EUROPEAN UROLOGY ONCOLOGY XXX (2018) XXX–XXX

available at www.sciencedirect.com
journal homepage: euoncology.europeanurology.com

European Association of Urology

Development and External Validation of Nomograms To Predict Adverse Pathological Characteristics After Robotic Prostatectomy: Results of a Prospective, Multi-institutional, Nationwide series

Lorenzo Tosco [a,b], *Greet De Coster* [c], *Thierry Roumeguère* [d], *Wouter Everaerts* [a], *Thierry Quackels* [d], *Peter Dekuyper* [e], *Ben Van Cleynenbreugel* [a], *Nancy Van Damme* [c], *Elizabeth Van Eycken* [c], *Filip Ameye* [e], *Steven Joniau* [a,*],

for the Be-RALP: the Belgian RALP consortium

[a] *Urology, Department of Development and Regeneration, UZ Leuven, Leuven, Belgium;* [b] *Division of Nuclear Medicine and Molecular Imaging, KU Leuven, Leuven, Belgium;* [c] *Belgian Cancer Registry, Brussels, Belgium;* [d] *Department of Urology, Erasme Hospital ULB, Brussels, Belgium;* [e] *Department of Urology, AZ Maria Middelares, Gent, Belgium*

Article info

Article history:
Accepted April 11, 2018

Associate Editor:
Gianluca Giannarini

Keywords:
Prostate cancer
Robotic surgery
Nomogram
Prediction
Validation

Abstract

Background: The possibility of predicting pathologic features before surgery can support clinicians in selecting the best treatment strategy for their patients. We sought to develop and externally validate pretreatment nomograms for the prediction of pathological features from a prospective multicentre series of robotic-assisted laparoscopic prostatectomy (RALP) procedures.

Design, setting, and participants: Between 2009 and 2016, data from 6823 patients undergoing RALP in 25 academic and community hospitals were prospectively collected by the Belgian Cancer Registry. Logistic regression models were applied to predict extraprostatic extension (EPE; pT3a,b–4), seminal vesicle invasion (SVI; pT3b), and high-grade locally advanced disease (HGLA; pT3b–4 and Gleason score [GS] 8–10) using the following preoperative covariates: prostate-specific antigen, clinical T stage, biopsy GS, and percentage of positive biopsy cores. Internal and external validation was performed.

Outcome measurements and statistical analysis: The stability of the model was assessed via tenfold cross-validation using 80% of the cohort. The nomograms were independently externally validated using the test cohort. The discriminative accuracy of the nomograms was quantified as the area under the receiver operating characteristic curve and graphically represented using calibration plots.

Results and limitation: The nomograms predicting EPE, SVI, HGLA showed discriminative accuracy of 77%, 82%, and 88%, respectively. Following external validation, the accuracy remained stable. The prediction models showed excellent calibration properties.

Conclusions: We developed and externally validated multi-institutional nomograms to predict pathologic features after RALP. These nomograms can be implemented in the clinical setting or patient selection in clinical trials.

Patient summary: We developed novel nomograms using nationwide data to predict postoperative pathologic features and lethal prostate cancer.

© 2018 Published by Elsevier B.V. on behalf of European Association of Urology.

* Corresponding author. Urology, Department of Development and Regeneration, University Hospitals Leuven, 3000 Leuven, Herestraat 49, Belgium. Tel.: +32 1 6346930; Fax: +32 1 6346931.
E-mail address: steven.joniau@uzleuven.be (S. Joniau).

https://doi.org/10.1016/j.euo.2018.04.008
2588-9311/© 2018 Published by Elsevier B.V. on behalf of European Association of Urology.

Please cite this article in press as: Tosco L, et al. Development and External Validation of Nomograms To Predict Adverse Pathological Characteristics After Robotic Prostatectomy: Results of a Prospective, Multi-institutional, Nationwide series. Eur Urol Oncol (2018), https://doi.org/10.1016/j.euo.2018.04.008

1. Introduction

Prostate cancer (PCa) is the most common malignancy among men, representing 22.8% of cancers and causing 9.5% of male cancer mortality in Europe [1]. Therapeutic strategies are generally based on prognostic risk classification relying on preoperative features such as clinical TNM stage, biopsy Gleason score (bGS), initial prostate-specific antigen (iPSA) levels, number of positive biopsy cores [2,3], and multiparametric magnetic resonance imaging (mpMRI) [4]. Clinical stage and grade, for example, might under- or overestimate the pathologic stage and grade of the disease; up to 45% of high-grade PCa at biopsy (bGS 8–10) is downgraded to final GS $\leq$7 [5] and up to 33% of cT3a–4 PCa cases are downstaged at definitive pathology to pT2 [6]. In the absence of generally implemented validated biomarkers, the combination of preoperative clinicopathological features into nomograms represents the most accurate predictive or prognostic instrument. Preoperative nomograms can be useful for predicting survival [7] or specific postoperative pathological characteristics [8,9]. Pretreatment prediction of pathological stage can greatly improve our ability to counsel patients regarding treatment options. Nomograms often perform better than other predictive tools [10] and can reach greater predictive accuracy compared to clinical expertise [11,12]. Training populations usually involve patients from single institutions, typically academic and/or tertiary centres; thus, nomograms must be externally validated in different clinical settings before wider use, such as in centres in other states or continents, or community hospitals instead of academic hospitals [13]. The Kattan nomogram [14], for example, was externally validated in a community-based population and can be expected to be reasonably applicable in this setting, yet it overestimates recurrence-free survival for patients with a low-risk profile [15]. The development and validation of specific nomograms for each institution would represent the ideal scenario, but not all centres have a sufficient caseload to support the statistical methodology to develop and validate such instruments.

We aimed to develop and validate nomograms to predict adverse pathologic features using a nationwide data set from 25 academic and nonacademic hospitals.

2. Patients and methods

From 2009 onwards, academic and nonacademic Belgian hospitals have maintained a prospective data registry of consecutive patients treated with robotic-assisted laparoscopic radical prostatectomy (RALP) +/- lymph node dissection (the Be-RALP project). The project is supported by the Belgian government and has been implemented by the Belgian Cancer Registry. Between 2009 and 2016, clinical and pathologic data of 8922 patients treated in 25 hospitals were collected. The study was approved by the Steering Committee of the Be-RALP project, originating from a collaboration between the Belgian Association of Urology, the Belgian Cancer Registry, and RIZIV/INAMI (Rijksinstituut voor ziekte- en invaliditeitsverzekering/Institut national d'assurance maladie-invalidité).

The Belgian Cancer Registry has a legal basis for collection of data for all cancer types (diagnosis, treatment, and follow-up) as outlined in the Health Care Law of December 13, 2006 (www.kankerregister.org/media/docs/Wetgeving/Staatsbladgezondheidswet13122006pub22122006.pdf). Data collection for all consecutive patients in an electronic case report form (eCRF) was mandatory for reimbursement of the robotic instruments. Diagnostic evaluation, surgical indication, technique (nerve-sparing, lymph node dissection), and multimodal regimens followed the preferences of the individual institutions. Clinical T stage was based on digital rectal examination (DRE). We applied the following exclusion criteria to the overall group: previous medical treatment for urological disease (yes or unknown) to avoid any effect of neoadjuvant treatment on postoperative pathologic features; metastatic disease, including patients with PSA >100 ng/mL as a possible proxy of metastatic disease; and missing data for cT stage, iPSA, bGS, number of positive cores, and number of biopsy cores, as well as values considered to be inconsistent (Fig. 1). All GS $\leq$6 values were converted to GS 6 [16]. There were no data available on primary and secondary bGS. Clinical or pathological stage T3 cases were excluded if one of the T3 subcategories (ie, T3a, T3b) was not specified.

The covariates were chosen considering their common availability and use in clinical practice. We assessed the relationship between all available covariates and the following outcomes: (1) extraprostatic extension (EPE; pT3a,b–4); (2) seminal vesicle invasion (SVI; pT3b); and (3) high-grade locally advanced disease (HGLA; pT3b–4 and pathologic GS [pGS] 8–10).

Logistic regression models were applied to analyse the endpoints by testing their relationship with the following specific covariates: clinical T stage stratified as cT1 (reference), cT2, cT3a, and cT3b–4; bGS stratified as bGS 6 (reference), bGS 7, bGS 8, and bGS 9–10; iPSA (continuous); and the percentage of positive biopsy cores (continuous). The overall data set (100%) was randomly split in two sets containing 80% and 20% of the centres. The data set with 80% of the centres was used to develop the nomogram and tenfold cross-validation was applied to internally validate the stability of the model [17]. This was performed by randomly splitting the patients into ten equal samples. Nine-tenths of these samples were used to construct logistic regression models and the model coefficients were applied to the remaining sample (1/10). This process was repeated ten times and the variability in accuracy is summarised as the mean of the area under the receiver operating characteristic (ROC) curve (AUC) and the 95% confidence interval (CI). The final nomogram was derived from the data set containing 80% of the centres. For external validation, the data set containing the remaining 20% of the centres (test cohort) [17] was applied to the coefficients of the final model, and calibration and ROC curves were computed to check the discriminative accuracy of the model. Moreover, we assessed the net benefit of the model using decision curve analysis (DCA) [18]. Analyses were performed with SAS v.9.3 for Windows (SAS Institute, Cary, NC, USA). The significance level was set at $\alpha = 0.05$, and all tests were two-sided.

3. Results

After applying the exclusion criteria, 6823 patients remained for analyses; after eliminating patients with missing data for the specific outcomes, three subgroups were defined (Fig. 1). Descriptive statistics for the entire cohort are shown in Table 1. Three different nomograms (EPE, SVI, and HGLA) were developed based on coefficients from the logistic regression for the 80% cohort (Table 2). All the covariates were significant predictors for each outcome; only cT2 did not differ relative to cT1 in the prediction of risk of HGLA ($p = 0.08$). The nomograms based on the 80% cohort

Please cite this article in press as: Tosco L, et al. Development and External Validation of Nomograms To Predict Adverse Pathological Characteristics After Robotic Prostatectomy: Results of a Prospective, Multi-institutional, Nationwide series. Eur Urol Oncol (2018), https://doi.org/10.1016/j.euo.2018.04.008

Download English Version:

https://daneshyari.com/en/article/11017617

Download Persian Version:

https://daneshyari.com/article/11017617

Daneshyari.com