Inguinal Recurrence Following Therapeutic Lymphadenectomy for Node Positive Penile Carcinoma: Outcome and Implications for Management

Niels M. Graafland, Luc M. F. Moonen, Hester H. van Boven, Erik van Werkhoven, J. Martijn Kerst and Simon Horenblas*

From the Departments of Urology (NMG, SH), Pathology (LMFM), Radiation Oncology (HHV), Biometrics (EVW) and Medical Oncology (JMK), The Netherlands Cancer Institute - Antoni van Leeuwenhoek Hospital, Amsterdam, The Netherlands

Abbreviations and Acronyms

ENE = extranodal extension

pN+ = pathological node positive

TPF = docetaxel plus cisplatin and fluorouracil

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Nothing to disclose.

* Correspondence: The Netherlands Cancer Institute - Antoni van Leeuwenhoek Hospital, Plesmanlaan 121, 1066 CX Amsterdam, the Netherlands (telephone: +31-(0)20-5122611; FAX: +31-(0)20-5122553; e-mail: s.horenblas@nki.nl).

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Editor's Note: This article is the third of 5 published in this issue for which category 1 CME credits can be earned. Instructions for obtaining credits are given with the questions on pages 1164 and 1165.

Purpose: We investigated the treatment results and outcomes of patients with pathological node positive penile carcinoma who experienced an inguinal recurrence after therapeutic lymphadenectomy, and determined the clinicopathological features predictive of such recurrences.

Materials and Methods: Data of 161 patients with pN+ penile carcinoma were analyzed. Ipsilateral postoperative radiotherapy was given if histopathology revealed 2 or more metastases and/or extranodal extension. Medium observed followup was 60 months. The 5-year incidence of inguinal recurrence was estimated using a competing risk analysis considering death a competing risk.

Results: An inguinal recurrence developed in 26 patients following lymphadenectomy after a median of 5.3 months. The overall estimated 5-year inguinal recurrence rate was 16%. Of the 26 patients with inguinal recurrence ipsilateral adjuvant radiotherapy was indicated in 22 but given in 11. The other 11 patients had recurrence in the groin before the start of adjuvant radiotherapy. Median survival after inguinal recurrence was 4.5 months. Only 2 of 26 patients (8%) underwent successful salvage after inguinal recurrence. Pronounced differences in estimated recurrence rates were found among several clinicopathological variables indicating extensive penile cancer. Patients with 3 or more unilateral metastatic inguinal nodes and/or extranodal extension and/or pelvic nodal involvement defined a subgroup with high risk pN+ penile cancer.

Conclusions: Most inguinal recurrence following therapeutic lymphadenectomy in pN+ penile carcinoma occurs within a short time. Patients experiencing such a recurrence have a poor outcome with limited salvage options. Patients with 3 or more unilateral metastatic inguinal nodes and/or extranodal extension and/or pelvic nodal involvement represent a high risk group that may benefit from multimodality treatment.

Key Words: radiotherapy, adjuvant; lymph node excision; lymphatic metastasis; penile neoplasms; recurrence

PENILE squamous cell carcinoma is a relatively rare disease in the Western world. Surgery is considered the cornerstone of locoregional treatment, with ±80% cure in patients with 1 or 2 involved inguinal nodes without ENE.[1–6] At our institution postoperative radiotherapy is given to the inguinal lymphatic region if histopathology reveals more tumor than 1 intranodal metastasis to improve local control.

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Several studies have shown that local recurrence only has little impact on survival in patients with penile carcinoma.[7,8] There are few data on inguinal recurrence following therapeutic lymphadenectomy.[1,2,6,8] Previous studies on this topic are often biased by various patient populations of men treated with and without therapeutic lymphadenectomy. Moreover the incidence is probably underreported. If distant recurrence is found as well, the focus is usually on distant recurrence that is regarded as decisive for survival. Finally, data on the identification of clinicopathological features predictive of inguinal recurrences following lymphadenectomy in penile cancer are lacking. In our experience inguinal relapses are difficult to manage and cause a lot of suffering because of pain, fetor and lymphedema, often leaving the patient bedridden and debilitated. We investigated the treatment results and outcome of patients with pN+ penile carcinoma in whom inguinal recurrence developed following lymphadenectomy. In addition, we determined the clinicopathological features predictive of inguinal recurrences.

PATIENTS AND METHODS

At our tertiary referral institution inguinal lymphadenectomy in patients with penile squamous cell carcinoma is generally performed for therapeutic reasons only (tumor positive sentinel node biopsy/excision biopsy/cytology). Elective lymphadenectomy has not been part of our standard management since 1994, when dynamic sentinel node biopsy was introduced for patients with clinically node negative disease. The technique and results of dynamic sentinel node biopsy have been described in detail previously.[9]

Between 1956 and December 2007, 208 patients underwent inguinal lymphadenectomy. We analyzed 169 consecutive patients who had undergone therapeutic inguinal lymphadenectomy since January 1988 only because this period had more consistent, standardized treatment and followup, together with prospective data collection. Our indications for regional lymphadenectomy, surgical approach and boundaries of inguinal and pelvic node dissection have been published before,[4,10] and they have not changed during the study period. Eight patients were excluded from study, including 6 because of palliative treatment only, and 2 who experienced a simultaneous penile and inguinal recurrence in the contralateral nondissected groin. The remaining 161 patients with pN+ penile carcinoma were the focus of this report (table 1). Median age was 64 years (range 33 to 91). Most patients (110, 68%) were treated since 2000. Seven men with advanced penile carcinoma had induction treatment before lymphadenectomy consisting of preoperative radiotherapy in 3 (2%, in the early years of this study) and neoadjuvant chemotherapy in 4 (2%).

The primary tumor was treated surgically. In general, local excision was performed in distal T1 and T2 tumors smaller than 2 cm whenever oncologically feasible. More proximal and larger tumors were treated with partial or total amputation. The tumors were staged according to the 2002 TNM classification.[11] Patients were followed according to a standard protocol consisting of outpatient visits every 2 months during the first 2 years, with 3-month intervals in the third year and 6-month intervals thereafter. This included physical examination and imaging (with ultrasound or computerized tomography) on indication. A total of 60 patients (37%) died of disease during followup with a median time to death of 9 months (range 0.8 to 37) since lymphadenectomy. Median followup duration was 60 months (range 16 to 165).

Table 1. *Patient and tumor characteristics*

	No. (%)
pT category (TNM 2002):	
pT1	33 (20)
pT2	107 (66)
pT3	14 (9)
pT4	3 (2)
Not assessable*	4 (2)
Differentiation grade penile tumor:	
Well (G1)	32 (20)
Intermediate (G2)	78 (48)
Poor (G3)	47 (29)
Not assessable*	4 (2)
pN category (TNM 2002):	
pN1	58 (36)
pN2	66 (41)
pN3	37 (23)
No. pts with:	
Nonpalpable nodes (cN0)	51 (32)
Palpable nodes + fine needle aspiration cytology proven metastasis (cN+)†	110 (68)
Side of pathological metastatic inguinal nodes:	
Unilat	89 (55)
Bilat	72 (45)
No. unilat metastatic inguinal nodes:	
2 or Less	117 (73)
3 or Greater	40 (25)
Unknown, mass of metastases	4 (2)
ENE of metastatic inguinal nodes:	
No	80 (50)
Yes	81 (50)
Surgical margin inguinal specimen:	
Tumor neg	154 (96)
Tumor pos	7 (4)
Pathological metastatic pelvic nodes:	
No	124 (77)
Yes	37 (23)
Adjuvant radiotherapy given:	
No	93 (58)
Yes	67 (42)

No histopathological review of the primary tumor was done.

* In 4 patients no histopathological data were available of the primary tumor. They underwent inguinal lymphadenectomy at our institute for groin metastases while the penile tumor was treated previously elsewhere.

† Some patients were referred after excision of groin metastasis elsewhere.

Histopathological Analysis

Nodal tissue was examined by palpation, inspection and sectioning. All macroscopically detected nodes were completely embedded in paraffin. The total number of histopathologically confirmed lymph node metastases was re-