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External validation of the pretreatment nomogram to predict acute urinary retention after ^{125}I prostate brachytherapy

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ABSTRACT

PURPOSE: Acute urinary retention (AUR) after ^{125}I prostate brachytherapy has a negative impact on quality of life. Recently, the authors developed a nomogram to predict the risk of AUR preoperatively. The aim of this study was to assess the external validity of the nomogram.

METHODS AND MATERIALS: The nomogram was initially developed on 714 patients treated with ^{125}I prostate brachytherapy at the University Medical Center Utrecht, the Netherlands. Predictive factors included in the nomogram were prostate volume, international prostate symptom score, neoadjuvant hormonal treatment, and prostate protrusion. For external validation, the data of 715 consecutive patients treated between January 2003 and July 2008 at the Princess Margaret Hospital, Toronto, were used. The performance of the nomogram was evaluated by discrimination (ability to distinguish between patients who develop AUR yes or no) and calibration (agreement between observed and predicted numbers of AUR).

RESULTS: Of the 715 patients treated at the Princess Margaret Hospital, 67 patients (9.4%) developed AUR compared with 8.0% in the University Medical Center Utrecht cohort. In the validation data set, the discriminatory ability of the nomogram was good (receive operating characteristic area: 0.86; 95% confidence interval: 0.82–0.91), and comparable to the derivation data set (receive operating characteristic area: 0.82; 95% confidence interval: 0.77–0.88). Comparison between the predicted risks and the observed frequencies of AUR showed underestimation of the nomogram in the validation data set for high AUR risks values. Still, the negative predictive value for the risk of AUR, using a cutoff value of 5%, was high (98.1%).

CONCLUSION: External validation of the nomogram shows adequate discrimination of patients with and without AUR. Therefore, the nomogram can aid in individualized treatment decision making. © 2012 American Brachytherapy Society. Published by Elsevier Inc. All rights reserved.

Keywords: Prostate cancer; Acute urinary retention; Prostate brachytherapy; Predictive nomogram; External validation

Introduction

The most predominant severe acute toxicity after prostate brachytherapy is acute urinary retention (AUR). Published AUR rates vary from 6% to 34% (1–5). It is known that AUR negatively influences quality of life (6, 7). Preoperative prediction of AUR is useful for patient counseling and for clinical decision making in patients with localized prostate cancer.

In a previous study, the authors developed a clinical nomogram to predict the risk of AUR after ^{125}I prostate brachytherapy preoperatively, using the data of 714 consecutive patients treated at their center (Appendix) (8). The nomogram was based on the most important pretreatment risk factors for AUR, that is, prostate volume, international prostate symptom score (IPSS), neoadjuvant hormonal treatment (HT), and the extent of prostate protrusion into

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The research was conducted at the Princess Margaret Hospital, Toronto, ON, Canada and at University Medical Center Utrecht, Utrecht, The Netherlands.

The authors declare no conflicts of interest.

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the bladder. Both calibration and discrimination were adequate (receiver operating characteristic [ROC] area: 0.82). The nomogram showed that among patients with a very low sum score (<18 points), the risk of AUR was only 0–5%, and that in patients with a high sum score (>35 points), the risk of AUR was more than 20%.

However, as the nomogram was based on single-center data and patient selection and treatment techniques may differ between centers, its predictive value in other patient populations is unknown (9–11). The aim of this study was to perform external validation of the nomogram, by using data of patients treated at the Princess Margaret Hospital (PMH) in Toronto, Canada.

Methods and materials

Patients

The derivation study population consisted of 714 consecutive patients with localized prostate cancer treated with ^{125}I seed implantation between January 2005 and December 2008 at the University Medical Center Utrecht (UMCU), the Netherlands (8). The validation population consisted of 715 consecutive patients with localized prostate cancer treated with ^{125}I seed implantation between January 2003 and July 2008 at the PMH, Toronto, Canada. The PMH was chosen for external validation for two main reasons: (*1*) MR imaging for postimplant dose evaluation is performed, which is required for adequate determination of prostate protrusion (8, 12, 13), (*2*) it is a high-volume center with meticulous followup and documentation of toxicity.

The implantation techniques and dosimetric analyses were similar and according to the guidelines of Groupe-Européen de Curiethérapie-European Society for Therapeutic Radiology and Oncology and American Brachytherapy Society (14, 15). Table 1 summarizes the similarities and differences in ^{125}I prostate brachytherapy procedures between the centers. The UMCU and the PMH brachytherapy procedures have both been extensively described previously (4, 6, 16, 17). All patients were treated in lithotomy position. The radioactive seeds were inserted transperineally according to the preplan in a modified peripherally loaded Seattle technique (4). All implants were evaluated at 1 month, by using CT and 1.5 or 3.0 T MRI fusion. Implant quality was defined in terms of the standard dosimetric parameters D_{90}, V_{100}, V_{150}, and V_{200} (14, 15). Urinary function was assessed using IPSS questionnaires, which were completed at baseline and at each followup visit. AUR was defined as any need for urinary catheterization within 3 months after implantation (18).

Research Ethics Board approval was obtained to access the data from the PMH prospective database. A consecutive cohort of patients was selected between January 2003 and July 2008, ensuring adequate patient numbers and a substantial followup. Baseline characteristics and post-treatment sequelae were retrieved, including the dates and duration of retention and catheterization.

Determination of prostate protrusion

The extent of prostate protrusion into the bladder was recently shown to be a strong independent predictor of AUR (8, 13). It relates to the large median lobes and was defined as the maximum distance from bladder base to prostate base (13). The extent of prostate protrusion was determined retrospectively on sagital MR images at 1 month after implantation for all patients at PMH (Fig. 1). All delineations were performed by the same physician (EMR), who was blinded to patient's AUR status.

The authors previous study (8) showed that the inter- and intraobserver variability of prostate protrusion measurements were good (i.e., 0.7 mm [standard deviation ± 0.9] and 0.4 mm [standard deviation ± 0.7], respectively). Pearson correlation coefficients (r) were calculated and showed that both inter- and intraobserver repeatability of prostate protrusion measurements were high ($r = 0.97$ and $r = 0.94$, respectively).

Statistical analysis

Patient characteristics of the UMCU and PMH were compared using independent sample t tests (continuous variables) or χ^2 tests (categorical or dichotomous variables). Multivariate logistic regression analysis was performed to explore the predictive values of the predefined predictors (i.e., prostate volume, IPSS, neoadjuvant HT, and the extent of prostate protrusion) of AUR in the validation data set (8).

Proper validation requires the use of the fully specified existing prognostic model to predict outcomes for the patients in the validation data set and then compare these predictions with the patients' actual outcomes. Therefore, the risk of AUR was calculated for each individual patient in the validation data set using the following equation (Appendix) (8):

$$\text{Risk of AUR} = 1/[1 + \exp(-\text{linear predictor})] \times 100\%$$

The predictive accuracy of the nomogram was quantified using discrimination and calibration measures. Differences in discriminative ability (i.e., the ability of the model to distinguish patients who develop AUR: yes or no) between the derivation and validation model were quantified by the area under the ROC curve (ROC area). The ROC area may theoretically range from 0.5 (discrimination equivalent to that of chance) to 1.0 (perfect discrimination). Calibration of the model (i.e., agreement between observed and predicted numbers of AUR) was determined by comparing the predicted and the observed numbers of AUR among five risk groups. In addition, calibration was statistically tested across deciles of predicted risks with the Hosmer–Lemeshow test, where an insignificant test indicates good model fit (11). Furthermore, the negative predictive value using a cutoff value of 5% was computed. The 5% cutoff value was chosen because the AUR rate in our population was 8.0% and a reduction in AUR rate is aimed for.

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