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Early Wound Complications After Inguinal Lymphadenectomy in Penile Cancer: A Historical Cohort Study and Risk-factor Analysis

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Abstract

Background: Complication rates after inguinal lymph node dissection (ILND) are high. Risk factors for early wound complications after ILND in patients with penile carcinoma have not yet been studied.
Objectives: To assess the frequency of early wound complications in a contemporary series and to identify clinical risk factors for early wound complications after ILND for penile carcinoma.
Design, setting, and participants: We evaluated 237 ILNDs in 163 patients with penile cancer treated between 2003 and 2012 at the Netherlands Cancer Institute.
Outcome measurements and statistical analysis: We assessed the occurrence of wound infection, skin-flap problems, and seroma formation and graded complications using the modified Clavien system. Univariable and multivariable penalised mixed effects logistic regression was used to identify clinical risk factors for occurrence of any complication (grade $\geq$1) and of moderate to severe complications (grade $\geq$2).
Results and limitations: One complication or more occurred in 58% of the procedures, and 10% of those complications were severe. Wound infection occurred in 43%, seroma formation occurred in 24%, and skin-flap problems occurred in 16%.

Palpable disease was the only factor associated with grade $\geq$1 complications in the univariable analysis (odds ratio [OR]: 0.43; $p = 0.02$). In the multivariable model, after penalisation, no statistically significant risk factors remained.

Univariable associations for grade $\geq$2 complications were present for body mass index (BMI; OR of 1.66 for a 5.8-point change in BMI; $p = 0.05$) and sartorius muscle transposition (OR: 2.64; $p = 0.04$). In the reduced multivariable model, the OR for sartorius muscle transposition was 2.12 ($p = 0.06$) and for BMI was 1.76 ($p = 0.03$). In addition, bilateral dissection approached significance in the multivariable model (OR: 2.17; $p = 0.06$). This study is limited by its observational nature.
Conclusions: Wound complication rates after ILND are high in this cohort. BMI, sartorius muscle transposition, and bilateral dissection were the factors most strongly associated with the occurrence of grade $\geq$2 wound complications.

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1. Introduction

Inguinal lymph node dissection (ILND) is performed in penile cancer patients at high risk for lymph node metastases or in patients with established regional lymph node metastases. ILND can also be performed after a tumour-positive sentinel node procedure or following tumour-positive fine needle aspiration cytology. ILND is

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carried out simultaneously with the removal of the primary tumour or as an elective procedure. In cases of pelvic lymph node involvement or in patients at high risk for pelvic involvement, simultaneous pelvic lymph node dissection (PLND) is performed.

ILND is associated with a high morbidity rate. Short-term surgical complications include wound infection, seroma formation, skin-flap problems, and wound breakdown. The reported incidence of early postoperative wound complications varies strongly in the current literature but can be as high as 77% [1–6]. Over a longer period, lymphedema of the leg and/or the genital area may occur in varying degrees [2,6–9].

Previous studies in melanoma patients and vulvar cancer patients have tried to identify clinical risk factors for the occurrence of surgical complications after ILND [1,4,5,7,10]. To our knowledge, such attempts have not yet been made explicitly in patients with penile carcinoma, although complication rates have been compared for prophylactic dissection versus therapeutic and palliative dissection [11] and for radical ILND versus modified ILND [12].

Risk factors for any early surgical complication after ILND, as reported in the surgical literature, in patients with melanoma or vulvar cancer are age [1,10], diabetes [10] and other comorbidity [1], body mass index (BMI) [1,7], and drain production [10]. However, the presence of each risk factor is inconsistent and varies among studies [1,7,10].

Identification of risk factors for wound complications is clinically relevant. Therefore, we performed a historical cohort study, with two objectives: (1) to assess the frequency of early surgical wound complications after groin dissection for penile carcinoma and (2) to identify patient, tumour, and treatment characteristics as risk factors for the occurrence of early wound complications after ILND.

2. Methods

2.1. Data collection

We performed a chart review of all patients with penile cancer and ILND between 2003 and 2012 at the Netherlands Cancer Institute, a high-volume, specialised cancer hospital. Patients for whom the ILND was part of extensive resection that involved reconstructive surgery with myocutaneous flaps were excluded. We collected patient characteristics, tumour type and treatment characteristics, and data on early surgical wound complications, which were defined as complications occurring within 30 d after the operation. The complications of interest were wound infection, skin-flap problems, and seroma formation.

2.2. Definition and grading of outcome variables

All complications were strictly defined and graded in concordance with the modified Clavien system that allows for reporting complications of general surgery in a uniform manner [13,14]. Complications were defined as follows:

- Wound infection: any occurrence of inflammation for which oral (grade 1) or intravenous (grade 2) antibiotics were prescribed.
- Skin-flap problems: any wound dehiscence or skin edge necrosis. Skin-flap problems were classified as grade 1 if no intervention other than wound care was necessary, and those that required surgical intervention outside the operating room or readmission to the hospital were classified as grade 2.
- Seroma formation: serous fluid collection that developed under the skin flap that required needle aspiration (grade 1) or reopening of the wound (grade 2) after removal of the drain.
- Any complication that led to initiation of negative-pressure wound therapy was graded 3a, and any complication that required surgical reintervention in the operating room under general anaesthesia was graded 3b.

Complications were graded by two researchers independently (M.S. and R.D.), and any discrepancies were resolved in consensus.

2.3. Surgical technique of inguinal and additional pelvic lymphadenectomy

The technique of the inguinal lymphadenectomy as performed in all patients has been described in detail [15,16]. Briefly, all connective, fat, and lymphatic tissue is removed through an incision parallel and 2 cm inferior to the inguinal crease between the following boundaries: the proximal boundary, the inguinal ligament; the distal boundary, the adductor longus muscle at the crossing with the sartorius muscle; the medial boundary, the adductor muscle; and the lateral margin, the sartorius muscle. The floor of the dissection consists of the fascia lata, the pectineus muscle, and the ventral surface of the femoral vein and artery.

In cases of former dynamic sentinel node biopsy or skin involvement, the biopsy scar or involved skin is removed with an elliptical incision. A separate infraumbilical midline incision is used for the PLND. This consists of removal of all lymphatic tissue between the following boundaries: the proximal boundary, the bifurcation of the aorta; the lateral boundary, the genitofemoral nerve; the medial boundary, the prostate, the bladder, and the internal iliac artery; the distal boundary, the inguinal canal and the bottom, the obturator fossa. In rare cases, en bloc removal of the primary tumour and bilateral ILND are performed.

Prophylactic antibiotics were not always used routinely but have been part of the standard protocol in recent years. Suction drains are placed in the dissected area and generally are removed after $<$50-ml production per 24 h or after a maximum of 15 d.

2.4. Statistics

We report medians and ranges for continuous data and frequencies and percentages for nominal data.

For the assessment of risk factors, preselection of variables was based on biological plausibility and/or a previously reported association with the occurrence of complications. This initial set of variables included age, BMI, number of removed lymph nodes, number of tumour-positive lymph nodes, smoking status, type II diabetes, bilateral dissection in a single procedure, simultaneous PLND, indication for ILND, concomitant removal of skin, transposition of the sartorius muscle, sparing of the greater saphenous vein, and continuation of prophylactic antibiotics.

The association between clinical factors and occurrence of complications, both any complication (grade $\geq$1) and moderate to severe complications (grade $\geq$2), was assessed using univariable and multivariable mixed effects logistic regression. Mixed effects regression was used to account for within-patient correlations.

The multivariable analysis consisted of least absolute shrinkage and selection operator (LASSO; L1) penalised mixed effects logistic regression [17], with k-fold cross-validated likelihood (k = 40) used to determine the optimal penalty parameter [18,19]. Variables with nonzero coefficients were subsequently entered into a (nonpenalised) mixed effects logistic regression model for comparison with the