

Differences in Survival Associated with Performance of Lymph Node Dissection in Patients with Invasive Penile Cancer: Results from the National Cancer Database



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Abbreviations and Acronyms

CCI = Charlson comorbidity index
CoC = Commission on Cancer
I-LND = inguinal lymphadenectomy
NCCN® = National Comprehensive Cancer Network®
NCDB = National Cancer Database
SEER = Surveillance, Epidemiology and End Results

Purpose: Inguinal lymphadenectomy remains under performed in patients with invasive penile cancer. Using a large national cancer registry we assessed temporal trends in inguinal lymphadenectomy performance and evaluated the impact of the procedure on survival in patients in whom inguinal lymphadenectomy was an absolute indication (T1b-4 N0/x-1) according to NCCN® (National Comprehensive Cancer Network®) Guidelines®.

Materials and Methods: We queried the National Cancer Database for all cases of nonmetastatic, T1b-4 N0/x-1 squamous cell carcinoma of the penis from 2004 to 2014. Multivariable logistic regression models adjusting for patient, demographic, and clinicopathological characteristics were used to examine the association between available covariates and receipt of inguinal lymphadenectomy. Cox proportional hazards regression analysis was then done to assess the impact of clinical and pathological variables on overall survival. Propensity score weighted analysis was performed to assess the effect of inguinal lymphadenectomy on overall survival.

Results: A total of 2,224 patients met analysis criteria, of whom 606 (27.2%) underwent inguinal lymphadenectomy. Following adjustment the procedure was more likely in younger patients, those who presented with palpable adenopathy (cN1), those treated at an academic facility and those with a more contemporary diagnosis. On survival analysis controlling for all known and measured confounders inguinal lymphadenectomy was associated with improved overall survival (HR 0.79, 95% CI 0.74–0.84, $p < 0.001$).

Conclusions: At hospitals that report to the National Cancer Database the overall rate of inguinal lymphadenectomy in patients with invasive penile cancer was only 27.2%. Inguinal lymphadenectomy was associated with increased overall survival, justifying the procedure as an important quality metric for performance reporting in patients with invasive penile cancer.

Key Words: penile neoplasms; carcinoma, squamous cell; lymph node excision; mortality; morbidity

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SQUAMOUS cell carcinoma of the penis is a rare condition diagnosed in approximately 1/100,000 men, accounting for less than 1% of cancers diagnosed in men in the United States.¹ Although the disease is rare, it carries significant morbidity and mortality with approximately 50% 5-year cancer specific survival. Given its rarity, the management of penile cancer has been based on small retrospective studies and consequently there is significant variation in the treatment of the disease.

I-LND remains the most important staging and therapeutic intervention that can be performed in patients with invasive penile cancer.^{2,3} Despite this, recent population studies showed that in the United States only 19% to 37% of patients with high grade or invasive penile disease undergo lymphadenectomy as recommended by NCCN Guidelines.^{4,5} A major factor limiting inguinal lymphadenectomy is the high risk of postoperative complications associated with the procedure.⁶ Recent retrospective reports have shown the importance of I-LND in microscopic or low volume nodal disease, prompting the NCCN recommendation that I-LND should be offered to any patient with high grade or invasive penile cancer (pT1b-T4) and who present with no, or unilateral or low volume adenopathy (cN0-N1).⁷ In patients with bilateral (cN2) or bulky (cN3) adenopathy the recommendation is for neoadjuvant chemotherapy followed by I-LND in select candidates.

In this study we assessed the performance of I-LND in patients in whom I-LND was absolutely indicated according to NCCN Guidelines, including those with high grade or invasive penile cancer (T1b-4) with minimal or no nodal involvement (N0/x-N1). We also assessed the association of receipt of I-LND with overall survival using the NCDB.

METHODS

Data Source

The NCDB, a program of the ACS® (American College of Surgeons) CoC and American Cancer Society®, is a national cancer registry established in 1989 which serves as a comprehensive clinical surveillance resource for cancer care in the United States. The NCDB compiles data from more than 1,500 CoC accredited cancer programs in the United States and Puerto Rico, and captures approximately 70% of all newly diagnosed cancer cases.⁸

Definitions

Cohort and Primary Outcome. Patients with penile squamous cell carcinoma were identified in the NCDB based on ICD-O-3 site and histology codes. Cases were selected based on squamous cell histology (8070 and 8071). Our study cohort included patients diagnosed between 2004 and 2014. Men were selected for analysis based on invasive pathology findings, defined as T1b-4, the lack of or unilateral low volume inguinal

adenopathy (N0/x-N1), known surgical excision (partial or radical penectomy) and a known lymph node procedure. Patients who died within 30 days of diagnosis, had clinical N2-3 nodal involvement or metastatic disease at presentation, did not receive treatment at the reporting hospital or had a history of a prior malignancy were excluded from study (fig. 1).

When pathological stage was not available, clinical stage was used. To further limit any coding errors only patients with a reported nodal count were included in the lymphadenectomy group. Any patient with a lymph node count was excluded from the group without lymphadenectomy. Our primary outcome measures were the receipt of inguinal lymphadenectomy and overall survival.

Covariates. Patients were evaluated using the clinical, demographic and pathological characteristics available in the NCDB. Variables included patient characteristics such as year of diagnosis, age, race, Charlson-Deyo comorbidity classification,⁹ insurance status, median household income and demographic location. Disease characteristics included pathological stage and grade, clinical and pathological nodal stage, and receipt of I-LND. Hospital characteristics included facility type and location.

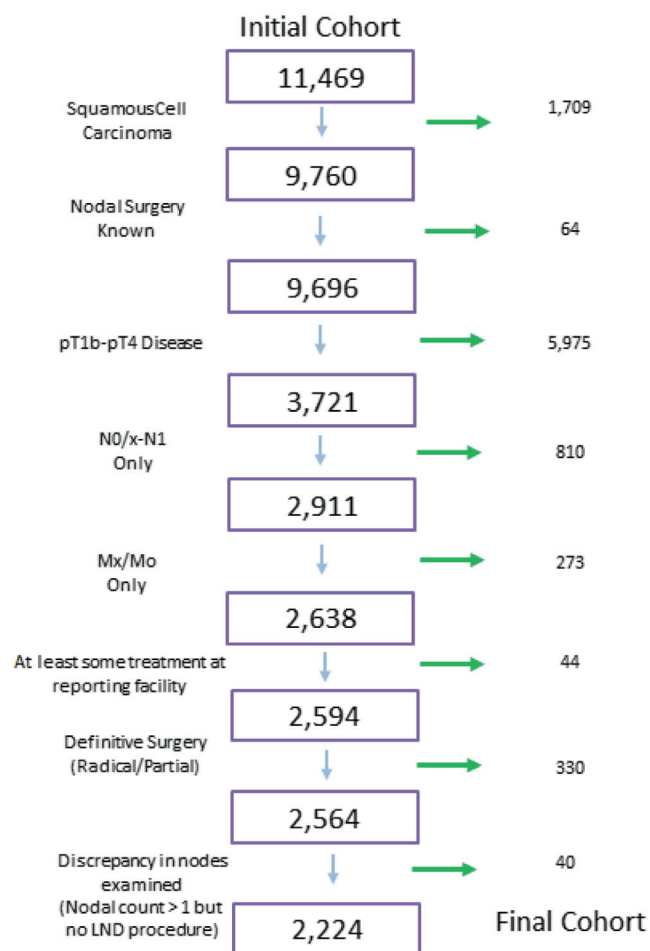


Figure 1. CONSORT (Consolidated Standards of Reporting Trials) diagram shows inclusion criteria for analyzed cohort.

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