



Original article

High incidence of clinically significant concomitant prostate cancer in patients undergoing radical cystectomy for bladder cancer: A 10-year single-center experience

Isabel Heidegger, M.D., Ph.D.^{a,*}, Willi Oberaigner, Ph.D.^b, Wolfgang Horninger, M.D.^a,
Renate Pichler, M.D.^a

^a Department of Urology, Medical University Innsbruck, Innsbruck, Austria

^b Department of Clinical Epidemiology, Tyrolean State Hospitals, Cancer Registry of Tyrol, Tyrol, Austria

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Abstract

Aim: To analyze prostate cancer (PCa) incidence, clinical significance, and recurrence in 213 patients who underwent radical cystectomy (RC) for advanced bladder cancer (BC).

Patients and methods: We conducted a 10-year retrospective analysis of a single-center database comprising the effect of PCa in RC specimens.

Results: In total, 113/213 male patients (53.1%) had PCa in the RC specimen. Patients' age, prostate-specific antigen (PSA), and also free PSA% were significant predictors for PCa. In addition, adverse bladder histology (\geq pT3) was found in 63.7% of patients with PCa. A total of 52.2% (59/113) of patients had at least a Gleason score (GS) 7 in final pathology and 10.6% of RC specimens showed an organ border growth (\geq pT3a). It was noted that 28.3% of patients experienced a biochemical recurrence (PSA \geq 0.2 ng/ml), among them 86.7% had GS \geq 7 in the RC specimen; however, 2 patients were diagnosed with a GS 5. Moreover, we found that 80% of patients with biochemical recurrence had an organ-extended (\geq pT3) histology of the bladder and 40% of patients with biochemical recurrence died of PCa rather than from BC.

Conclusion: Concomitant PCa is occurring in $>50\%$ of RC specimens with a significant proportion having characteristics (GS, pathological stage) of clinically relevant disease. Adverse bladder histology is a risk factor for both PCa and biochemical PSA recurrence. Follow-up analyses after RC should include PSA measurements also in low-risk PCa as a considerable number of patients develop biochemical recurrence and metastases from PCa partly ending up with death related to PCa in patients suffering from BC. © 2016 Elsevier Inc. All rights reserved.

Keywords: Bladder cancer; Incidental prostate cancer; Radical cystectomy; PSA; Free PSA; Biochemical recurrence; Prostate cancer-specific mortality

1. Introduction

Bladder cancer (BC) and prostate cancer (PCa) are the most common genitourinary malignancies worldwide associated with significant morbidity and mortality [1].

Radical cystectomy (RC) with extended bilateral pelvic lymphadenectomy is currently the standard treatment for

patients suffering from localized muscle-invasive or recurrent high-risk non-muscle-invasive BC according to the European Association of Urology (EAU) guidelines (www.uroweb.org).

Especially in younger men, there is a recent strong trend toward prostate or at least “prostate apex or capsule-sparing” techniques, whose clear advantages are the functional improvement of voiding and sexual function, whereas oncological outcomes have been reported not as inferior in comparison to standard RC [2].

However, one has to consider that “prostate-sparing” surgery techniques harbor still the risk of a prostate

* Corresponding author. Tel.: +43-512-504-24811; fax: +43-512-504-28365.

E-mail address: Isabel-maria.heidegger@tirol-kliniken.at (I. Heidegger).

involvement from BC or even the existence of PCa as a second malignancy [3–5]. Furthermore, no exact consensus exists regarding which approach preserves function best, varying from “prostate-, capsule-, seminal-, and nerve-sparing” techniques [6]. Therefore, regarding the current knowledge, “prostate-sparing cystectomy” may be an option only in a subset of carefully selected patients with BC without primary involvement of the prostatic urethra and without known PCa.

Currently, only few studies analyzed the effect of PCa in RC specimens while most of them argue that PCa is insignificant in patients undergoing RC and that “prostate-sparing cystectomy” technique can be safely offered to patients with bladder-confined disease.

The aim of the present study was to analyze the PCa incidence, histology, and clinical significance, as well their implication for management in patients with advanced BC undergoing standard RC. In addition, we aimed to determine the effect of PCa recurrence in this 10-year single-center analysis including 213 patients.

2. Patients and methods

The study was approved by the local ethics committee (study no. UN3532; 274/4.4 and AN2015-0085; 348/4.10).

We retrospectively analyzed 213 male consecutive patients who underwent standard RC including removal of the bladder, prostate, seminal vesicles, distal ureters, bilateral extended pelvic lymphadenectomy, and urinary diversion from January 2006 to December 2015 at our department. All patients met the European Association of Urology (EAU) criteria for cystectomy (www.uroweb.org), with localized muscle-invasive BC or recurrent high-risk non-muscle-invasive BC. BC was previously histologically confirmed by transurethral resection of the bladder. Patients who underwent neoadjuvant chemotherapy before RC were excluded from the study. Histopathological examination was performed by an experienced uropathologist of our University hospital.

Routine diagnostic preoperative evaluation included measurement of prostate-specific antigen (PSA), the percentage of free PSA (fPSA%), and digital rectal examination. Furthermore, all patients underwent imaging (computed tomography, positron emission tomography-computed tomography, or magnetic resonance imaging) before surgery where no signs of local or distant metastatic spread was confirmed. None of the patients included in the study had a previous histologically confirmed PCa at the time of BC diagnosis.

All demographic and baseline characteristics as well as histopathological and biochemical parameters were analyzed descriptively using Excel. Fisher exact test and Mann-Whitney test were performed for group comparisons. A significance level of $\alpha = 0.05$ (two-tailed) was applied.

Table 1

Overview about histopathological findings in radial cystectomy specimens

	<i>n</i> (%)
Pathological stage	
Primary carcinoma in situ	26 (12.2%)
pT1	51 (23.9%)
pT2a	25 (11.7%)
pT2b	34 (16.0%)
pT3a	27 (12.7%)
pT3b	25 (11.7%)
pT4	21 (9.9%)
Tumor free	3 (1.4%)
Concomitant carcinoma in situ	127 (59.6%)
Lymph node status	
N0	162 (76.1%)
N1	19 (8.9%)
N2	2 (0.9%)
N3	16 (7.5%)
Lymphovascular invasion	
Positive	44 (20.7%)
Negative	142 (66.7%)
Unknown	20 (9.4%)

3. Results

We analyzed 213 male patients who underwent RC. Histology and pathology of BC specimens are demonstrated in [Table 1](#).

Of 213 male patients, 113 patients (53.1%) were diagnosed with PCa in the RC specimen. Among them, all patients showed the histology of an acinar adenocarcinoma. None of our patients included in the study had a transrectal or perineal prostate biopsy before RC. Further, no prostate biopsies were performed as part of the transurethral resection of the prostate or bladder mapping.

The median age of patients with PCa in the RC specimen was 71 years (mean = 69.7 y), whereas patients without PCa in the RC had a median age of 68 years (mean = 67.2 y) indicating that PCa occurred significantly more frequently in older men ($P = 0.003$).

Comparing preoperative PSA levels of patients with and without PCa, our data show that both PSA and fPSA% were significantly increased in those patients with PCa (PSA, $P = 0.014$; fPSA%, $P \leq 0.001$) ([Table 2](#)).

Analyzing the aggressiveness of PCa, our data clearly show that 52.2% (59/113) of patients had at least a Gleason score (GS) 7 in final pathology report indicating that they have a significant tumor grade in the prostate tissue. Concerning the pathological stage, we found that pT2c (both prostate lobes interspersed with carcinoma, but organ confined) was the predominant histology. However, 10.6% of RC specimens showed an organ border growth (\geq pT3a). Detailed analyses of histology and GS are shown in [Table 3](#).

To the best of our knowledge, there are no data available evaluating if the histology of the bladder in the RC specimen correlates with the incidence of PCa. For this,

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