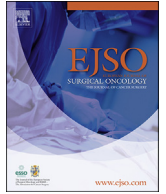




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Prostate sparing cystectomy for bladder cancer: A two-center study

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ABSTRACT

Purpose: To assess long-term functional and oncologic outcomes of prostate sparing cystectomy (PSC) as a sexuality-preserving alternative to radical cystectomy in a selected group of bladder cancer (BC) patients.

Materials and methods: Between 1995 and 2014, 185 BC patients underwent PSC according to one of two standardized procedures at two centers. All patients had received extensive evaluation to rule out prostate cancer and BC at the bladder neck and prostatic urethra (PU), including prostate specific antigen blood analysis, transrectal ultrasound and/or prostate biopsies, PU biopsies and/or PU frozen section analysis. All patients received an orthotopic ileal neobladder. Overall survival (OS) was assessed by Kaplan–Meier estimates. Cumulative incidence of cancer specific mortality, any recurrence and loco-regional recurrence were calculated using competing-risk methods. Finally, functional outcomes (voiding, continence and erectile function) were evaluated.

Results: 185 patients (cT_a-3N0M0) with a mean age of 57 years (SD: 9) were included. Median follow-up was 7.5 years (IQR: 5.6–10.8). Five-year OS was 71% and 5-year cumulative incidence of recurrence was 31%. Twenty patients (10.8%) had a loco-regional recurrence, two recurrences were in the PU. During follow-up, prostate cancer was detected in six patients (3.2%). Erectile function was preserved in 86.1% of patients, complete daytime and nighttime continence in 95.6% and 70.2%, respectively.

Conclusion: This two-center study shows that in men with BC in whom the prostate and PU were proven free of malignancy, PSC would represent a valid treatment option with excellent functional outcome. Oncologic outcomes were comparable to what is known from radical cystoprostatectomy series.

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Abbreviations: BC, bladder cancer; BCG, bacillus Calmette–Guérin; CSM, Cancer specific mortality; CSS, Cancer specific survival; CIS, carcinoma in situ; CIC, clean intermittent catheterization; CI, Confidence interval; IMM, Institute Mutualiste Montsouris; NCI-AVL, Netherlands Cancer Institute – Antoni van Leeuwenhoek Hospital; OS, overall survival; PET, positron emission tomography; PLND, pelvic lymph node dissection; PSA, prostate specific antigen; PSC, prostate sparing cystectomy; PU, prostatic urethra; RC, radical cystectomy; RFS, recurrence-free survival; TRUS, transrectal ultrasound; TUR, transurethral resection.

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Introduction

Standard treatment for muscle-invasive bladder cancer (BC) and persistent non-muscle invasive BC is radical cystectomy (RC) [1]. In men, standard RC includes resection of the bladder, regional lymph nodes, prostate and seminal vesicles. This surgery has major impact on urinary continence and sexual function [2,3].

Over the years, several cystectomy techniques have been developed, aimed at minimizing postoperative incontinence and erectile dysfunction. Single center series report on preserving the neurovascular bundles and urinary sphincter function by sparing the vasa deferentia, the seminal vesicles and prostate capsule, or

the entire prostate [4–7]. Reported functional results of the prostate-sparing cystectomy (PSC) techniques are excellent [8]. In a recent systematic review, none of the included comparative studies found any differences in oncological results between PSC and RC⁹. However, PSC is still heavily debated for fear of jeopardizing oncologic outcome. In this two-center study, we investigated long-term functional and oncologic results following two standardized PSC techniques.

Materials and methods

Patient selection

Consecutive patients, who received PSC according to the standardized techniques at either one of two hospitals until 2014 were included. All patients had either muscle-invasive BC or persistent/recurrent non-muscle invasive BC despite intravesical bacillus Calmette-Guérin (BCG) treatment. In one center (Netherlands Cancer Institute-Antoni van Leeuwenhoek hospital; NCI-AVL), the entire prostate was left in situ and prostatic involvement with urothelial carcinoma was excluded with transurethral biopsies prior to surgery. In the other center (Institut Mutualiste Montsouris; IMM), peroperative frozen section analysis of the prostatic urethra (PU) was used for this purpose, and PSC was combined with a simple adenectomy.

At the NCI-AVL, patients were included from 1995; at the IMM, the standardized PSC technique was introduced in 2001. Our cohort concerns the combined, extended, and refined series previously described by Mertens et al. [6] and Rozet et al. [10]. PSC was offered to patients with cT_a-3 BC, normal preoperative erectile function and a strong wish to maintain sexual function. An overview of inclusion criteria and diagnostic evaluation in both centers is shown in Fig. 1. Preoperative evaluation included physical examination, cystoscopy, urinalysis, laboratory blood studies and imaging (at least abdominal/pelvic computed tomography and chest X-ray). All patients received digital rectal examination and transrectal ultrasonography. At the NCI-AVL, transurethral bladder neck and PU biopsies and at least sextant prostate biopsies were taken prior to treatment, irrespective of prostate specific antigen (PSA) measurements, as previously described [6]. At the IMM, prostate biopsies were only taken if patients had palpable nodules, PSA >4 ng/ml, free PSA <15% or hypoechoic lesions on transrectal ultrasound [4,10]. Work-up at the IMM did not include standard transurethral biopsies. Exclusion criteria were BC PU/bladder neck involvement or presence of prostate cancer.

Surgery

Surgical techniques were as previously described [4,6,10]. In brief, a pelvic lymph node dissection (PLND) was performed according to standardized templates. At the NCI-AVL the boundaries of PLND were distally the circumflex vein and node of Cloquet, laterally the iliac artery, medially the bladder and prostate, and dorsally the hypogastric artery and obturator nerve. Since 2000, the boundaries have been enlarged proximally to the crossing of the ureter over the common iliac artery, laterally to the genitofemoral nerve and dorsally/caudally the bottom of the obturator fossa. At the IMM, the latter template was used in all included patients. PLND was followed by resection of the bladder, leaving the prostate and seminal vesicles in situ. At the IMM, the procedure included a simple adenectomy. At the NCI-AVL, the prostate was left in place. At both institutes an orthotopic ileal neobladder was constructed and anastomosed to the prostate capsule. At the IMM, standard intraoperative frozen section analysis of the urethral prostate capsule was performed to confirm negative surgical margins. At the NCI-AVL, this was only performed if

there was a suspicion of bladder neck involvement despite negative preoperative transurethral biopsies.

Outcomes

Patients were followed according to the European Association of Urology guidelines and follow-up included urethro-cystoscopy, digital rectal examination, PSA and free PSA measurements [1]. Oncologic end-points for cancer-specific mortality (CSM), overall recurrence and local recurrence were date of death due to BC or treatment, date of disease recurrence, and date of local recurrence, respectively, or the last event-free follow-up date. Local recurrence was defined as recurrent lesion(s) in the surgical bed, specifically in the PU or bladder neck, or pelvic lymph nodes. Functional outcomes were assessed by interviews on continence, pad use, voiding and sexual function. Normal erectile function was defined as sufficient erectile function for intercourse with or without PDE-5 inhibitors. Complete continence was defined as completely dry both day and night with no need to wear pads. Continence was defined as satisfactory if a patient required 1 pad per day/night and poor for >1 pad per day/night. Clean intermittent catheterization (CIC) was indicated for post-void residual volume ≥150 cc as measured by ultrasound or transurethral catheterization.

Statistical analysis

Baseline characteristics and outcome data were analyzed using descriptive statistics. Probabilities of death from any cause were estimated using the Kaplan-Meier method. For CSM, overall recurrence and local recurrence cumulative incidence functions are provided in order to account for competing events. For CSM, death unrelated to bladder cancer was treated as competing event. For overall recurrence death without recurrence was treated as competing event. Finally, for local recurrence, recurrence other than in the surgical bed or pelvic lymph nodes and death without recurrence were treated as competing events. Median follow-up was calculated using the reverse Kaplan-Meier method [11]. Statistical analyses were performed using IBM SPSS Statistics version 22.0 (Armonk, NY, IBM Corp.) and R version 3.4.4 (R Foundation for Statistical Computing, Vienna, Austria).

Results

Patient and tumor characteristics

A total of 185 patients (122 NCI-AVL, 63 IMM) with a mean age of 57 years (SD: 9) underwent PSC. Patient and tumor characteristics are shown in Table 1. Before PSC, 42 (23%) patients received neoadjuvant chemotherapy. Histological examination of PSC specimens revealed ypT₀ in 35 (19%) patients. Patients treated at the NCI-AVL had relatively higher cT and cN classifications than patients treated at the IMM, and relatively more often received perioperative chemotherapy and/or radiotherapy (Table 1). Likewise, the NCI-AVL cohort contained more pN + BCs than the IMM cohort (Table 1).

Positive surgical margins were found in ten (5.4%) patients, of whom seven (3.8%) had positive urethral margins (all were NCI-AVL patients, Table 1). These urethral margins were all positive for carcinoma in situ (CIS) and none of these patients had undergone urethral frozen sections intraoperatively.

Survival

Median follow-up was 7.5 years (IQR 5.6–10.8 years). In total, 69 of 185 patients (37.3%) died, of whom 53 (28.6%) died of BC.

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