

Salvage Surgical Resection for Isolated Locally Recurrent Inguinal Lymph Node Metastasis of Penile Cancer: International Study Collaboration

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Abbreviations and Acronyms

CT = computerized tomography
DSS = disease specific survival
ILND = inguinal lymph node dissection
OS = overall survival
PET = positron emission tomography

Purpose: We assessed the merit of performing salvage inguinal lymph node dissection in those infrequent cases of penile cancer with locally recurrent inguinal lymph node metastases in the absence of other suspected sites of disease.

Materials and Methods: A total of 20 patients were retrospectively identified as having undergone salvage inguinal lymph node dissection for locally recurrent penile cancer. Patients were previously treated with primary inguinal lymph node dissection with curative intent. At the time of salvage inguinal lymph node dissection, superficial and deep inguinal lymph node dissection was performed with resection outside of the standardized surgical template if there was inguinal recurrence outside of this region.

Results: All cases were primary penile squamous cell carcinomas. Median time to recurrence from initial inguinal lymph node dissection was 7.7 months (range 3.1 to 35.0). At salvage inguinal lymph node dissection a median of 3 lymph nodes (range 1 to 17) was resected with a median of 2 (range 1 to 7) nodes positive for malignancy. Median overall survival after salvage inguinal lymph node dissection was 10.1 months (95% CI 1.9–18.3) and median disease specific survival after salvage inguinal lymph node dissection was 16.4 months (95% CI 5.1–27.8). Of the initial 20 patients 9 have no evidence of disease (median followup 12.0 months, range 7.1 to 70.1). Postoperative complications developed in 11 patients, including wound infections in 6, postoperative severe (debilitating) lymphedema in 4 and seroma in 1.

Conclusions: Salvage inguinal lymph node dissection is a potentially curative treatment in patients with penile cancer with locally recurrent inguinal lymph node metastases in the absence of occult disease. Patients undergoing such salvage surgery should be informed of the high likelihood of postoperative complications.

Key Words: lymph node excision, penile neoplasms, salvage therapy

SQUAMOUS cell carcinoma of the penis is a relatively rare disease with an incidence of 0.5 to 1.6 per 100,000 males in the United States and Europe.¹ It is characterized by an

insidious onset of locoregional disease before disseminated metastatic progression. The standardized treatment approach in a patient with inguinal lymph node metastasis is ILND with

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the therapeutic benefit being greatest in the absence of other sites of metastasis.²⁻⁵ The extent of lymph node metastasis is strongly correlated with cancer specific outcomes, with ILND having the greatest curative potential when performed early vs in a delayed clinical setting.⁶⁻⁹ Approximately 2% of patients with penile cancer initially present with distant metastatic disease indicating a poor prognosis.⁷ Therefore, the early management of inguinal lymph node metastasis is paramount in the optimization of treatment outcomes.

Multiple studies have shown that local recurrence has little impact on patient survival. However, there is currently a paucity of evidence-based data on the management of inguinal recurrence after therapeutic lymphadenectomy.^{3,10,11} It has been reported that most inguinal recurrences after ILND occur within 17 months of the initial lymph node dissection.³ Such recurrences are a sign of poor prognosis and currently are not associated with a standardized approach due to the lack of evidence-based data on which treatment, if any, may be beneficial. In this study the patients were offered surgical resection as a form of salvage therapy. We investigated the surgical outcomes and the clinical utility of salvage ILND in patients with penile cancer with locally recurrent inguinal lymph node metastases and no other sites of disease.

PATIENTS AND METHODS

Between October 2003 and August 2013 a total of 404 patients were retrospectively identified as having undergone inguinal lymph node dissection for penile carcinoma. These patients were treated at one of 3 tertiary referral institutions (Moffitt Cancer Center, Tampa, Florida; University College Hospital, London, UK and University Hospital, Rostock, Germany). Of these 404 patients 20 (5%) underwent salvage ILND for inguinal recurrence in the absence of distant metastatic disease. Patients with distant metastasis and those refusing surgery were excluded from the study. In an effort to exclude those patients in whom lymphadenectomy may have been incomplete at primary ILND, all patients included in the study had at least 5 lymph nodes resected at initial ILND (2 of the 20 patients had primary lymphadenectomy performed elsewhere). In addition, all patients included in the study underwent salvage ILND with curative intent. All 20 patients who underwent salvage ILND met our inclusion criteria.

Primary tumors were treated surgically with local excision, or partial or total amputation, depending on the size and location of the primary tumor. All tumors were staged according to the 2002 TNM classification.¹² Inguinal recurrence was defined as any histological or cytological evidence of tumor in the groin, in or near the original ILND incision. Before being offered salvage lymphadenectomy all patients underwent a physical examination and laboratory studies including a complete

blood count, basic metabolic panel and liver function studies. All patients also underwent CT or magnetic resonance imaging of the chest, abdomen and pelvis to rule out distant metastases (within 4 to 6 weeks of salvage surgery). In equivocal cases PET/CT was used.

The surgical boundaries of salvage ILND (provided there was no radiographic evidence of disease outside this template) were the inguinal ligament superiorly, the adductor longus muscle laterally and the sartorius muscle medially, with superficial and deep inguinal lymph node dissection performed in all cases. All operative pathology reports were formally reviewed by fellowship trained genitourinary pathologists at their respective institutions.

Demographics, primary tumor pathology, time to recurrence, location of recurrence, perioperative complications and outcomes were recorded. OS and DSS, which served as the primary end points of the study, were estimated using Kaplan-Meier methodology starting from the date of salvage ILND to the date of last followup or date of death. Overall and disease specific survival times are reported with their respective 95% CIs. Statistical analyses were conducted using SPSS® 21.0.

RESULTS

Patient and Tumor Characteristics

A total of 20 patients underwent salvage ILND for inguinal recurrences of penile cancer. Median followup was 9.7 months (range 4.9 to 70.1). Median patient age at salvage ILND was 65 years (range 38 to 80) and the majority of patients were white (95%). Median original tumor size was 2.25 cm (range 0.7 to 6.5). Overall 1 patient had T1 disease, 13 had T2 disease and 6 had T3 disease. Four patients were treated with glansectomy, 13 were treated with partial penectomy and 3 were treated with total penectomy. All patients underwent inguinal lymphadenectomy at the original surgery.

Salvage ILND

Median time to inguinal recurrence was 7.7 months (range 3.1 to 35.0) after initial ILND. At salvage ILND the median number of lymph nodes resected was 3 (range 1 to 17) and the median number of cancer positive lymph nodes was 2 (range 1 to 7). Twelve patients (60%) received adjuvant systemic chemotherapy after salvage ILND while 2 (10%) received adjuvant radiation therapy alone after salvage surgery.

Overall and Disease Specific Survival

Median OS after salvage ILND was 10.1 months (95% CI 1.9–18.3; mean 30.9, 95% CI 16.1–45.7). Median DSS after salvage ILND was 16.4 months (95% CI 5.1–27.8; mean 33.5, 95% CI 18.0–49.0). The figure shows the OS and DSS Kaplan-Meier curves. At last followup (median 12.0 months, range 7.1 to 70.1) 11 patients are alive and of these patients 9 currently have no evidence of disease.

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