

Prospectively Packaged Ilioinguinal Lymphadenectomy for Penile Cancer: The Disseminative Pattern of Lymph Node Metastasis

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Purpose: We prospectively evaluated the disseminative pattern of lymph node metastasis in penile cancer cases using packaged lymphadenectomy. In addition, we analyzed prognostic factors of the extent of lymph node metastasis.

Materials and Methods: Packaged inguinal lymphadenectomy was performed in 46 patients. A total of 24 patients with 1 or more positive inguinal lymph nodes underwent packaged iliac lymphadenectomy. Inguinal lymphadenectomy was divided into 3 packages, including medial inguinal, lateral inguinal and Cloquet's node packages. Medial and lateral inguinal packages were separated by the lateral surface of the femoral artery and the saphenous vein. Iliac lymphadenectomy was divided into 3 packages, including external iliac, obturator and common iliac packages. Clinicopathological features of the primary tumor and lymph nodes were correlated with the extent of lymph node metastasis.

Results: Of 92 groin basins 27 cases of inguinal lymphadenectomy and 7 of iliac lymphadenectomy had lymph node metastasis. Medial inguinal and external iliac packages were the most common involved regions in inguinal and iliac lymphadenectomy cases, respectively. No extended lymph node metastasis was observed in the absence of positive lymph nodes in the medial inguinal package. In groin basins with lymph node metastasis in the medial inguinal package extranodal extension was a significant predictor of extended lymph node metastasis. Cloquet's node was associated with iliac lymph node metastasis on univariate analysis. However, it was of limited predictive value in patients with 1 or 2 positive inguinal lymph nodes.

Conclusions: The medial inguinal package defined in our study was the first involved lymph node region in penile cancer cases. Extranodal extension was an important predictor of extended lymph node metastasis beyond the medial inguinal package.

Key Words: penis, penile neoplasms, neoplasm metastasis, lymph nodes, lymph node excision

IDEAL management of ilioinguinal LNs in patients with penile cancer is one of the concerns of greatest contention. Two major issues are the treatment of choice for cN0 cases and the extent of dissection in pN+ cases. Recently groups from 2 collaborative European

institutions reported that DSNB had 94% sensitivity for detecting micro-metastatic nodal disease in 599 cN0 groins.¹ However, their promising microinvasive technique requires ultrasound, nuclear imaging, surgical exploration and meticulous pathological

Abbreviations and Acronyms

DSNB = dynamic sentinel node biopsy

EAU = European Association of Urology

LN = lymph node

LNM = LN metastasis

MIL = modified inguinal lymphadenectomy

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Study received institutional ethics committee approval.

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examination.² Although inguinal LN dissection is associated with significant morbidity, it is a more practical staging approach when an experienced multidisciplinary team is absent. MIL, which was first introduced by Catalonia, was suggested to be an alternative choice for the possible balance between survival benefit and adverse effects.³ Although some investigators have reported the clinical outcome of MIL,^{4,5} the rationale and indications for this technique are still under discussion. In patients with inguinal pN+ disease the decision to perform iliac LN dissection and its extent are other open questions.

Our retrospective study has demonstrated that Cloquet's node could not predict microscopic pelvic LNM.⁶ To address the disseminative pattern of LNM in patients with penile cancer we prospectively evaluated a series of patients undergoing packaged ilioinguinal lymphadenectomy.

MATERIALS AND METHODS

Between January 2006 and January 2008 packaged lymphadenectomy was prospectively performed in 46 patients with penile cancer. Those who received neoadjuvant chemotherapy or underwent palliative surgery were excluded from study. Informed consent was obtained from all patients and the protocol was approved by the institutional ethics committee.

The primary tumor was managed by local excision in 8 patients, and by partial (32) and total (6) penectomy according to the depth of invasion, size and patient attitude toward postoperative sexual dysfunction. Most enrolled patients had nonpalpable inguinal LNs. Primary lymphadenectomy was suggested in intermediate and high risk cases. In patients at low risk the choice of surgery or surveillance was made according to patient preference. Of 92 groin basins 16 had palpable inguinal LNs. However, the longest diameter of palpable LNs was less than 4 cm in all groin basins. All patients received antibiotics for 1 to 5 weeks before lymphadenectomy.

Bilateral inguinal lymphadenectomy was performed in all enrolled patients. The borders of inguinal lymphadenectomy included 2 cm above the inguinal ligament superiorly, the apex of the femoral triangle inferiorly, the adductor longus medially and the sartorius muscles laterally. In cases of 1 or more positive inguinal LNs bilateral iliac lymphadenectomy was done. The limits of iliac LN dissection were 2 cm above the bifurcation of the common iliac artery as the cephalad limit, Cloquet's node as the caudal limit, the bladder as the medial limit and the genitofemoral nerve as the lateral limit. Three parallel vertical incisions were the choice of incisions for ilioinguinal lymphadenectomy at our institution. Primary lesions and regional LNs were staged according to the 2002 American Joint Committee on Cancer TNM system.⁷ Histological grade was classified according to the Broders system as G1—well, G2—moderately and G3—poorly differentiated.⁸

The ilioinguinal LNs were separated into 6 packages according to anatomical landmarks (see figure). Inguinal LNs were divided into 3 packages, including medial inguinal, lateral inguinal and Cloquet's node packages. The medial and lateral inguinal packages were separated by the lateral surface of the femoral artery and saphenous vein. In this study the saphenous vein was routinely resected and included in the medial inguinal package. After removing the medial inguinal package adipose tissue along the medial aspect of the femoral vein and under the inguinal ligament was removed as the Cloquet's node package. The 3 nodal packages included in iliac lymphadenectomy were the external iliac, obturator and common iliac packages.

Pathologists were blinded to the anatomical locations of the submitted nodal packages. A standard method of processing node packages was used, including dissecting the LNs from surrounding adipose tissue under bright light. Retrieved LNs were embedded into paraffin blocks and sliced using a 1-section cut. All tissue sections were stained with hematoxylin and eosin, and examined by ordinary light microscopy.

Statistical analysis was done using the chi-square and Fisher exact tests for multiple comparisons. In all analyses 2-sided statistical tests were used and $p \leq 0.05$ was considered significant.

RESULTS

Patient and Tumor Characteristics

Table 1 lists the characteristics of enrolled patients and tumors. Of 46 patients with penile cancer 21 had unilateral inguinal LNM and 3 had bilateral inguinal LNM. The LNM incidence was 11%, 38% and 69% in the low, intermediate and high EAU risk groups,⁹ respectively. Primary tumor stage was significantly associated with LNM ($p = 0.012$). However, primary tumor grade failed to achieve statistical significance in this cohort ($p = 0.26$). According to the treatment protocol 92 inguinal and 48 iliac packaged lymphadenectomies were performed.

Anatomical LN Distribution and LNM Disseminative Pattern at Ilioinguinal Lymphadenectomy

A median of 13 (range 9 to 19) and 11 LNs (range 6 to 19) were retrieved in inguinal and iliac lymphadenectomy cases, respectively. Table 2 shows the anatomical distribution of LNs in ilioinguinal lymphadenectomy cases.

In inguinal lymphadenectomy the medial inguinal package represented 47% of all inguinal LNs and it was the most commonly involved region. The incidence of LNM in the other packages correlated with the number of positive LNs in the medial inguinal package (table 3). Although the lateral inguinal package represented almost half of the retrieved inguinal LNs, we noted absent metastatic disease when there were fewer than 2 positive LNs in the

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