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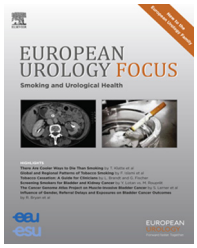

Bladder Cancer

Prognostic Model for Predicting Survival in Patients with Disease Recurrence Following Radical Cystectomy

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Abstract

Background: Although the natural history of urothelial carcinoma of the bladder (UCB) from radical cystectomy (RC) to disease recurrence (DR) has been investigated intensively, the course of patients who have experienced DR after RC for UCB remains poorly understood.
Objective: To evaluate the prognostic value of the Bajorin criteria that consists of two risk factors: Karnofsky performance status (KPS) and the presence of visceral metastases (VMs) in patients with DR after RC for UCB. Furthermore, to identify additional factors associated with cancer-specific mortality (CSM) and thus build a multivariable model to predict survival after DR.

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Bladder cancer
Transitional cell carcinoma
Metastasis
Disease recurrence
Prognosis
Survival
Model

Design, setting, and participants: We identified 967 patients with UCB who underwent RC at 17 centers between 1979 and 2012 and experienced DR. Of these, 372 patients had complete data we used for analysis.
Outcomes measurements and statistical analysis: Univariable Cox regressions analysis was performed. We used a forward stepwise selection process for our final multivariable model.
Results and limitations: Within a median follow-up of 18 mo, 266 patients died of disease. Cancer-specific survival at 1 yr was 79%, 76%, and 47% for patients with no ($n = 105$), one ($n = 180$), and two ($n = 87$) risk factors ($p < 0.001$; c-index: 0.604). On multivariable analyses, we found that KPS <80%, higher American Society of Anesthesiologists score, anemia, leukocytosis, and shorter time to DR (all p values <0.034) were independently associated with increased CSM. The combination of time to DR and KPS resulted in improved discrimination (c-index: 0.694).
Conclusions: We confirmed the prognostic value of KPS and VMs in patients with DR following RC for UCB. We also found several other clinical variables to be associated with worse CSM. We developed a model for predicting survival after DR inclusive of time to DR and KPS assessed at DR. If validated, this model could help clinical trial design.
Patient summary: We developed a model to predict survival following disease recurrence after radical cystectomy for urothelial carcinoma of the bladder, based on time to disease recurrence and Karnofsky performance status.

1. Introduction

Although the natural history of urothelial carcinoma of the bladder (UCB) from radical cystectomy (RC) to disease recurrence (DR) has been intensively investigated [1–7], that of patients who have experienced DR after RC for UCB still remains poorly understood. Indeed, it has been previously reported that poor patient Karnofsky performance status (KPS) and the presence of visceral metastases (VMs) (ie, the Bajorin criteria) are associated with decreased survival in patients with metastatic urothelial carcinoma (UC) treated with systematic cisplatin-based chemotherapy and could be used to stratify patients into risk groups [8]. Recent studies have reported that a shorter time to DR after RC is associated with unfavorable outcomes [9,10]. Improved understanding of the natural history of such patients and accurate prognostication after DR could help in patient counseling and in the design of clinical trials.

The aim of the study was therefore threefold. First, we assessed the prognostic value of the Bajorin criteria in a large multi-institutional cohort of patients who experienced DR after RC for UCB. Second, we evaluated additional clinical, pathologic, and/or biologic factors at the time of DR in these patients for an association with cancer-specific outcomes. Third, we aimed to create a multivariable model based on the identified variables that were associated with cancer-specific outcomes and to compare discrimination versus the Bajorin risk grouping.

2. Materials and methods

2.1. Patient selection

This study was approved by institutional review boards, with all participating sites providing the necessary data-sharing agreements before initiation. A total of 17 international centers provided data. The database was closed in October 2012.

Our multi-institutional cohort consisted of 967 patients who experienced DR after RC for UCB between 1979 and 2012. Of these, we identified 372 patients with complete data on all variables for analysis. Patients were excluded even when missing only one variable. We consider this step important to avoid selection bias. None of the patients had evidence of distant metastases at the time of RC. All patients underwent an RC with bilateral pelvic lymph node dissection and urinary diversion as described elsewhere [4]. No patient received neoadjuvant chemotherapy or pre- and/or postoperative radiation therapy to the bladder.

2.2. Pathologic evaluation

Tumors were staged according to the American Joint Committee on Cancer Union Internationale Contre le Cancer TNM classification, 7th edition [11]. Tumor grade was assessed according to the 1998 World Health Organization/International Society of Urologic Pathology consensus classification [12].

2.3. Follow-up regimen

Follow-up was performed according to institutional protocols. Postoperatively, patients were seen at least every 3–4 mo in the first year, every 6 mo in the second year, and annually thereafter. Diagnostic imaging of the upper tract (eg, ultrasonography and/or intravenous pyelography, computed tomography of the abdomen/pelvis with intravenous contrast) and chest radiography were performed annually and when indicated clinically. DR was defined as a tumor relapse in the operative field, regional lymph nodes, and/or distant metastases. DR was managed at the patient's and treating physician's discretion (ie, administration of salvage chemotherapy). Perioperative mortality (ie, death within 30 d of surgery) was censored at time of death for bladder cancer–specific survival analyses.

2.4. Statistical analysis

For statistical analysis, we only used patients with complete data on all variables ($n = 372$). Our first aim was to describe the association of the Bajorin criteria with cancer-specific mortality (CSM) [8]. Patients were thus categorized into three risk groups determined by KPS and/or the presence of VMs (no risk factors [RFs]: KPS ≥80% and no VMs; one RF: KPS <80% or presence of VMs; two RFs if both). Kaplan-Meier curves were generated (log rank).

Our next aim was to identify additional characteristics associated with cancer-specific survival (CSS) in these patients. There were four characteristics of interest (Table 1): clinical characteristics, characteristics at RC, biologic characteristics at DR, and treatment-related