extranodal extension, and the pelvic LN involvement have all been associated with worse 5-year cancer-specific survival [17]. Patients without palpable lymphadenopathy who undergo inguinal lymph node dissection have improved overall survival, showing a benefit for immediate resection of clinically occult LN metastases [16,18,19]. Additionally, survival is improved in patients with unilateral LN metastases who undergo bilateral pelvic lymph node dissection [20]. The 2016 NCCN guidelines provide recommendations suggesting which patients should undergo LN surveillance, inguinal lymph node dissection, or pelvic lymph node dissection [14]. Despite this, one previous population-based study using the SEER database demonstrated an inadequate number of LNs removed in patients undergoing lymph node dissection (LND) for penile cancer and showed better cause-specific survival in patients who underwent more extensive LND [21].

Previous studies have documented the use of conservative surgery at tertiary referral centers [22]. However, the use of PSS and LND nationwide and adherence to NCCN guidelines are largely unknown. The aim of the present study was to use the National Cancer Data Base (NCDB) to determine how closely management of the primary site and regional LN metastases in patients with penile cancer aligned with the subsequently introduced NCCN guidelines.

2. Materials and methods

The NCDB is a collaboration between the Commission on Cancer of the American College of Surgeons and the American Cancer Society. We included all penile squamous cell carcinomas (SCC) from 2004 to 2013 using specific codes for primary site (ICD code C60) and histological subtype (ICD code 807). Only patients with clinical or pathologic AJCC M0 disease and patients with penile SCC confirmed on histology were included. Patients were excluded if their diagnosis was determined at the reporting facility but they received treatment or decision not to treat elsewhere. This resulted in a final cohort of 6,396 cases.

Patient demographic information included age, race, Charlson-Deyo comorbidity index, insurance status, median income quartiles, percentage of the population with a high school degree, facility location (urban, rural, or metropolitan), facility location by region of the United States, and facility type. Severity of disease at diagnosis was determined according to the American Joint Committee on Cancer (AJCC) TNM staging [15]. Facility type was grouped into academic and nonacademic. Nonacademic facilities included community cancer programs, comprehensive community cancer programs, integrated network cancer program, and others. The following disease characteristics were retrieved: tumor grade, pathologic T stage, and clinical N stage.

Patients were stratified by T classification into the following groups: clinical Ta and Tis (cTa/is), pathologic T1 low grade (pT1, grade 1–2), pathologic T1 high grade (pT1, grade 3–4), and pathologic T234 (pT2, T3, or T4; any grade). These groups were chosen based on the treatment groups in the NCCN guidelines for penile cancer (Version 1.2016) [14]. Treatment was categorized as PSS or penectomy (partial, total, or radical). PSS included wide local excision, excisional biopsy, laser therapy, and electrocautery or fulguration. Because some of the steps included in the NCCN guidelines algorithm for regional LND involve variables that are not included in the NCDB, such as LN size and needle biopsy results, we were not able to exactly determine adherence to this section of the guidelines. Rather, we assessed overall trends in LN management. Management of LNs was stratified into regional LND vs. no LND.

Univariate chi-square and multivariable logistic regression analyses were performed to evaluate for associations between disease stage and treatment of both the primary site and regional metastases. We adjusted for clinically significant covariates on multivariable analyses, including AJCC T classification, patient race or ethnicity, Charlson-Deyo score, insurance status, median household income, and hospital type and geographic location. Statistical analyses were performed with Stata version 11.2 (StataCorp LP, College Station, TX). The threshold for statistical significance was defined as $P = 0.05$.

3. Results

We identified 6,396 patients with penile SCC diagnosed between 2004 and 2013. The median age was 65 (range: 54–75) years, and most patients were white (73.9%), had a Charlson-Deyo score of 0 (73.3%), were insured by Medicaid or Medicare (56.5%), and were treated at a metropolitan facility (80.5%) (Table 1). The tumors were most commonly pathologic T1 (29.5%) and clinical N0 (61.1%) (Table 1).

NCCN guidelines recommend that cTa/is penile cancer be treated with a penile-sparing approach, and our data confirm that the vast majority of these patients were being managed with PSS (989 of 1,021 or 96.9%), with only 3.1% (32 of 1,021) undergoing penectomy. For patients with T1 low-grade (T1LG) disease, the guidelines also recommend only PSS, and 91.4% (1,158 of 1,267) of these patients in our study did undergo PSS with no significant change in management over time (88.8% in 2004 to 91.8% in 2013, $P = 0.19$). Penectomy and PSS are both appropriate options for T1 high-grade (T1HG) disease. Our data show