Original Study

Radical Cystectomy in a Dutch University Hospital: Long-Term Outcomes and Prognostic Factors in a Homogeneous Surgery-Only Series

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Abstract

Limited survival data regarding muscle-invasive bladder cancer are available from outside the large tertiary referral centers. The aim of this study was to present survival outcomes and identify prognostic factors after oncologic cystectomy at a Dutch University Hospital with a moderate annual cystectomy volume. This study demonstrates a comparable 5-year recurrence-free survival (RFS) and overall survival (OS) in comparison with larger cystectomy centers.

Background: The aim of this study was to present survival outcomes and identify prognostic factors in patients undergoing radical cystectomy (RC) for urothelial bladder cancer (UBC) in a homogeneous surgery-only series. **Patients and Methods:** Patients who underwent RC for UBC with intent-to-cure between January 1998 and December 2010 without neoadjuvant or adjuvant treatment were included in this retrospective study. Clinical and histopathologic data were collected and institutional review board approval was obtained. Outcomes of interest were 30-day mortality (30dM), RFS, and OS. Univariable and multivariable analysis were performed. Median follow-up was 9.1 years. **Results:** Two hundred forty-five patients were included with a median age of 65 years (range, 34-92 years). 30dM rate was in 5 out of 245 patients (2.0%) and 5-year RFS and OS rates were 67% and 58%, respectively. A total of 223 patients (91%) underwent lymph node (LN) dissection. Median number of removed and positive LNs were 9 and 1.5, respectively. Variables independently associated with decreased OS and RFS were tumor stage and LN status. In addition, positive soft tissue surgical margin (STSM) status was independently associated with decreased OS. In LN-positive patients, presence of extranodal extension (ENE) was associated with decreased RFS (39.7% vs. 7.3%; $P = .005$). **Conclusion:** Radical cystectomy for UBC was associated with low perioperative mortality rate and provided 5-year disease control in approximately two-thirds of patients. Independent prognostic factors included tumor stage, LN status (RFS and OS), and STSM status (OS). Presence of ENE in LN-positive patients was univariably associated with decreased RFS and OS.

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Introduction

Bladder cancer is the second most common genitourinary malignancy worldwide.[1] Although most patients present with non–muscle-invasive bladder cancer (NMIBC), approximately 30% of patients present with muscle-invasive bladder cancer (MIBC). In addition, patients who present with NMIBC are at risk of progression to MIBC, with progression rates up to 50% to 75% for high-risk tumors.[2] The standard of care for MIBC is radical cystectomy (RC), lymph node (LN) dissection (LND), and urinary diversion. In addition, there is increasing evidence that

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neoadjuvant chemotherapy might benefit patients with locally advanced disease.[3]

A number of large, tertiary referral centers have reported on their experience with RC for urothelial bladder cancer (UBC). Consequently, most of our knowledge regarding survival outcomes and prognostic factors originate from large centers that perform an average volume of 40 to 50 RCs annually.[4,5] Such RC series are valuable because they present survival data from specialized centers of excellence that might be considered as the gold standard outcomes. Yet, limited survival data are available from outside these large tertiary referral centers, and substantial differences in the annual number of RCs, surgical techniques, use of (neo)-adjuvant chemotherapy and/or patient populations might be present.[6,7] The effect of these interinstitutional differences, in particular between high-volume centers and moderate-volume centers, on survival outcomes and on the prognostic value of proposed prognostic factors have only partially been explored.[6]

The goal of the current study was to present RC survival data and identify prognostic factors in a contemporary surgery-only series from a Dutch university hospital.

Patients and Methods

Cohort Assembly and Data Collection

We reviewed our Institutional Review Board-approved computerized database, including all patients (n = 426) who underwent RC between January 1998 and December 2011 at the Radboud University Nijmegen Medical Centre. Clinical and histopathologic data were collected by 2 dedicated data extractors using standardized retrospective medical record review. Excluded were patients who underwent RC: (1) after December 2010 (to assure a minimum of 2 years follow-up; n = 65); (2) for nononcological reasons or non-UBC (n = 61); (3) for palliative reasons (n = 18); or (4) and received neoadjuvant or adjuvant treatment (n = 37). A total of 245 patients were included in this study. Indications for RC were MIBC at transurethral resection of bladder tumor or NMIBC refractory for treatment.

Pathologic Variables

All patients underwent en bloc RC with urinary diversion. Pathologic tumor staging and grading was standardized to the 2002 American Joint Committee on Cancer (AJCC) and 1973 World Health Organization recommendations, respectively.[8,9] The extent of LND was determined by analyzing the operative reports, rather than the preoperatively intended LND template. Limited LNDs included LN removal in the obturator region only. Standard LND included LN removal at the common iliac bifurcation (proximal), LN of Cloquet (distal), lateral border of the external/common iliac vessels (lateral), and hypogastric vessels (posterior). Extended LND differed from standard LND by extending the proximal limit to the aortic bifurcation and inclusion of the presacral area. LNs were removed en bloc with the RC specimen. The specimen was macroscopically evaluated for the presence and number of LNs, individually dissected from the adipose tissue and completely embedded in 1 or more slices depending on the LN size. In addition, the remaining fatty tissue was completely embedded in paraffin. Next, microscopic evaluation was performed by a dedicated uropathologist. Presence of a LN was defined as aggregates of lymphocytes with presence of a nodal capsule and sinus. In case LNs were found on multiple slides, careful reconstruction with the macroscopic report was performed to prevent duplication in LN count. LN density was defined as the ratio between positive LNs and total removed LNs. Pathologic subgroups were defined as organ-confined (OC; pT0-pT2, pN0), extravesical (EV; pT3-pT4, pN0) or LN positive (LN+; pTany, pN1-3) disease. Soft tissue surgical margin (STSM) status was determined by evaluating the inked soft tissue margin of the RC specimen. In LN+ patients, presence of extranodal extension (ENE) was defined as extension of tumor tissue through the LN capsule into the perinodal tissue.

Follow-up and Statistical Analysis

Primary end points of this study were 30-day mortality (30dM), recurrence-free survival (RFS) and overall survival (OS). 30dM was defined as all deaths occurring within 30 days after RC. RFS

Table 1 Baseline Characteristics of All 245 Patients

Characteristic	Patients, n (%)
Age	
>65 years	122 (49.8)
≤65 years	123 (50.2)
Sex	
Male	185 (75.5)
Female	60 (24.5)
ASA Score	
1	64 (26.1)
2	128 (52.2)
3	46 (18.8)
4	–
Missing	7 (2.9)
Pathological Stage	
pT0	33 (13.5)
pTa	24 (9.8)
pTis	33 (13.5)
pT1	21 (8.6)
pT2a	25 (10.2)
pT2b	23 (9.4)
pT3a	39 (15.9)
pT3b	31 (12.6)
pT4a	11 (4.5)
pT4b	5 (2.0)
History of NMIBC	
Yes	105 (42.9)
No	140 (57.1)
Soft Tissue Surgical Margin Status	
Positive	7 (2.9)
Negative	238 (97.1)
30-Day Mortality	
Yes	5 (2.0)
No	240 (98.0)

Abbreviations: ASA = American Society of Anesthesiologists; NMIBC = non–muscle-invasive bladder cancer.