

# Contemporary Management of Regional Nodes in Penile Cancer—Improvement of Survival?

Rosa S. Djajadiningrat, Niels M. Graafland, Erik van Werkhoven, Wim Meinhardt, Axel Bex, Henk G. van der Poel, Hester H. van Boven, Renato A. Valdés Olmos and Simon Horenblas\*

From the Departments of Urology (RSD, NMG, WM, AB, HGvdP, SH), Biometrics (EvW), Pathology (HHvB) and Nuclear Medicine (RAVO), The Netherlands Cancer Institute, Amsterdam, The Netherlands

## Abbreviations and Acronyms

CSS = cancer specific survival  
DSNB = dynamic sentinel node biopsy  
ENE = extranodal extension  
iLND = inguinal lymph node dissection  
SCCp = squamous cell carcinoma of the penis

Accepted for publication July 26, 2013.

Study performed in accordance with institutional ethical guidelines and based on good clinical practice.

Nothing to disclose.

\* Correspondence: Department of Urology, The Netherlands Cancer Institute, Plesmanlaan 121, NL-1066 CX Amsterdam, the Netherlands (telephone: +31 20 512 9083; FAX: +31 20 512 2554; e-mail: [s.horenblas@nki.nl](mailto:s.horenblas@nki.nl)).

**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 276 and 277.

**Purpose:** The management of regional nodes of penile squamous cell carcinoma has changed with time due to improved knowledge about diagnosis and treatment. To determine whether changes in the treatment of regional nodes have improved survival, we compared contemporary 5-year cancer specific survival of patients with squamous cell carcinoma of the penis with that of patients in previous cohorts.

**Materials and Methods:** In an observational cohort study of 1,000 patients treated during 56 years 944 were eligible for analysis. Tumors were staged according to the 2009 TNM classification, and patients were divided into 4 cohorts of 1956 to 1987, 1988 to 1993, 1994 to 2000 and 2001 to 2012, reflecting changes in clinical practice regarding regional nodes. Kaplan-Meier survival curves with the log rank test and Cox proportional hazards modeling were used to examine trends in 5-year cancer specific survival.

**Results:** The 5-year cancer specific survival of patients with cN0 disease treated between 2001 and 2012 was 92% compared to 89% (1994 to 2000), 78% (1988 to 1993) and 85% (1956 to 1987). The 5-year cancer specific survival improved significantly since 1994, the year dynamic sentinel node biopsy was introduced, at 91% (1994 to 2012) vs 82% (1956 to 1993) ( $p = 0.021$ ). This conclusion still holds after adjustment for pathological T stage and grade of differentiation (HR 2.46,  $p = 0.01$ ). Extranodal extension, number of tumor positive nodes and pelvic involvement in node positive (pN+) cases were associated with worse 5-year cancer specific survival.

**Conclusions:** Despite less surgery being performed on regional nodes, 5-year cancer specific survival has improved in patients with cN0 disease. The number of tumor positive nodes, extranodal extension and pelvic involvement were highly associated with worse cancer specific survival in patients with pN+ disease. In this group other treatment strategies are needed as no improvement was observed.

**Key Words:** survival; penile neoplasms; carcinoma, squamous cell; sentinel lymph node biopsy; lymphatic metastasis

SQUAMOUS cell carcinoma of the penis is a rare disease in Western countries with an age standardized incidence of approximately 1/100,000.<sup>1</sup> The single

most important prognostic factor for cancer specific survival is the presence of nodal metastases.<sup>2-4</sup> Nevertheless, cure is still possible with

tumor positive lymph nodes and is inversely related to the metastatic load. Therefore, early detection and treatment of metastases are of great importance.<sup>5,6</sup> Patients with clinically node negative groins (cN0), ie no evidence of tumor on preoperative physical examination, ultrasound or fine needle aspiration cytology, have an approximately 20% chance of harboring occult metastases.<sup>7</sup> The detection of these metastases in patients with cN0 disease has changed in recent decades. The management of cN0 cases has shifted from observation to risk adapted inguinal lymph node dissection<sup>1</sup> and dynamic sentinel node biopsy instead of prophylactic iLND.<sup>8</sup>

The most important change was the introduction of DSNB in 1994 for cN0 cases.<sup>9</sup> As shown in a recent cohort, induction chemotherapy is also being used more frequently in selected patients with advanced locoregional disease.<sup>1,10</sup> Thus, in theory, contemporary survival may have improved in SCCp. Therefore, we assessed the contemporary 5-year CSS of patients with SCCp treated at our institute, and compared the outcomes with those of previous cohorts stratified by treatment periods.

## MATERIALS AND METHODS

### Patients

This study was performed in accordance with institutional ethical guidelines and based on good clinical practice. The recorded data of 1,000 patients with SCCp who presented at our institute from 1956 until 2012 were retrieved from our consecutive SCCp database. Detailed information on patient characteristics, primary tumor characteristics and regional lymph node characteristics at presentation, treatment and followup were prospectively registered from 1988. In previous years only primary tumor stage, primary treatment, recurrence and survival data were registered. Missing items were collected retrospectively.

Overall 36 patients were excluded from study because all histological data were missing (grade, pathological T and N stage [pT/pN]). The majority of these patients were treated with primary radiation in the early years. In addition, 20 patients were excluded because they refused treatment or died before they were treated. Thus, a total of 56 patients were excluded, leaving 944 eligible for analysis. All patients were treated with surgical resection of the penile tumor.

### Staging

All tumors were (re)staged according to the 2009 TNM classification.<sup>1</sup> Major changes were the presence of ENE and pelvic lymph node involvement discriminators in the pN classification. Patients who underwent close surveillance of the regional lymph nodes without pathological examination had disease staged pN0 if there was no evidence of lymph node involvement 2 years after primary treatment, or pN1, pN2 or pN3. Disease was staged pNx if

patients were subjected to close surveillance and had less than 2 years of followup or died of another cause within 2 years, or if treatment of the groin consisted of radiotherapy only.

Until 2008 all histopathology was revised by a single experienced uropathologist. Since then, all histopathological examinations were not revised, but reported by experienced uropathologists. Grade was assigned as well, moderately or poorly differentiated based on the amount of undifferentiated cells in the tumor on histopathological examination according to Broders.<sup>11</sup> Lymphovascular invasion was defined as the presence of embolic tumor cells in thin walled, vessel-like structures using routinely stained sections. Finally, ENE was defined as extension of tumor through the lymph node capsule into the perinodal fibrous-adipose tissue.

### Treatment of Regional Lymph Nodes

Until 1988 patients with cN0 disease were usually treated with surveillance of the inguinal nodes, whereas most patients with clinically node positive disease (cN+) underwent ipsilateral radical iLND. In 1988 elective bilateral radical iLND was introduced for patients with cN0 disease considered at high risk (T2G3 or higher) for lymphatic invasion. Low and intermediate risk cN0 cases were managed with close surveillance.

In 1994 DSNB was introduced for patients with cN0 disease with T2 or greater tumors, and since 2004 for all patients with T1G2 or greater tumors.<sup>12</sup> In 2001 several procedural changes were made.<sup>8</sup> Only in patients with a tumor positive sentinel node was a completion ipsilateral radical iLND performed.<sup>13</sup>

If histopathology revealed 2 or more positive inguinal nodes and/or ENE in the removed inguinal specimen, a subsequent ipsilateral pelvic lymphadenectomy and adjuvant inguinal radiotherapy followed. In patients with tumor positive pelvic nodes, irradiation to the pelvic region followed. In general the radiotherapy dose was 50 Gray (25 fractions of 2 Gy). Induction chemotherapy was administered for locally advanced and/or inoperable regional disease without evidence of distant metastasis as described by Leijte et al.<sup>14</sup> Between 2008 and 2012 a combination of docetaxel, cisplatin and 5-fluorouracil was used. Patients presenting with or with progression to inoperable advanced disease received chemotherapy and/or radiotherapy for palliation only, together with the best supporting care.

### Followup

Since 1988 followup has been standardized at our institute. This involves physical examination of the penis and groin at the outpatient clinic every 2 months during the first 2 years, at 3-month intervals in the third year and at 6-month intervals thereafter. Computerized tomography is only performed on indication and ultrasound of the groin has been regularly performed since 2001. Patients were discharged from followup after 10 years without evidence of disease. The followup scheme was altered after analysis of recurrence patterns and now consists of a more risk adapted followup scheme.<sup>15</sup> Compliance with followup was almost 100% with only 11 patients lost to followup (range 4 to 36 months).

Download English Version:

<https://daneshyari.com/en/article/3863538>

Download Persian Version:

<https://daneshyari.com/article/3863538>

[Daneshyari.com](https://daneshyari.com)