

Assessing the density of lymph node metastasis in various inguinal regions of penile cancer using the nine-section method: A prospective study

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Abstract. Inguinal lymph node (ILN) metastasis in patients diagnosed with penile squamous cell cancer (PSCC) is a notable factor that leads to a substantial decrease in patient survival rates. Current guidelines differ in terms of the scope of radical ILN dissection (rILND) and a unified consensus has not yet been reached. The present study aimed to optimize the standardized surgical lymph node dissection boundaries for rILND and to explore the rILND range suitable for the population. This prospective study included 26 patients with PSCC who underwent rILND. Anatomically, the ILNs were divided into 9 regions centered on the saphenofemoral junction and the bifurcation of the great saphenous vein, and a detailed pathological examination was performed. Positive ILNs were mainly concentrated in regions 1 and 2; however, 9.1% of positive ILNs were found in the surrounding regions 3, 4 and 7. Region 1 had the highest lymph node metastatic density among all regions. In patients with single or regional lymph node metastasis, positive ILNs were detected in regions 1, 2, 5 and 8. The pathway of ILN metastasis may first invade regions 1, 2, 5 and 8 and

subsequently spread to other areas. Region 1 positivity was preliminarily associated with inferior disease-free survival but was not associated with overall survival. A detailed distribution map of ILNs with metastatic density using the nine-section method was established and an optimized dissection range was formed including region 1. This study was registered with the Chinese Clinical Trial Registry under clinical trial number ChiCTR2200064529 (registration date, 2022-10-11).

Introduction

There is a notable variation in survival rates among individuals diagnosed with penile squamous cell cancer (PSCC). For patients diagnosed with localized PSCC (N0 stage), the 5-year OS rate is ~90% (1). Once the tumor metastasizes to the lymph nodes, the prognosis becomes markedly worse. In a previous study, patients with unilateral inguinal lymph node (ILN) involvement and ≤ 2 lymph nodes (N1 stage) experienced a 5-year OS rate of 80%, those with bilateral or pelvic lymph node involvement (N2 or N3 stage) experienced an OS rate of 10-20% and those patients with extranodal lymph node involvement had a survival rate of <10% (2). Therefore, early diagnosis and treatment are critical factors in determining patient survival (2). Lymph node metastasis is a recognized determinant of prognosis in PSCC, and early radical ILN dissection (rILND) has been reported to confer a survival advantage. For patients with positive lymph nodes, early rILND can achieve a 5-year overall survival (OS) rate of 71-80% compared with those waiting for observation (3-5). However, complications following rILND, such as lymphatic fistula, necessitating prolonged periods with drainage tubes, and occasionally leading to lower limb edema, flap infection/necrosis at the incision site and hernia formation, could significantly impact the patient's quality of life in the long term. Appropriate boundaries for dissection are therefore crucial to ensure tumor-free resection, achieve a complete cure and reduce surgical complications.

In rILND for PSCC, the standards for the extent of resection are not uniform across various guidelines; for example,

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the scope of dissection in Mei Hui Urology (6) surgical area is larger than that in the NCCN guidelines (7). Daseler *et al* (8) introduced the concept of rILND and its approximate boundaries in 1948; however, a detailed summary on the number and anatomical distribution of ILNs remains lacking, especially the locations of pathologically positive nodes (8). This has led to current and ongoing controversy over different surgical approaches for rILND in recent decades (9-14).

When discussing the boundaries of rILND, three main scopes are primarily considered: i) The traditional rILND scope (8) (Fig. 1A; purple outlined area); ii) the standard rILND scope (15) (Fig. 1A; red outlined area); iii) the modified rILND scope (9,12,16) (the external boundary narrowed from the sartorius muscle to the femoral artery, resulting in a smaller dissection range; Fig. 1A; blue outlined area). The controversy surrounding the boundaries of rILND is mainly attributed to the lack of detailed anatomical partitioning data for ILNs and corresponding pathological results.

In the clinical process at Yunnan Cancer Hospital (Kunming, China), it had been observed that, occasionally, there was recurrence and metastasis of the lymph nodes in the area above the pubic bone after bilateral rILND, which is currently excluded in several rILND scopes. Furthermore, it was suggested that the number of all resected lymph nodes, the number of pathologically positive lymph nodes and the lymph node metastasis density after rILND in different regions could guide the surgical strategy, reduce unnecessary dissection ranges, prevent the omission of micro-metastases and reduce the recurrence rate in affected patients.

The present study aimed to optimize the scope of lymphadenectomy, specifically to include the suprapubic lymph nodes. Building upon Daseler's five-region framework, a nine-region model (regions 1-9) is proposed, centered around the saphenous opening and the bifurcation of the great saphenous vein as the key anatomical landmarks. This model involves expanding the superomedial dissection boundary and independently designating the suprapubic area as region 1. By calculating the lymph node metastasis density within each predefined region, the present study sought to achieve a more precise evaluation of metastasis density and patterns, ultimately aiming to reduce unnecessary surgical interventions and improve patient survival rates.

Materials and methods

Study population and ethics statement. The present prospective study enrolled patients diagnosed with PSCC at Yunnan Cancer Hospital between November 2021 and December 2024. All patients provided informed written consent for participation, and the study protocol was approved by the Medical Ethics Committee of Yunnan Cancer Hospital (approval no. KYLX2022051) before data collection. The study was conducted in accordance with the Declaration of Helsinki (2013 revision) and was registered with the Chinese Clinical Trial Registry under the clinical trial number ChiCTR2200064529 (registration date, 2022-10-11). All patients underwent simultaneous or elective (within 3 months) bilateral rILND.

The dissection scope was expanded based on the traditional rILND range (6), with the upper boundary extending

up to 2 cm above the inguinal ligament and the inner upper boundary extending to the pubic symphysis, adding an area in front of the pubic bone (Fig. 1A; black outlined area).

The traditional rILND (Mei Hui Urology) (6) scope includes the following: A line from the external ring to the anterior superior iliac spine; the lateral boundary represented by a line extending 20 cm downward from the anterior superior iliac spine; and the medial boundary, represented by a line extending 15 cm downward from the pubic tubercle (Fig. 1A; purple area).

Inclusion and exclusion criteria. The inclusion criteria were as follows: i) Diagnosed with PSCC and undergoing rILND concurrently/electively; ii) age ≥ 18 years; and iii) willingness to participate in the research protocol and undergo follow-up.

The exclusion criteria were as follows: i) Previous rILND or biopsy; ii) prior systemic treatment (chemotherapy, radiotherapy, immunotherapy, etc.); iii) pathology with other differentiation types; iv) patients with incomplete medical records or unable to obtain required clinical information; and v) patients unwilling to provide clinical information.

In summary, the present study included patients who underwent partial or total penectomy with rILND. All patients had complete imaging information, clinical pathological data and biochemical parameters.

rILND boundaries and the nine-section anatomical division of ILNs. In the present study, the boundaries of rILND are presented in Fig. 1A (black outlined area). The surgical templates proposed by the NCCN (7) and EAU (17) guidelines define the standard scope (superior: inguinal ligament; inferior: saphenofemoral junction; lateral: sartorius muscle; medial: adductor longus muscle) and the modified scope (narrowed laterally to the femoral artery and inferiorly to the femoral canal, with preservation of the great saphenous vein). By contrast, the rILND boundaries in the present study adopted traditional radical margins (8) but further extended this dissection range by expanding the superior boundary to 2 cm above the inguinal ligament and the medial limit to the pubic symphysis, thereby incorporating the prepubic anatomical area. Superficial ILNs were completely removed and zonally diagnosed according to anatomical landmarks (Fig. 1B and C). The inguinal region was divided using the nine-region method as follows: Taking the saphenofemoral junction and the bifurcation of the great saphenous vein as the center, 4 lines (a, b, c and d) were drawn 1 cm above, below, medial, and lateral to this center, respectively, forming 9 regions. Lymph nodes from each region were collected for pathological examination. Line 'a' was located 1 cm medial to the saphenofemoral junction, line 'b' was 1 cm lateral to the saphenofemoral junction, line 'c' was at the level of the midpoint of the inguinal ligament and line 'd' was located at the inferior border of the femoral triangle below the saphenofemoral junction (Fig. 1B and C). Region 1 is an area not included in the dissection ranges recommended by current guidelines, and during surgery, lymph nodes in regions 1 through 9 were each subjected to separate pathological examinations. The anterior and posterior sides, as well as the superior and inferior directions, were marked with sutures or Hem-o-locks. The actual division according to the nine-section method is

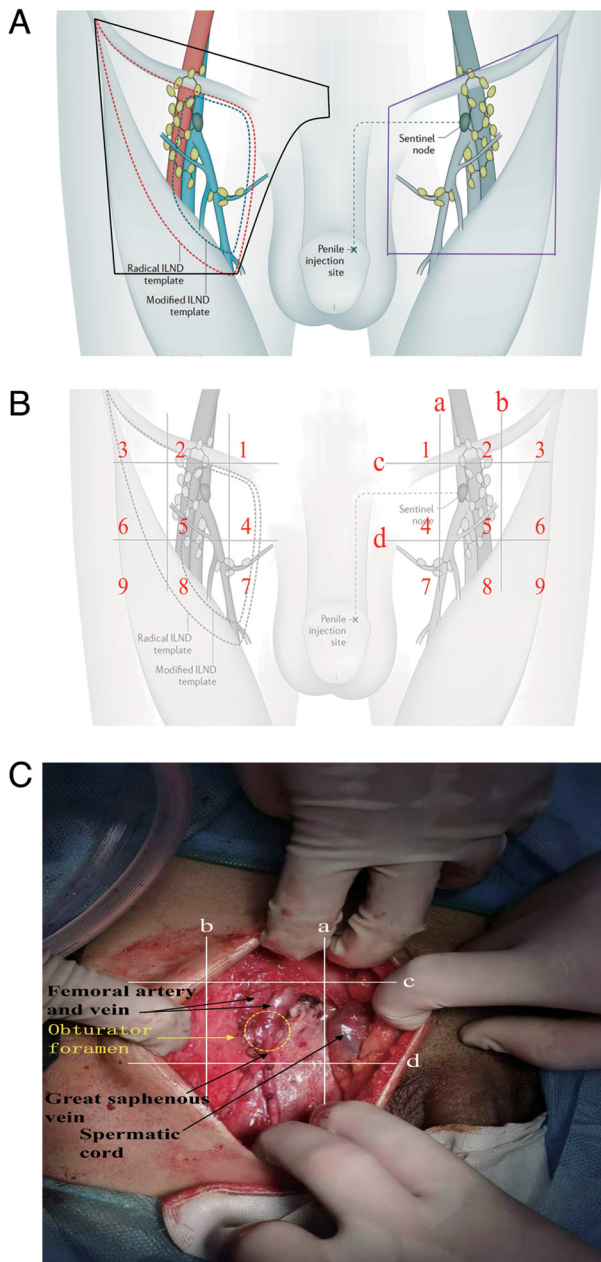


Figure 1. Surgical boundaries of ILND and the regional division of ILNs according to the nine-section method. (A) The area inside the purple line represents the Campbell rILND range. The area inside the red line represents the NCCN radical ILND range. The area inside the blue line represents the NCCN modified ILND range. The area inside the black line represents the nine-section dissection range. (B) The nine-section regional division: Line 'a' is located 1 cm medial to the saphenofemoral junction, line 'b' is located 1 cm lateral to the saphenofemoral junction, line 'c' is at the midpoint level of the inguinal ligament and line 'd' is at the lower edge of the femoral triangle below the saphenofemoral junction. (C) The actual division according to the nine-section method. ILN, inguinal lymph node; ILND, ILN dissection; NCCN, National Comprehensive Cancer Network.

shown in Fig. 1C. The rILND was performed by experienced surgeons with the credentials of Associate Chief Physician or higher. The ILNs harvested after dissection were categorized by trained Resident Physicians to ensure consistency.

Pathological examination. Primary tumors and the 9 regions of ILNs were fixed in 10% neutral buffered formalin at room

temperature for 24 h, cut into 4- μ m sections for standard hematoxylin and eosin staining, and subsequently evaluated under a light microscope at x20 and x100 magnification by experienced genitourinary subspecialty pathologists. All isolated lymph nodes were analyzed using 5-mm-thick longitudinal whole-tissue sections to ascertain the status of lymph node metastasis. Clinical pathological characteristics were documented according to the 8th Edition of the Tumor-Node-Metastasis Staging System for penile cancer (18).

Tx staging was assigned to patients who were referred to Yunnan Cancer Hospital specifically for rILND following initial excision of the primary tumor at an external hospital, where the definitive pathological specimen was retained, thus precluding an accurate T-stage assessment. The T1 category represents a broad classification. This is because the original pathology reports for the specimens obtained after primary tumor resection lacked the detailed descriptions necessary to consistently discriminate among the Tis, Ta and T1 substages. Consequently, the broader T1 category was used in the present study to encompass all non-invasive and early invasive diseases that were not classified as T2 or higher.

Statistical analysis. Data were collected and analyzed using SPSS version 26.0 (IBM Corp.) and R version 4.2.1 (R Core Team, R Foundation for Statistical Computing). The number of lymph nodes is expressed as the mean \pm standard deviation, and differences between groups were compared using unpaired Student's t-test. $P < 0.05$ was considered to indicate a statistically significant difference. Fisher's exact test was used to compare the proportion of positive lymph nodes between the right and left inguinal regions. The Kaplan-Meier method was used to estimate survival curves, and differences between groups were compared with the log-rank test. Multivariate Cox proportional hazards regression models were used to identify independent prognostic factors. The results are presented as hazard ratios (HRs) with corresponding 95% confidence intervals (CIs).

Results

Baseline characteristics of 26 patients with PSCC undergoing rILND. A total of 26 patients with PSCC underwent extended bilateral rILND. Detailed baseline data are summarized in Table I. A total of 8 patients with PSCC (30.8%) were found to have regional lymph node metastasis (pN+). Overall, 26 left-sided and 26 right-sided ILNs were analyzed.

Distribution of resected and positive ILNs in PSCC. In this study, a mean of 18.81 ± 7.22 left ILNs and 18.69 ± 7.35 right ILNs were resected (Fig. 2A; Table II). The number of ILNs in each region was relatively uniform. Comparing the upper and lower regions unilaterally, regions 4, 5 and 6 exhibited a slightly higher number of ILNs. Unilaterally comparing the left and right regions unilaterally, regions 2, 5, and 8 had a slightly higher number of ILNs. However, there was no significant difference between the bilateral groins (Fig. 2A; Table II).

In these cases, 19.2% (5/26) of the right ILNs and 23.1% (6/26) of the left ILNs (Fig. 2B) had metastatic lymph nodes. Notably, region 2 was the most frequently metastatic area, accounting for >40% of patients with pN+, followed by regions

Table I. Baseline characteristics of 26 patients with PSCC^a.

Variables	Value
Median age (IQR), years	54 (41.8-59.5)
pT stage, n (%)	
Tx	15 (57.7)
≤T1	6 (23.1)
T2	2 (7.7)
T3	3 (11.5)
AJCC 8th edition pN, n (%)	
pN0	18 (69.2)
pN1	3 (11.5)
pN2	5 (19.2)
Lymph node dissection method, n (%)	
Unilateral	0 (0.0)
Bilateral	26 (100.0)
pM, n (%)	
pM0	26 (100.0)
pM1	0 (0.0)
Grade, n (%)	
G1	9 (34.6)
G2	13 (50.0)
G3	4 (15.4)
Adjuvant therapy, n (%)	9 (34.6)

^aAll lymph node data were based on pathological diagnosis. PSCC, penile squamous cell carcinoma; IQR, interquartile range; AJCC, American Joint Committee on Cancer; ENE, extranodal extension; pM, pathological metastasis; pN, pathological node; pT, pathological tumor.

1, 5, and 8. Lymph node metastasis in regions 3, 4, 6, 7 and 9 was less common, accounting for 0-20% of patients with pN+. The number of positive ILNs is presented in Table III, with no statistically significant differences shown between the two groups. Region 1 had the highest lymph node metastasis density, followed by regions 2, 5 and 8, with lower densities in regions 3, 4, and 7, and no lymph node metastasis in regions 6 and 9. The metastasis density of ILNs is presented in Fig. 2C. The results indicated that positive ILNs were distributed in most areas within the extended radical boundaries (excluding regions 6 and 9), and were mainly concentrated in the upper medial regions (regions 1 and 2). This suggests that traditional rILND may not achieve adequate tumor-free resection, and that there is an over-resection in the lower lateral areas. Notably, the current guidelines for rILND do not include region 1. Therefore, the results of this study suggested that the boundaries of the dissection range during rILND should be appropriately adjusted based on the traditional boundaries. The upper medial boundary should be extended medially upwards to include the area in front of the pubic bone, to reduce the recurrence rate, while the lower lateral boundary can be appropriately reduced to minimize unnecessary damage and surgical complications. The lymph node dissection range recommended by the present study is shown in Fig. 2D.

Table II. Mean number of lymph nodes dissected in each region.

Region	Right ILNs (n=26)	Left ILNs (n=26)	P-value
Total	18.69±7.35	18.81±7.22	0.985
Region 1	0.85±1.52	1.50±1.68	0.147
Region 2	1.96±2.46	2.35±2.06	0.543
Region 3	1.69±2.11	2.15±2.11	0.434
Region 4	2.38±2.10	1.96±1.71	0.429
Region 5	3.23±2.25	4.04±3.01	0.279
Region 6	2.62±2.56	2.27±2.20	0.604
Region 7	1.65±1.85	1.42±2.16	0.681
Region 8	2.46±2.27	2.00±2.64	0.502
Region 9	1.85±1.76	1.04±1.68	0.097

ILN, inguinal lymph node.

Table III. Number of positive lymph nodes.

Region	Positive right ILNs (n=5)	Positive left ILNs (n=6)	P-value
Case	5/26 (19.2%)	6/26 (23.1%)	0.711
Total	0.35±0.85	0.35±0.75	1.000
Region 1	0.08±0.27	0.08±0.27	1.000
Region 2	0.08±0.27	0.12±0.33	0.646
Region 3	0.04 ±0.20	0.00±0.00	0.327
Region 4	0.04 ±0.20	0.00±0.00	0.327
Region 5	0.04±0.20	0.04±0.20	1.000
Region 6	0.00±0.00	0.00±0.00	-
Region 7	0.04±0.20	0.00±0.00	0.327
Region 8	0.04±0.20	0.04±0.20	1.000
Region 9	0.00±0.00	0.00±0.00	-

ILN, inguinal lymph node.

First station metastasis distribution of single positive ILN or region and lymphatic drainage patterns. The sentinel lymph node is the first lymph node on the lymphatic drainage pathway of the primary tumor, acting as a barrier to prevent the spread of tumor cells through the lymphatic system (17,19,20). During the process of cancer dissemination, cancer cells typically first metastasize to this lymph node, making the sentinel lymph node the first stop for cancer cells to spread from the primary tumor area to other locations (17,19,20). The metastatic pathway of PSCC usually first flows through the superficial lymphatics of the penis to the superficial ILNs, then transfers downward to the deep ILNs, where it finally reaches the iliac lymph nodes (21).

In the present study, single metastatic lymph nodes in the unilateral inguinal region were analyzed to obtain direct pathological evidence regarding the distribution of the first positive sentinel lymph nodes in the superficial ILNs of PSCC

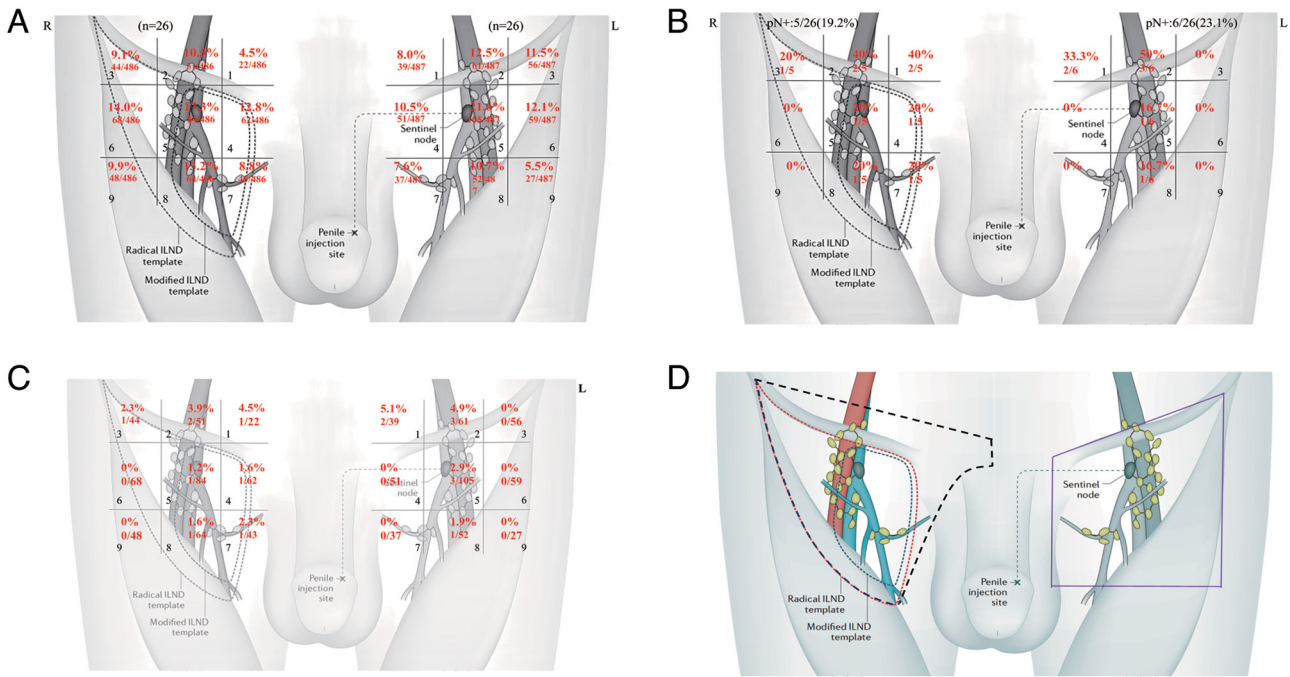


Figure 2. Proportions, quantities and lymph node metastasis densities of dissected or positive ILNs. (A) Total number and proportion of dissected lymph nodes. (B) Proportion of patients with positive lymph nodes. (C) Lymph node metastasis density. (D) The ILN dissection range recommended in this study (dashed black outlined area). ILN, inguinal lymph node.

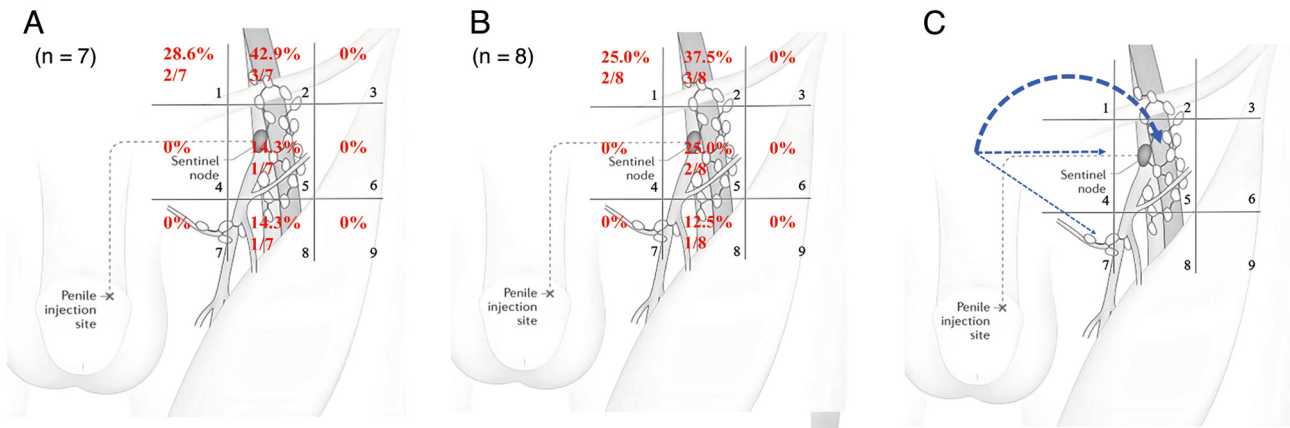


Figure 3. Distribution of single-positive and first-station positive ILNs. (A) Single positive ILN distribution. (B) Single positive region distribution. (C) Lymphatic drainage patterns of ILNs in penile squamous cell cancer. Blue arrows represent the areas where the first-station positive lymph nodes may occur, with thicker lines indicating a higher probability. ILN, inguinal lymph node.

(Fig. 3A). In this study cohort, 7 cases that fulfilled the criteria for a single positive lymph node in the inguinal region were analyzed separately (Fig. 3A). The distribution of single-positive lymph nodes included regions 1, 2, 5 and 8. Region 2 was the most frequent site for positive lymph nodes, accounting for 42.9%, followed by regions 1, 5 and 8, which accounted for 28.6, 14.3 and 14.3%, respectively (Fig. 3A). Additionally, the location of the first-station metastatic region in each inguinal region was investigated, which was defined as the only metastatic region in each inguinal region (Fig. 3B). It was found that the first-station metastatic regions occurred in regions 1, 2, 5 and 8. Region 2 was the most common, accounting for 37.5%, followed by regions 1, 5 and 8, which accounted for 25.0, 25.0 and 12.5%, respectively (Fig. 3B). Based on the

current data, it was possible to infer the potential lymphatic metastatic pathway involved according to postoperative pathological findings, and further studies may be conducted using a dynamic sentinel node biopsy approach (Fig. 3C).

Region 1 had a high proportion of positive sentinel lymph nodes, and the traditional rILND had limitations in the medial upper boundary of the dissection range, which may omit metastatic lymph nodes. This finding is of importance for the treatment strategy of PSCC, as it suggests that it may be necessary to reevaluate and adjust the scope of rLND to ensure more effective treatment outcomes.

Region 1 lymph node positivity is a risk factor for a poor prognosis. With a median follow-up time of 30 months

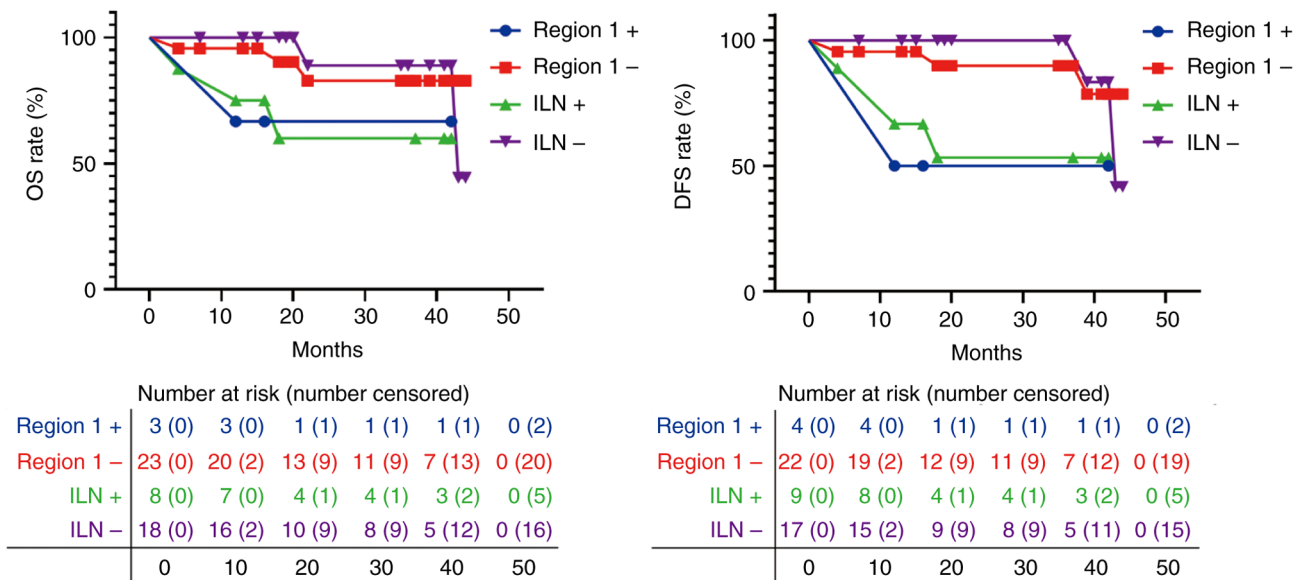


Figure 4. K-M analyses of lymph node-negative, lymph node-positive, region 1 lymph node-negative and region 1 lymph node-positive statuses. OS, overall survival; DFS, disease-free survival; K-M, Kaplan-Meier; HR, hazard ratio; CI, confidence interval; ILN, inguinal lymph node.

(interquartile range, 16.0-63.5 months) for the 26 enrolled patients, 5 experienced recurrence and 4 died. Kaplan-Meier survival analysis revealed that ILN positivity was associated with inferior OS (HR, 8.9; 95% CI, 1.0-76.3; log-rank P=0.0207) and inferior DFS (HR, 8.7; 95% CI, 1.3-57.6; log-rank P=0.0082) compared with ILN negativity. Region 1 positivity was preliminarily associated with inferior DFS (HR, 11.0; 95% CI, 0.8-152.3; log-rank P=0.0464), but not associated with OS (HR, 6.4; 95% CI, 0.2-188.0; log-rank P=0.2342) compared with region 1 negativity, as shown in Fig. 4 and Table IV.

Discussion

ILN metastasis is a notable prognostic factor in patients with PSCC. According to the NCCN (16) and EAU guidelines (17,22), patients with intermediate to high-risk PSCC should undergo concurrent rILND, which has a significant curative value for the treatment of early- to intermediate-stage disease. However, there is currently no international consensus regarding the extent of rILND, and incomplete dissection may lead to tumor recurrence and affect treatment outcomes.

Since the concept of rILND was introduced by Daseler *et al* (8) in 1948, the optimal boundaries of rILND have been controversial due to a lack of high-quality pathological data from patients with PSCC (9-14,23). The root of this controversy is in the scarcity of clinical evidence regarding the distribution and metastatic patterns of ILNs in PSCC (14). In 2024, a retrospective summary was conducted for clinical pathological data from 414 patients with PSCC who underwent concurrent rILND, and for the first time, the distribution of ILNs in PSCC was mapped, particularly the distribution patterns of pathologically positive lymph nodes (14). It was concluded that the upper part of the lymph nodes had the highest positivity rate for metastatic disease, which is similar to the conclusion of the present study. It was also found that the upper inner part of the saphenofemoral junction had the

highest positivity rate (51.7%) (14), a location similar to region 1 in this study, thus indirectly demonstrating the importance of region 1.

At Yunnan Cancer Hospital, occasional lymph node recurrence and metastasis have been observed in the area anterior to the pubic bone, which is currently excluded from the existing rILND ranges. Incomplete rILND may lead to cancer recurrence in the inguinal region, which may become an extremely serious situation. Even when patients undergo salvage rILND, nearly one-half of the patients die after ~16.4 months, and these patients also experience more complications (24). To explore more effective dissection boundaries and improve the treatment outcomes of PSCC, Yunnan Cancer Hospital has adopted a method of extending rILND boundaries, including the area anterior to the pubic bone, and pioneered the nine-section method to clarify the number of lymph nodes, positivity rate and lymph node density in each region, aiming to further clarify the standard of radical dissection range of ILNs to ensure the best tumor control effect for patients.

Within the expanded radical dissection boundaries, ILNs appeared anywhere within the observed boundaries (in all 9 regions), with a cross-shaped distribution of ILNs, high density in the central areas and lower density in the peripheral areas. A greater number of ILNs were located in the central regions of 2, 4, 5, 6 and 8; however, up to 4.5-8.0% of ILNs were found in the superior medial area of region 1. Compared with the five and six-region division methods, the further anatomical division refined the superficial ILNs (regions 1-9), appropriately extending the upper boundary of the dissection range on the traditional boundaries, and adding the ILNs in the anterior region of the pubic symphysis (region 1).

Additionally, the results confirmed to some extent the safety and feasibility of the reduced rILND proposed by Catalonia (15) and the common femoral triangle-limited laparoscopic rILND in the laparoscopic era, which narrowed the lateral boundary of dissection. More importantly, it was

Table IV. K-M and Cox regression model for OS and DFS.

Variables	OS				DFS			
	K-M analysis		Cox		K-M analysis		Cox	
	HR	95% CI	P-value	P-value	HR	95% CI	P-value	P-value
Age, years								
<52	Reference	0.113-5.828	0.847	0.482	Reference	0.103-5.621	0.928	0.968
≥52	0.811				0.761			
Smoking status								
No	Reference		0.002	0.268	Reference		0.002	0.218
Yes	44.045	4.726-410.513			30.902	3.538-269.931		
N stage								
0	Reference			0.011	Reference			0.093
1	10.421	0.259-418.398	0.085	0.003	15.245	0.305-761.467	0.172	0.030
2	21.503	1.211-381.795	0.014	0.099	18.021	1.072-302.871	0.052	0.285
Histological type								
Well-differentiated	Reference			0.321	Reference			0.191
Moderately differentiated	4.752	0.405-55.753	0.220	0.151	5.561	0.516-59.907	0.165	0.074
Poorly differentiated	25.790	0.369-1802.026	0.134	0.216	25.79	0.369-1802.026	0.134	0.139
Total number of left ILNs								
<18	Reference	0.123-6.377	0.885	0.529	Reference	0.144-7.600	0.823	0.899
≥18	0.885				1.046			
Total number of right ILNs								
<18	Reference	0.555-30.080	0.156	0.463	Reference	0.634-37.659	0.090	0.162
≥18	4.084				4.885			
Total number of ILNs								
<37	Reference	0.212-11.938	0.691	0.868	Reference	0.242-15.375	0.429	0.443
≥37	1.589				1.930			
Region 1-positive								
No	Reference	0.218-188.016	0.234	0.097	Reference	0.792-152.282	0.046	0.285
Yes	6.405				10.984			
ILN-positive								
No	Reference	1.036-76.260	0.021	0.003	Reference	1.329-57.558	0.008	0.030
Yes	8.889				8.747			

K-M, Kaplan-Meier; OS, overall survival; DFS, disease-free survival; HR, hazard ratio; CI, confidence interval.

confirmed that metastatic ILNs could be found in region 1, which is not included in the traditional rILND range. This suggested the necessity of including the anterior region of the pubic symphysis (region 1) in the rILND range.

Penile cancer has a relatively low incidence rate, with only 87 patients with penile cancer treated at Yunnan Cancer Hospital between November 2021 and December 2024. Among these, 48 patients fulfilled the inclusion criteria and, after applying the exclusion criteria, 26 remained. The small sample size may have resulted in statistical bias. In small cohorts, the Cox model often yields excessively wide confidence intervals (95% CI, 0.8-52.3), resulting in insufficient statistical power to confirm the significance of the hazard ratio. Consequently, the prognostic value of region 1 positivity is interpreted as a preliminary clinical trend that warrants further validation in larger, multicenter cohorts. Therefore, future studies may require multi-center collaboration to obtain more reliable and generalizable findings. Compared with the traditional dissection range, the inclusion of region 1 in the surgical field may increase the potential risks of retropublic lymphatic leakage, infection, flap necrosis and hernia formation. Since all enrolled patients to date have developed ≥ 1 of these complications, further studies with an expanded sample size and using the standardized complication grading systems are necessary to confirm these findings. Future investigations will also integrate surgical optimizations from multiple centers to determine the most effective surgical approach (such as single-port laparoscopic techniques) (25) and the optimal dissection range.

In summary, the present study used the nine-section method to detail the distribution of ILNs in PSCC, firstly including the pubic symphysis area in the rILND range for PSCC, and provided direct pathological evidence of the distribution of ILNs in PSCC. The results of the study emphasized the necessity of including the area anterior to the pubic symphysis in the dissection range and adjusting the traditional dissection boundaries to reduce recurrence rates and surgical complications. These findings provide clinical guidance for optimizing surgical strategies for treating PSCC.

In conclusion, a metastatic density map of ILN metastases in penile cancer was established using a the nine-section method. Region 1 contained positive lymph nodes and was recommended for surgical inclusion. Regions 1, 2, 5 and 8 may be the first-station regions of ILN metastasis. Region 1 positivity was preliminarily associated with inferior DFS.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

CH was responsible for study design, conceptualization, methodology, access to and verification of the underlying data, formal analysis, validation, visualization, writing of the original draft, and reviewing and editing of the manuscript. LD performed database establishment, statistical analysis and visualisation, and writing, reviewing and editing of the manuscript. HW was responsible for conceptualization. YB was responsible for the literature search and methodology and performed the surgical resection. HY, YB, HJ, WW, JL performed sample collection, management and labeling. RL performed the surgical resection and project supervision. HS was responsible for conceptualization, reviewing and editing of the manuscript, project supervision, administration and funding acquisition. All authors have read and approved the final manuscript. CH and HS confirm the authenticity of all the raw data.

Ethics approval and consent to participate

The study was approved by the Ethics Committee of Yunnan Cancer Hospital (Kunming, China; approval no. KYLX2022051) and was registered with the Chinese Clinical Trial Registry, with the clinical trial number ChiCTR2200064529 (registration date, 2022-10-11). All patients have provided consent for participation.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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