



Original article

Nomogram for predicting survival of postcystectomy recurrent urothelial carcinoma of the bladder

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Abstract

Purpose: We aimed to identify prognostic clinicopathological factors and to create a nomogram able to predict overall survival (OS) in recurrent urothelial carcinoma of the bladder (UCB) after radical cystectomy (RC).

Materials and methods: Among 1,087 patients with UCB who had undergone RC at our 11 institutions between 1990 and 2010, 306 patients who subsequently developed distant metastasis or local recurrence or both were identified. Clinical data were collected with medical record review. Univariate and multivariate Cox regression models addressed OS after recurrence. A nomogram predicting postrecurrence OS was constructed based on Cox proportional hazards model, without using postrecurrence factors (systemic chemotherapy and resection of metastasis). The performance of the nomogram was internally validated by assessing concordance index and calibration plots.

Results: Of the 306 patients, 268 died during follow-up with a median survival of 7 months (95% CI: 5.8–8.5). Postrecurrence chemotherapy was administered in 119 patients (38.9%). Multivariable analysis identified 9 independent predictors for OS; period of time from RC to recurrence (time-to-recurrence), symptomatic recurrence, liver metastasis, hemoglobin level, serum alkaline phosphatase level,

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serum lactate dehydrogenase level, serum C-reactive protein level, postrecurrence chemotherapy, and resection of metastasis. A nomogram was formed with the following 5 variables to predict OS: time-to-recurrence, symptomatic recurrence, liver metastasis, albumin level, and alkaline phosphatase level. Concordance index rate was 0.75 (95% CI: 0.72–0.78) by internal validation using Bootstraps with 1,000 resamples. Calibration plots showed that the nomogram fitted well.

Conclusions: We identified 9 clinicopathological factors as independent OS predictors in postcystectomy recurrence of UCB. We also created a validated nomogram with 5 variables that efficiently stratified those patients regardless of eligibility for chemotherapy. The nomogram would be useful for acquiring relevant prognostic information and for stratifying patients for clinical trials. © 2016 Elsevier Inc. All rights reserved.

Keywords: Bladder cancer; Urothelial carcinoma; Radical cystectomy; Recurrence; Nomogram

1. Introduction

Radical cystectomy (RC) with pelvic lymph node (LN) dissection is the standard treatment for muscle-invasive or high-risk non-muscle-invasive urothelial carcinoma of the bladder (UCB) [1]. Unfortunately, postsurgical recurrence is highly probable; however, the 5-year recurrence-free survival rate after RC is reportedly 48% to 68% [2–6]. Prognosis of recurrent UCB is variable but generally dismal: 1-year overall survival (OS) rate after recurrence is reportedly 32% to 70%, and the median survival time (MST) rate is merely 4.0 to 11.2 months [7–11].

Precise prediction of prognosis is mandatory in patient counseling and patient stratification for clinical trials. Nomogram is one of the most popular prediction models, and has several advantages over other prediction models [12,13]. Overall, 3 major prognostic models, including 2 nomograms, have been proposed for metastatic UCB undergoing systemic chemotherapy [14–16]. However, those models excluded patients ineligible for systemic chemotherapy [14–16]. In an era of emerging immunotherapies and targeted therapies, even the patients ineligible for chemotherapy are to be considered for them because their toxic profiles differ from conventional cytotoxic chemotherapy [17]. Although previous studies identified potential prognostic factors and proposed prediction models for all patients after disease recurrence [7–11], a prognostic nomogram has not been available so far for these patients.

In this study, we aimed to develop a prognostic nomogram predicting survival of postcystectomy recurrence of UCB irrespective of eligibility for systemic chemotherapy.

2. Patients and methods

2.1. Patient population

The present study is approved by the institutional review board of each participating institute. We retrospectively reviewed medical records of 1,087 patients who underwent RC for bladder cancer at the University of Tokyo Hospital and 10 affiliated hospitals between January 1990 and December 2010. Patients who developed distant metastasis or local recurrence or both of UCB during post-RC follow-

up were identified. Recurrence in the preserved urothelium (i.e., upper urinary tract and retained urethra) was not included in the study population. Patients were excluded if they had pure nonurothelial cancers histologically (i.e., squamous cell carcinoma, adenocarcinoma, or small cell carcinoma), distant metastases at the time of surgery, or synchronous or metachronous invasive upper urinary tract or urethral cancers. On this basis, 306 patients with recurrent UCB were available for analysis (Supplementary Fig. 1).

2.2. Diagnosis and follow-up

All cystectomy specimens were subjected to routine pathological examination. Histological diagnosis was determined according to the World Health Organization classification system [18]. Primary tumors and LNs were restaged based on the 2009 UICC TNM system [19].

All patients were followed routinely after surgery according to each institution's protocol. Although the retrospective and multi-institutional nature of this study precluded a standardized follow-up protocol, patients were generally seen every 3 months in the first year, every 3 to 6 months in the second and third year, every 6 months in the fourth and fifth year, and annually thereafter. Patients who presented between scheduled visits with

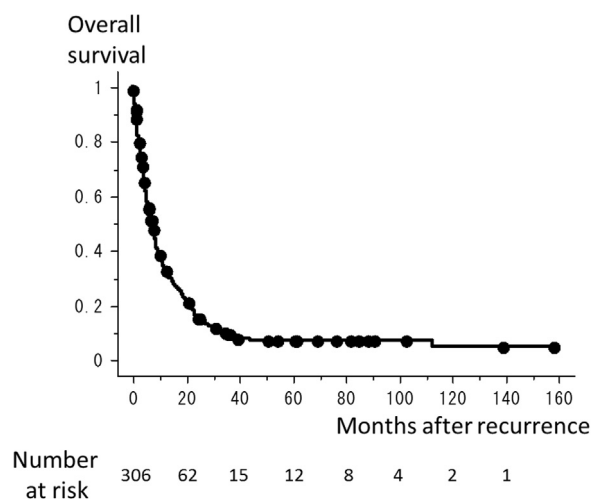


Fig. 1. Overall survival of the 306 patients with recurrent UCB analyzed using the Kaplan-Meier method.

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