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Bladder Cancer

Prediction of 90-day Mortality After Radical Cystectomy for Bladder Cancer in a Prospective European Multicenter Cohort

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Abstract

Background: Despite recent improvements, radical cystectomy (RC) is still associated with adverse rates for 90-d mortality.
Objective: To validate the performance of the Isbarn nomogram incorporating age and postoperative tumor characteristics for predicting 90-d RC mortality in a multicenter series and to generate a new nomogram based strictly on preoperative parameters.
Design, setting, and participants: Data of 679 bladder cancer (BCa) patients treated with RC at 18 institutions in 2011 were prospectively collected, from which 597 patients were eligible for final analysis.
Intervention: RC for BCa.
Outcome measurements and statistical analysis: An established prediction tool, the Isbarn nomogram, was applied to our cohort. For the purpose of external validation, model discrimination was measured using the receiver operating characteristics–derived area under the curve. Calibration plots examined the relationship between predicted and observed probabilities. Univariable and multivariable logistic regression models were fitted to assess the impact of preoperative characteristics on 90-d mortality.
Results and limitations: The 30-, 60-, and 90-d mortality rates in the development cohort ($n = 597$) were 2.7%, 6.7%, and 9.0%, respectively. The Isbarn nomogram predicted individual 90-d mortality with an accuracy of 68.6%. Our preoperative multivariable model identified age (odds ratio [OR]:1.052), American Society of Anesthesiologists score (OR: 2.274), hospital volume (OR: 0.982), clinically lymphatic metastases (OR: 4.111), and clinically distant metastases (OR: 7.788) (all $p < 0.05$) as

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independent predictors of 90-d mortality (predictive accuracy: 78.8%). Our conclusions are limited by the lack of an external validation of the preoperative model.
Conclusions: The Isbarn nomogram was validated with moderate discrimination. Our newly developed model consisting of preoperative characteristics might outperform existing models. Our model might be particularly suitable for preoperative patient counseling.
Patient summary: The current report validated an established nomogram predicting 90-d mortality in patients with bladder cancer after radical cystectomy (RC). We developed a new prediction tool consisting of strictly preoperative parameters, thus allowing clinicians an optimal consultation for RC candidates.

1. Introduction

Radical cystectomy (RC) with bilateral pelvic lymph node dissection is one of the most challenging procedures in urologic surgery and represents the standard-of-care treatment for muscle-invasive bladder cancer (BCa), as well as high-risk non–muscle-invasive BCa [1]. RC is associated with significant perioperative morbidity and mortality, varying between 30% and 70% and between 0.3% and 7.9%, respectively [2–16]. Weighing individual treatment benefits against the potential risks of RC represents one of the key challenges for medical providers treating BCa patients, particularly in the context of a demographic shift toward more elderly and sick patients [17]. Therefore, understanding the factors associated with morbidity and mortality at RC is essential for treatment planning and informed decision making prior to surgery.

There have been efforts to adapt existing prediction tools or to develop new ones for mortality after RC [13–15]. Prasad et al. and Smaldone et al. applied existing scores consisting of intraoperative parameters [13], as well as preoperative and intraoperative parameters [14] for outcome prediction in their cohorts. Isbarn and colleagues [15] developed a model for individual prediction of 90-d mortality after RC with a predictive accuracy of 70.1%. Taylor et al. externally validated the Isbarn model in a single-center cohort and developed a simple model consisting of two preoperatively readily available parameters [16]. Despite these efforts, a comprehensive assessment tool for prediction of 90-d mortality after RC based on readily available preoperative parameters, including the patient's comorbidity profile, is lacking.

The aim of the present study was to externally validate the Isbarn nomogram, as well as to develop an assessment tool for prediction of 90-d mortality based on preoperative patient characteristics in a contemporary prospective European multicenter cohort.

2. Patients and methods

2.1. Study population

The Prospective Multicenter Radical Cystectomy Series 2011 (PROMETRICS 2011) was an institutional review board–approved study, with all participating sites providing the necessary data-sharing agreements (Appendix). A total of 18 European centers (15 German, 2 Austrian, and 1 Italian center) prospectively collected data, resulting in a database consisting of 679 consecutive patients undergoing RC for muscle-invasive or high-risk BCa from January 1 to December 31, 2011. A computerized data collection sheet, including a comprehensive definition of all variables, was generated for data transfer. After combining the data sets, preliminary reports were generated to identify data inconsistencies and other data integrity problems. Regular communication among all participating centers ensured that all identified anomalies were resolved before starting the final analyses. Eighty-two patients (12.1%) were excluded because of incoherent data assessment. In total, 597 patients were considered for final analyses.

2.2. Assessment of data

Preoperative baseline patient characteristics were evaluated and documented at admission for RC and comprised continuous variables such as age, body mass index (BMI), and American Society of Anesthesiologists (ASA) score, as well as categorical variables such as gender and Charlson comorbidity index (CCI) (coded as <3 or ≥ 3) prior to RC.

Clinical and histopathologic stages were classified according to the 2009 TNM classification [18]. Histologic examination of the surgical specimens was performed by experienced uropathologists at each center. Clinical stage was assessed by radiologic imaging (computed tomography/magnetic resonance imaging) and history of transurethral resection of bladder tumor (TURBT). Treatment characteristics included the time interval between the last TURBT and RC (in months), hospital volume (number of RCs per year), preoperative histology (coded as urothelial carcinoma [UC], squamous cell carcinoma [SCC], other), clinical T stage (coded as $<$T3 or $\geq$T3), preoperative grading (coded as 1–2, 3, or unspecified), preoperative presence of carcinoma in situ (CIS), administration of neoadjuvant chemotherapy, and presence of a clinically lymphatic and distant metastatic disease (all coded as none, cN+, or cM1).

2.3. Statistical analyses

Medians and interquartile ranges (IQRs) were generated for continuously coded variables; frequencies and proportions were generated for categorical variables. The Mann-Whitney and chi-square tests were used to assess differences in medians and proportions, respectively. Regression coefficients from Isbarn's initial report were obtained for

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