

Penile Sparing Surgery for Penile Cancer: A Multicenter International Retrospective Cohort



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Purpose: We evaluated recurrence outcomes of penile sparing surgery in what is to our knowledge the largest multicenter cohort of patients to date.

Materials and Methods: We retrospectively identified patients treated with penile sparing surgery from May 1990 to July 2016 at 5 tertiary referral institutions. Treatments consisted of circumcision, wide local excision, laser therapy with or without local excision, partial or total glansctomy and glans resurfacing. The study primary end point was local recurrence-free survival, defined from initial treatment to time of local recurrence and estimated with the Kaplan-Meier method.

Results: After applying study exclusion criteria 1,188 patients were included in analysis. During the median followup of 43.0 months there were 252 local recurrences (21.2%), of which 99 (39.3%) developed in year 1. Median time to local recurrence was 16.3 months and the 5-year local recurrence-free survival incidence was 73.6%. When stratified by stage, the 5-year local recurrence-free survival rate was 75.0%, 71.4% and 75.9% in Ta/Tis, T1 and T2 cases, respectively (log rank $p = 0.748$). Of the recurrences 58.3% were treated with repeat organ sparing procedures and the secondary partial (total) penectomy rate was 19.0%. Only margin status was significantly associated with local recurrence on multivariate analysis ($p = 0.001$). Study limitations included the retrospective design and the heterogeneous clinical approach.

Conclusions: Penile sparing surgery can provide excellent local control for superficial penile tumors as well as for appropriately selected invasive lesions. Strict followup in the early postoperative period is highly recommended.

Abbreviations and Acronyms

CIS = carcinoma in situ

LRFS = local recurrence-free survival

PSS = penile sparing surgery

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PENILE cancer is a rare neoplasm representing 0.4% to 0.6% of all malignancies in the United States and Europe.¹ Approximately 80% of tumors develop on the glans or prepuce and the most common histology is

squamous cell carcinoma.² For many years radical surgery has been the mainstay of treatment but this can be potentially disfiguring, and lead to significant psychological distress and sexual dysfunction.³

Treatment of penile cancer has evolved with time. Historically the goal of surgery was complete tumor resection with at least a 2 cm negative margin.⁴ However, an excision margin of only a few mm has been widely accepted in the last several years with similar oncologic outcomes.^{5,6} Several PSS options have been popularized for select penile lesions, including glansectomy, wide local excision and laser ablation.

Due to the rarity of penile cancer clinical trial data on the oncologic efficacy of PSS is scarce and unlikely to be forthcoming. In this international multicenter study we present our overall experience with PSS for squamous cell carcinoma of the penis in what is to our knowledge the largest cohort to date.

MATERIAL AND METHODS

Study Design and Patients

We reviewed the records of 1,351 consecutive patients who underwent PSS at a total of 5 academic institutions in Europe, Asia and North America between May 1990 and July 2016. Treatment of cancer lesions included circumcision, partial or total glansectomy, wide local excision, laser ablation using Nd:YAG or CO₂ medium with or without local excision and partial or total glans resurfacing. This study was performed according to the ethical guidelines of the institutional review board at each participating center.

Patient and Disease Specific Characteristics

Recorded characteristics included patient age at the time of the procedure, primary penile tumor stage (pT), tumor diameter in cm, and tumor grade and location. Recurrence was classified as local—penile treatment bed, regional—inguinal or pelvic lymph nodes or distant—visceral or distant metastasis.

Primary Tumor Treatment

Surgical treatment was decided according to patient and surgeon discretion at each respective institution. As a result the indications for PSS were not uniform across institutions. However, management during the last 5 years of the study period was based on NCCN (National Comprehensive Cancer Network®) Guidelines® and EAU (European Association of Urology) guidelines for penile cancer.^{4,7} This included penile preserving strategies for small noninvasive lesions as well as smaller invasive tumors confined to the glans that were amenable to negative surgical margins. No perioperative chemotherapy or postoperative radiation was done to manage primary lesions.

Staging

All tissue was examined by expert genitourinary pathologists at each center according to the local institutional protocol and based on the 7th edition of the AJCC (American Joint Committee on Cancer) TNM staging system.⁸ Cases prior to 2010 were reclassified according to this edition.

End Point

The study primary end point was LRFS, defined as the period between primary local treatment and the date of local recurrence or censoring on the day of the last followup visit. Factors associated with local recurrence were analyzed in men with invasive lesions (pT1 and pT2)

Statistical Analysis

Continuous variables are reported as the median and IQR, and categorical variables are reported as the frequency count and percent. Univariable analysis was performed using the Pearson chi-square and Kruskal-Wallis tests for categorical and numerical outcomes, respectively. The Kaplan-Meier method was applied to estimate LRFS while differences in survival between the groups were determined with the log rank test. Clinicopathological factors were evaluated using univariate and multivariate Cox proportional hazard regression models to find predictors of local recurrence. Statistical analyses were performed with IBM® SPSS®, version 24.

RESULTS

We retrospectively identified 1,351 patients treated with PSS from May 1990 to July 2016. Of these men 233 were excluded from analysis due to missing treatment data on 3 (0.2%), unrecorded recurrence outcomes in 35 (2.6%), missing pT stage in 26 (1.9%), disease coded pT3/4 in 51 (3.8%) and a missed last followup or surgery date in 118 (8.7%). A total of 1,188 patients were included in the final analysis.

Supplementary table 1 (<http://jurology.com/>) shows an overview of patient characteristics. Median followup was 43.0 months (IQR 27.9–60.4). Of the patients 394 (33.2%) had pT2 disease. There were 234 local recurrences (19.7%). Median time to local, regional and distant recurrence was 16.3 (IQR 12.6–20.0), 7.8 (6.6–8.9) and 29.6 months (2.2–57.0), respectively. One, 2 and 5-year LRFS was 90.7%, 85.2% and 73.6%, respectively (fig. 1).

Of pT2 tumors 60.9% were treated with glansectomy while 55.2% of pT1 and 56.8% of pTa/Tis tumors were treated with wide local excision or circumcision (supplementary table 2, <http://jurology.com/>). Larger and poorly differentiated tumors were also seen in men with pT2 disease (each $p < 0.001$). Margin data were available on 585 cases (49.2%). This can partially be explained by the fact that a large number of patients underwent laser therapy and so margin data were obviously not available. The positive margin rate did not differ based on stage. It ranged from 28.7% for T2 tumors to 30.9% and 35.9% for Ta/Tis and T1 tumors, respectively ($p = 0.214$).

Of the 252 local recurrences 88.1% developed within 5 years of treatment, including 99 (39.3%) in year 1 (table 1). Organ sparing treatment was repeated in 147 patients (58.3%) (supplementary table 3, <http://jurology.com/>). When stratified by tumor stage, 5-year LRFS was 75.0%, 71.4% and

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