

# National Trends and Predictors of Organ-sparing for Invasive Penile Tumors: Expanding the Therapeutic Window

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## Abstract

**Current guidelines for the management of lower stage penile tumors advocate for organ-sparing whenever oncologically feasible. In this study, we aim to analyze current national trends in organ-sparing treatment as well as evaluate predictors influencing local treatment management. In total, 49% (2073 of 4172) of patients received organ-sparing treatment over the study period ( $P = .009$ ). Demographic and socioeconomic differences were found as predictors in treatment management for these patients. In a subgroup analysis of pT2 patients, older age, black race, comorbidity, node status, and grade were associated with increased overall mortality, whereas organ-sparing did not have an effect (hazard ratio, 0.83; 95% confidence interval, 0.52-1.31) in these patients. More studies are needed to evaluate the oncologic efficacy in select, invasive penile tumors.**

**Introduction:** The purpose of this study was to analyze contemporary trends and predictors in the use of organ-sparing treatment (OST) for low-stage invasive penile tumors as well as to ascertain its impact on overall mortality (OM) in those with high-risk (pT2) disease. **Patients and Methods:** The National Cancer Data Base was queried for patients with clinically nonmetastatic penile cancer and available pathologic tumor (pT) and treatment data from 1998 to 2012. Independent predictors for performance of OST were analyzed. Multivariable Cox proportional hazard regression was used to identify factors of OM in a subset of patients with pT2 disease. **Results:** A total of 4231 patients with  $\leq$  pT2cN0cM0 primary penile cancer were identified over a median follow-up of 39.6 months. Approximately 49% of patients received OST over the study period ( $P = .009$ ). Older age, Hispanic ethnicity, urban counties, academic facilities, and pT2 disease were negative predictors for OST (all  $P < .05$ ), whereas grade and years of diagnosis were associated with increased performance ( $P < .01$ ). In subgroup analysis of pT2 patients, older age, black race, comorbidity, node status, and grade were associated with higher OM (all  $P < .05$ ). When compared with radical penectomy, partial penectomy was associated with decreased OM (hazard ratio, 0.67; 95% confidence interval, 0.52-0.87;  $P = .002$ ), whereas organ-sparing did not affect survival (hazard ratio, 0.83; 95% confidence interval, 0.52-1.31;  $P = .419$ ) in these patients. **Conclusion:** Ethnic and socioeconomic differences exist in the local management of penile tumors. No impact on OM was observed for those with high-risk cases treated with organ-sparing at intermediate follow-up. More studies are needed to evaluate oncologic efficacy of organ-sparing in carefully selected invasive penile tumors.

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## Introduction

Penile cancer is a rare malignancy in the Western world.<sup>1,2</sup> The overall incidence in the United States (US) is approximately 0.69 per 100,000 men, with incidence associated with increasing age at

diagnosis.<sup>3</sup> Approximately 80% of tumors occur on the glans or prepuce, and the most common histology is squamous cell carcinoma.<sup>4</sup> The etiology of penile cancer is multifactorial with many risk factors identified, including phimosis, smoking, chronic inflammatory states, number of sexual partners, and human papillomavirus infection.<sup>5</sup>

The goals of local control include complete tumor removal while achieving negative surgical margins, with a 2-cm clear margin long considered the standard approach to organ-sparing procedures.<sup>5</sup> However, excision margins of only a few millimeters have been widely accepted owing to acceptable oncologic outcomes.<sup>5-7</sup> Thus, the use of organ-sparing treatments (OSTs) in penile cancer have

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## Organ-sparing for Penile Cancer in the United States

been increasingly characterized and recommended for lower stages of the disease.<sup>5,8,9</sup>

OST allows for voiding standing upright and maintaining the ability for sexual intercourse.<sup>10,11</sup> However, studies reporting the survival outcomes of OST are scarce, with few monocentric series reported in the literature to date. In this study, we evaluate contemporary patterns in the surgical management of superficial (pTa/is) and invasive penile tumors (pT1/2) as well as explore clinical and socioeconomic predictors associated with treatment modality. Because current national comprehensive guidelines do not endorse organ-sparing for tumors invading the corporal bodies (pT2),<sup>8</sup> we also aim to assess the incidence of OST in this group of patients and ascertain its impact on overall mortality (OM) using a nationwide cancer registry.

### Patient and Methods

#### Data Source

The National Cancer Data Base (NCDB) is a nationwide cancer registry that serves as a comprehensive surveillance resource for cancer care in the US. The NCDB includes about 70% of new cancers in the US and collects data from more than 1400 hospitals that have cancer treatment programs accredited by the US Commission on Cancer.<sup>12</sup> Institutional review board approval was not required for this study, given that no patient, physician, or hospital identifiers were examined.

#### Study Population

The NCDB was queried for primary squamous cell carcinoma of the penis diagnosed from 1998 to 2012. From a population of 14,395 men, we identified 7340 who presented with clinically localized (cN0M0) disease. We defined organ-confined disease for

verrucous (Ta) or in-situ (Tis) tumors, and those confined to sub-epithelial connective tissue (pT1) or corporal bodies (pT2), but not urethra or surrounding structures (pT3/4) (n = 478). Patients with missing pathology were also excluded (n = 2476). Of the remaining 4386 patients in the cohort, 155 were excluded (treatment data was missing in 95 patients, surgery coded as debulking in 5, or not otherwise specified in 55). A total of 4231 patients were included in the final analysis (Figure 1).

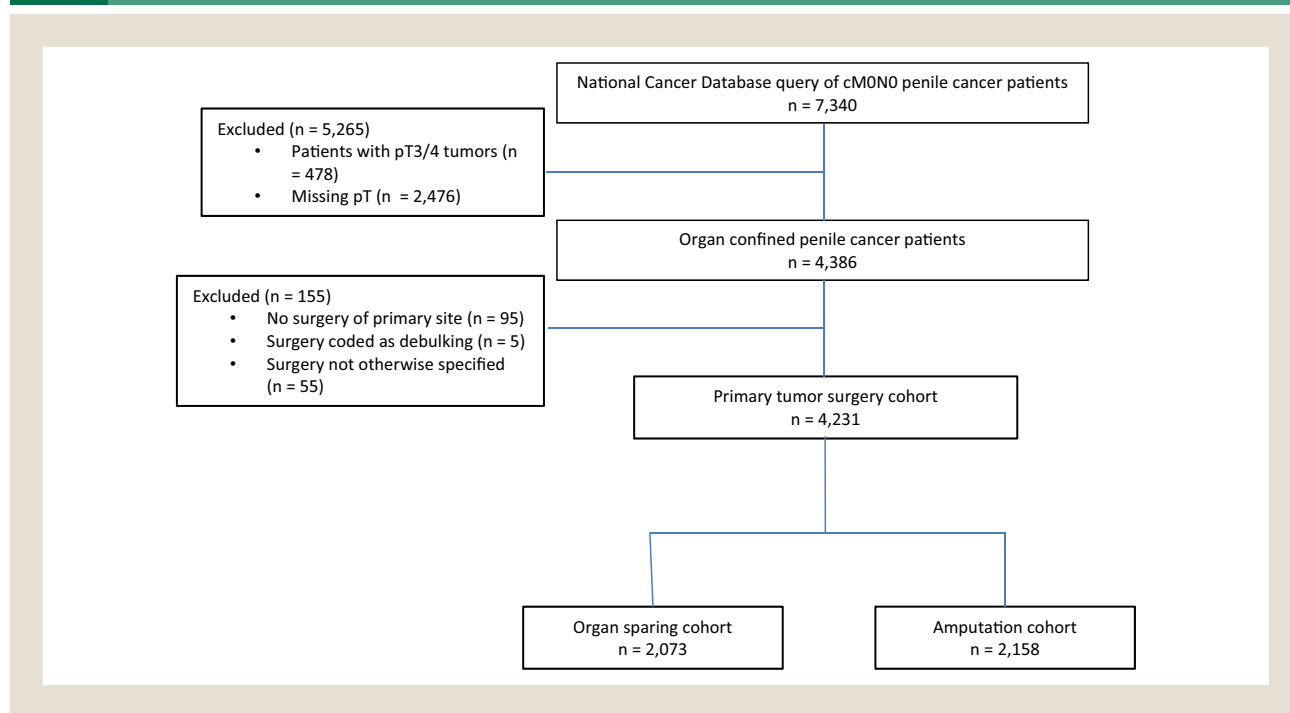
#### Endpoint

Trends and predictors for performance of OST were evaluated across the study period. Organ-sparing was coded as local tumor destruction (ie, laser therapy using neodymium-doped yttrium aluminium garnet or carbon dioxide mediums) or excisional organ-sparing surgery (ie, Mohs surgery, circumcision, glansectomy, and/or glans resurfacing). Amputation was defined as partial or total surgical removal of the penis. A secondary analysis was performed to assess the effect of OST in pT2 patients. Survival time was calculated from date of diagnosis to date of last contact or death from any cause. The NCDB does not specify recurrence or cause of death.

#### Definition of Covariates

Age was grouped as < 55, 55-64, 65-74, or ≥ 75 years. Race was categorized as white, black, or other. Ethnicity was defined as Spanish/Hispanic origin of any race. Insurance status was defined as the primary insurance carrier at the time of diagnosis and was categorized into private insurance, Medicaid, Medicare or other government, and uninsured. Facility type was defined as community, comprehensive community, or academic, depending on case volume and available services. Patients' zip code and 2008 to 2012 American Community Survey data were used to determine

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



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