



Original article

Lymph node yield as a predictor of overall survival following inguinal lymphadenectomy for penile cancer

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Abstract

Objective: To determine whether a specific lymph node yield (LNY) affects overall survival (OS) in patients with penile cancer.

Materials and Methods: Using the National Cancer Database, we identified 364 men diagnosed with pSCC who underwent ILND between 2004 and 2013. Men diagnosed on autopsy or at the time of death, patients with preoperative chemotherapy or radiotherapy, M+ and N3 disease, or with less than 3-month of follow-up were excluded. Kaplan-Meier analysis was used to compare Overall Survival (OS). A multivariable Cox regression model was developed to assess predictors of OS.

Results: The median number of LN retrieved was 16 (IQR: 9–23). There was no significant difference in race, stage, grade for men with LNY ≤ 15 vs. > 15 . However, men with LNY ≤ 15 were significantly older than those with LNY > 15 (65 vs. 59 years, $p < 0.001$). On multivariable analysis, radical surgery, age, N+ disease, and LNY ≤ 15 were independent predictors of worse OS. Patients with LNY ≤ 15 showed significantly worse 5-year OS versus those with LNY > 15 (49% vs. 67%, $p = 0.008$). Nodal density (ND) $\geq 12.5\%$ was also associated with decreased 5-year OS versus ND $< 12.5\%$ (31% vs. 70%, $p < 0.0001$).

Conclusions: LNY following ILND for pSCC appears to be an independent predictor of OS. A total LNY of > 15 following ILND may have a beneficial impact on OS and serve as the threshold for defining an adequate ILND. © 2018 Elsevier Inc. All rights reserved.

Keywords: Lymph node yield; Penile cancer; National Cancer Database; Inguinal lymphadenectomy; Lymph node dissection

Introduction

Penile cancer is rare in the United States (US) with an incidence of 0.58/100,000 [1]. The majority of cases are squamous cell carcinoma. Management of penile squamous cell carcinoma (pSCC) is based on local invasiveness of the tumor, tumor grade, and staging of regional (inguinal and

pelvic) lymph nodes (LNs) [2]. Involvement of the regional LNs is an adverse pathological finding and has been demonstrated to influence cancer-specific survival (CSS) and overall survival (OS) [3]. Inguinal lymphadenectomy (ILND) is, therefore, an important part of the treatment algorithm for clinically node positive disease (cN+) [4]. In addition, clinically node-negative patients with high-risk

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Table 1
Sociodemographic and treatment characteristics for penile squamous cell carcinoma patients: National Cancer Database 2004–2013

Variable	LNy ≤15 (Row%)	LNy > 15 (Row%)	Total (Col%)	P value
Median age (IQR)	65(55–72)	59(50–70)	62(52–70.5)	0.001
Race				0.955
White	136(43.7)	175(56.3)	311(85.4)	
Black	16(43.2)	21(56.8)	37(10.2)	
Others	7(43.8)	9(56.3)	16(4.4)	
Ethnicity				0.586
Non-Hispanic	126(45.2)	153 (54.8)	279(76.6)	
Hispanic	22 (38.6)	35 (61.4)	57(15.7)	
Unknown	11 (39.3)	17 (60.7)	28(7.7)	
Charlson/Deyo				0.685
0	108 (43.0)	143 (57.0)	251(69.0)	
1	50 (43.2)	50 (56.8)	88(24.2)	
2	13 (52.0)	12 (48.0)	25(6.9)	
Income				0.310
< \$38,000	33 (40.7)	48 (59.3)	81(22.3)	
\$38,000–\$47,999	48 (41.4)	68 (58.6)	116(31.9)	
\$48,000–\$62,999	32 (40.0)	48 (60.0)	80(22.0)	
\$63,000 +	45 (52.3)	41 (47.7)	86(23.6)	
Facility type				0.083
Academic center	93 (40.3)	138 (59.7)	231(63.5)	
Community center	66 (49.6)	67 (50.4)	133(36.5)	
Post-op chemotherapy N (%)				0.595
Yes	18 (40.0)	27 (60.0)	45(12.4)	
No	141 (44.2)	178 (55.8)	319(87.6)	
Post-op radiation N (%)				0.779
Yes	17 (45.9)	20 (54.1)	37(10.2)	
No	142 (43.4)	185 (56.6)	327(89.8)	
Median follow-up (IQR)	27.8(15.7–55)	35(20.6–56.6)	32(18.5–55.7)	N/A

IQR = interquartile range; LNy = lymph node yield.

disease (stage \geq cT1b, moderate to poorly differentiated tumors and presence of lymph vascular invasion (LVI)) may benefit from ILND due to an approximately 23% risk of occult metastases [5,6]. However, there is a limited consensus regarding optimal management and lack of appropriate outcome metrics on the extent of ILND.

Lymph node yield (LNy) has been demonstrated to be a surrogate marker for the quality of Lymph Node Dissection (LND) and oncologic outcome in melanoma, oral, rectal, gastric, and thyroid malignancies [7–11]. Specific thresholds for LNy vary among different malignancies and are used as a metric for surgical adequacy of LND and overall survival [12–15]. In pSCC, there is no consensus regarding specific LNy or, whether a particular number of nodes retrieved has prognostic significance. Johnson et al. reported that a LNy of 8 nodes per groin might be associated with a 5-year OS benefit for pSCC [16]. Similarly, Li et al. assessed data from SEER and demonstrated that a LNy of 16 nodes combined from the regional nodes in node-negative patients might improve OS [17]. However, these findings have not been confirmed by other studies and, a specific threshold for LNy that may impact survival outcome following ILND, has yet to be established.

Despite the integral role of ILND in pSCC management, the limited data regarding LNy precludes any consensus

toward defining an optimal threshold that may serve as a metric for adequate ILND. Furthermore, it is unclear whether a specific LNy has an impact on survival in pSCC. Using the National Cancer Database (NCDB) registry, we sought to assess the quantitative distribution of lymph nodes retrieved following ILND in pSCC and to define an optimal threshold for LNy that impacts OS.

Materials and methods

Patient population

The NCDB is a nationwide oncology registry in the United States, jointly sponsored by the American College of Surgeons and the American Cancer Society. It collects information on 70% of all newly diagnosed invasive cancers [18]. The data from NCDB can be used to conduct clinical studies assessing outcomes related to cancer care. Institutional review board approval was acquired, and the study was classified as exempt as no identifiable data was examined.

Sample population

We identified 10,273 men with pSCC in NCDB diagnosed between 2004 and 2013. Patients who had undergone

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