



Original article

Predictive factors for local recurrence after glansectomy and neoglans reconstruction for penile squamous cell carcinoma

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Abstract

Objectives: To investigate predictive pathological factors for local recurrence (LR) after glansectomy for penile squamous cell carcinoma (SCC) and to develop a risk score for prediction of LR after glansectomy.

Patients and methods: In this retrospective study, we analyzed 117 patients operated between February 2005 and January 2016 in a supraregional penile cancer center in the UK for LR after glansectomy and glans reconstruction. Univariate and multivariate Cox proportional hazards regression was used to identify 4 prognostic indicators for LR. The hazard ratio (HR) of LR was estimated in Kaplan-Meier analysis, and based on these data, we designed a postoperative model for prediction of LR based on 3 risk groups.

Results: Median follow-up period was 33.7 (95% CI: 26.8–40.3) months; 12.8% of the patients experienced LR. Univariate Cox proportional hazards regression revealed that the risk factors for recurrence were the presence of perineural invasion, carcinoma in situ, positive margin on definitive pathology, and high-grade disease. Based on Kaplan-Meier analysis stratified by number of factors present, we defined 3 risk groups for LR: low (0,1 risk factors) as reference, intermediate (2,3 risk factors) with HR of 13.9 (95% CI: 1.81–107.04, $P = 0.0115$), or high risk (all 4 risk factors present) with a HR of 34.2 (95% CI: 3.07–381.81, $P = 0.0041$). Limitations include the retrospective design and low number of events inherent to the rare nature of penile SCC.

Conclusions: Perineural invasion, carcinoma in situ, positive definitive margins, and the presence of high-grade SCC predict LR following glansectomy. These factors can be used to stratify patients into low-, intermediate-, and high-risk groups for recurrence which may be used to tailor follow-up. © 2017 Published by Elsevier Inc.

Keywords: Penile cancer; Recurrence; Model; Carcinoma in situ; High grade; Margins; Perineural invasion; Risk factors; Organ-sparing surgery

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1. Introduction

Penile cancer is a rare malignancy in Europe and North America with an age standardized incidence of approximately 1 per 100,000 males, although this increases to 4.4 per 100,000 for men in South America and Africa [1]. Approximately 80% of tumors are located on the glans or the prepuce or both [2]. Based on the original concept that a 2-cm clear resection margin was required for local control, partial and total penectomy were for a long time the standard surgical techniques used to manage penile squamous cell carcinoma (SCC) [1]. However, over the past 2 decades, it has become clear that distal penile tumors can be safely treated using a much smaller resection margin of only a few millimeters [3,4]. This has now led to the development of novel penile-preserving surgical techniques that not only preserve penile length but also allow voiding standing upright, preserve the ability to have sexual intercourse, as well as maintain a satisfactory esthetic appearance [5].

In 1966, Jackson described that tumors confined to the glans and prepuce should be considered a separate stage, which is in contrast to the modern TNM staging [6]. In 1994 and 1996, Pisani et al. [7] raised the suggestion that the corpora cavernosa are a distinct entity and can remain perfectly functional when separated from the glandulospongio-urethral unit. These suggestions led to a final illustrated technique describing glansectomy and reconstruction using a split-thickness skin graft (STSG) by Bracka in 2010, which uses well-defined anatomical planes as the resection margins [8]. Our adaptations to Bracka's technique and functional and oncological outcomes in a series of 177 patients have recently been published [9]. Previously small series have reported excellent cosmetic, functional, and oncological results for glansectomy with STSG reconstruction, with the largest series published in the literature so far comprising 87 and 72 patients as parts of series on penile-preserving surgery [10,11]. The rarity of penile cancer and the small sample size of previous publications have complicated the statistical analysis of local recurrence (LR) patterns and predictors, while the assumption that LR does not affect on cancer-specific survival (CSS) or overall survival (OS) has further limited interest [1,12–14]. Nevertheless, an estimation of the risk of LR may assist in counseling patients, tailoring follow-up, and reducing subsequent anxiety [15]. It may further guide the extent of the resection indicated.

In this retrospective cohort study, we report on the largest series of patients with penile SCC treated with glansectomy and STSG in a supraregional penile cancer center and aim to identify pathological risk factors for LR.

2. Patients and methods

Between February 2005 and January 2016, 177 patients with histologically proven—or with a strong clinical

suspicion of—invasive SCC involving the glans penis underwent a glansectomy and reconstruction to form a neoglans covered with a STSG from the thigh. Of these, 117 patients had complete histological and follow-up data and were included in final analysis. In the 60 cases that were not included in this analysis, 2 recurrences occurred. Surgery was performed by, or under the supervision of, surgeons who all have extensive experience in penile cancer treatment and penile reconstructive procedures in the same unit. All of the patients were discussed preoperatively at a dedicated multidisciplinary team meeting comprising a pathology review and radiological review. Where there was a clinical suspicion of distal corporal tip invasion, a penile magnetic resonance imaging of the erect penis was performed. Glansectomy was combined with circumcision if this was not already previously performed, and a plane between Bucks fascia and the glans cap was developed. Alternatively, for more extensive lesions, Bucks fascia was lifted off the underlying tunica albuginea and dissected off the corporal heads with the glans cap. The distal urethra was transected, spatulated, and then splayed over the corporal tips. In the majority of cases, frozen section analysis of samples from each corporal head was performed intraoperatively, and the corporal heads were transected followed by reconstruction in patients with frozen-sections showing the presence of residual tumor [16]. Reconstruction of a neoglans was performed by covering the corporal tips with an STSG harvested from the thigh using an air dermatome (thickness typically 0.012–0.018 in). A Foley catheter was inserted and removed at the same time-point as removal of the dressing.

Positive margins on definitive histopathological examination were managed by revision surgery in 9/17 cases to ensure negative margins, while the others were followed up by clinical surveillance. The latter pathway was used only when perioperative frozen section analysis of the corporal tips was negative, but the tumor reached the inked margin of the pathological specimen. Regional and systemic staging, treatment, and follow-up were conducted as per the European Association of Urology (EAU) guidelines following surgery at the time of treatment.

A retrospective review of patient records was conducted to record the clinicopathological features and local, regional, and distant recurrences as well as CSS and OS. The actuarial probabilities of LR were calculated using the Kaplan-Meier method. Clinicopathological variables were dichotomized as follows: (1) high grade vs. low/intermediate disease, (2) carcinoma in situ (CIS), (3) lymphovascular invasion (LVI), (4) perineural invasion (PNI), and (5) basaloid subtype vs. other subtypes. Pathological review was verified by 2 expert pathologists. Staging was classified or when needed re-classified, and according to the 2009 TNM classification, pT stage was subdivided into pT1 or CIS vs. pT2 vs. pT3. pN stage was subdivided into pN1 vs. pN2 vs. pN3.

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