

External validation of the PRECE nomogram model in a Central America cohort

Abstract

Introduction: This is an external validation study of the PRECE prostate cancer nomogram in a Central American population.

Methods: We present 102 consecutive cases of robotic radical prostatectomy, performed with preservation of the anterior fascia and we use the PRECE nomogram as a guide to preserve the prostatic neurovascular pedicles. We compared the predicted extra-capsular extension from the PRECE nomogram to the final prostatectomy pathology.

Results: Analysis of post-prostatectomy pathological samples revealed that 61% patients had pT2; 27% had a pT3a and 12% had a pT3b, respectively

The ROC curve for the PRECE nomogram at one (1) mm showed a model AUC of 0.91 (95% CI), which implies a high agreement with the PRECE nomogram in the prediction of extraprostatic disease.

Conclusion: This is the first report of external validation of the PRECE nomogram in a Central American population. PRECE demonstrated high discrimination for the prediction of extraprostatic disease in an independent Latin American cohort. More external validation studies, from different geographic settings, are expected to confirm the reliability and reproducibility of PRECE in other clinical settings.

Keywords: PRECE nomogram, extraprostatic disease

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Introduction

Prostate cancer is the most frequent and lethal tumor in Panama.¹ Worldwide, it is the fourth in incidence and eighth in mortality.² Radical surgery is one of the pillars in the treatment of the disease. Since the initial descriptions of Dr. Walsh, it has been known that the preservation of the prostatic pedicles is of value to avoid erectile dysfunction and urinary incontinence.³

The challenge of preserving the prostatic neurovascular pedicles is avoiding positive margins and not to preserve them in the presence of extraprostatic disease.

Several techniques have been published for pedicle preservation,⁴ and the current trend is gradual preservation,⁵ a procedure performed in patients who have undergone robotic surgery. The decision whether or not to perform pedicle preservation depends on the preoperative prediction of extraprostatic extension, based on clinical staging, the International Society of Urological Pathology (ISUP) score, multiparametric MRI and the use of different nomograms.

There are several nomograms: Briganti, Memorial Sloan Kettering Cancer Center, among others.⁶ Dr. Patel's group has published the use of the PRECE nomogram (Predicting Extracapsular Extension in Prostate Cancer), available online at the website www.prece.it. This nomogram uses a database of more than 6,000 patients⁷ from the United States and is proposed as a tool for predicting extraprostatic extension and as a guide for the surgeon, so that he can decide the degree of preservation to be performed in radical robotic surgery.

The PRECE nomogram⁷ proposes in a graded way the risk of extraprostatic disease, in the capsule and at different distances (1, 2, 3, 4 mm outside the capsule). The model is applied to each prostate

lobe for a separate prediction and is composed of simple co-variables such as age, prostate-specific antigen, clinical stage (American Joint Committee on Cancer TNM staging 1992/2002), Gleason score and percentage of positive biopsy, the latter distributed topographically within the prostate gland. Despite the successful performance in internal validation (AUC 0.81), the model still lacks an external validation study in Latin American populations. It has only been published in Italian population, with an AUC of 0.80 in the capsule.⁷

The objective of this study is the external validation of the PRECE nomogram in a Latin American population group undergoing robotic radical prostatectomy, from a geographic area different from those already described in the literature.

Methodology

This is an external validation study based on a retrospectively collected database of 102 consecutive patients who underwent robotic-assisted radical prostatectomy between January 2021 and June 2024, in Panama City, Panama. The robotic radical prostatectomies were performed by one surgeon using the Patel technique.⁷ In total, 204 prostate lobes from 102 patients were considered and constituted the validation data set. All patients underwent surgery for clinically localized or locally advanced prostate cancer and by the same group of surgeons. Preoperative clinical variables included patient age, total prostate-specific antigen (PSA) level, and clinical stage (American Joint Committee on Cancer TNM staging 1992/2002). In addition, a specific clinical T stage was determined on one side, that is, when a patient is assigned to cT2a, the abnormally palpable lobe was considered to be stage T2a, while the normal lobe was assigned to stage T1c. On the other hand, a patient with abnormally palpable tumor on both sides was considered to have cT2c in each lobe. The

biopsy variables considered for each lobe were the total number of biopsies with tumor and the Gleason score. In addition, the percentage of each biopsy positive for cancer was considered.^{8,9}

The main endpoint of the study is to externally validate the PRECE model for the prediction of Extraprostatic at one millimeter (1 mm) of the prostatic capsule.

For the analysis, the statistical program Datatab (www.datatab.net) was used for the creation and analysis of the database and Microsoft Excel for the preparation of tables.

The external validation was performed with the evaluation of receiver operating characteristic (ROC) curves, to address the ability of the prediction model to discriminate between patients with or without ECE. The area under the ROC curve (AUC) was estimated with a 95% confidence interval (CI). The AUC ranges from 0.5 to 1; a value of 0.5 indicates no discrimination, $0.5 < \text{AUC} < 0.7$ poor discrimination, $0.7 \leq \text{AUC} < 0.8$ acceptable discrimination, $0.8 \leq \text{AUC} < 0.9$ excellent discrimination, $0.9 \leq \text{AUC} < 1$ outstanding discrimination, and 1 indicates perfect discrimination. The criteria used in the validation model of Chiara Sighinolfi¹⁰ were applied. Sensitivity, specificity, Chi square, and the Cox & Snell analysis of the regression model were applied.

Results

Preoperative characteristics

The characteristics of our patients in the validation cohort are summarized as follows: mean age was 63 (Range: 41-76) years, mean PSA value was 9.4 (Range: 3.2-20.0) ng/ml. Clinical staging was stratified as follows: 76.5% had a cT1 (78/102), and 23.5% had a cT2 (24/102).

Postoperative characteristics

Analysis of postprostatectomy pathological specimens revealed that 61% of patients had pT2; 27% had pT3a and 12% had pT3b, respectively. Regarding the International Society of Urological Pathology (ISUP) histological analysis, between the 100 patients it revealed ISUP 1 in 20%, ISUP 2 in 17%, ISUP 3 in 45%, ISUP 4 in 14% and 4% with ISUP 5. Overall, extraprostatic disease was found in 39% of cases and of these pT3 patients, 4% had bilaterally positive seminal vesicles.

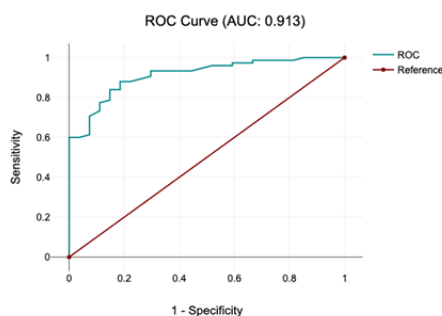


Figure 1 Estimated ROC curve and AUC for a Latin American cohort.

The ROC curve for the PRECE nomogram at one (1) mm showed a model AUC of 0.91 (95% CI) (Figure 1). Sensitivity was 96% and specificity was 44% with 95% of confidence interval (CI: 0.84-0.92). Chi² was 74.62. The Chi square measures the difference between the observed and expected frequencies of the outcome of the model. 74.62 suggest that the model's predictors have a significant relationship with the outcome. The Cox & Snell logistic regression

analysis of the model was 0.31. This indicates the amount of variance in the dependence variable was explained by the model.

Discussion

Our objective is the external validation in a Latin American population of a preoperative nomogram (PRECE), whose advantage in our geographic area is to use accessible clinical and pathological variables in prostate biopsy.

The previously published internal validation is an AUC of 0.81.⁷ The results of our study in a Latin American population (Panama) are similar and yield a performance of 0.91. Although there are already publications validating these nomograms in other latitudes, there are no specific publications for our region and this reality is also applicable to other nomograms.

PRECE is easy to use and freely available online (prece.it). Once the data is entered, a color graphic interface is presented that actively provides a value and range of probability of extraprostatic invasion at different distances from the prostatic capsule for each lobe. The graphic, through three traffic-light type colors, provides elements for the surgeon to decide on the dissection plane, according to the risk of extraprostatic disease.⁷

There are different nomograms that use more complex parameters (magnetic resonance) and that are not always accessible in our geographic region.¹¹ Moreover, these nomograms have been validated in other latitudes, which do not necessarily represent the behavior in our geographic region.¹² PRECE is based on simple, standardized and universally available variables, which carry a low degree of variability (i.e. age, PSA, clinical stage); pathological covariates of the systematic biopsy (i.e. Gleason score) are the ones that may differ,⁹ but ultimately do not affect the reproducibility of PRECE in a different population.¹⁰

For external validation studies, the minimum sample size required to achieve statistical value is 200 events (100 events and 100 non-events).^{13,14} Our study conforms to this requirement, although it is the minimum, and can be considered a weakness in this series. It should be kept in mind that the PRECE model originates from a cohort of 6360 patients who underwent robotic radical prostatectomy between January 2008 and January 2016.⁷ The Italian cohort includes patients elected for robotic surgery between the years 2018 to 2019.¹⁰ The current series is more recent, from 2021-2024, in order to have the 200 prostate lobes required for validation, given the lower number of cases per year performed robotically in our center.^{15,16}

In the case of the Italian external validation study, prediction is performed at the capsule level. In that review it is established that the prediction of extraprostatic disease at the capsule is the most difficult, as it involves the prediction of the smallest amount well within the definition of "focal" extraprostatic disease. Therefore, if the model performs adequately at this level, it is expected to perform even better for a larger amount of extraprostatic extension.⁹ In our case, one millimeter was used. From the operational point of view, the predictability is shown to be higher (0.91).

The visualization of the prostatic neurovascular pedicle artery is constant¹⁷ and can be appreciated as a constant reference at one millimeter from the capsule, in all robotic, laparoscopic and open surgery.

External validation studies in open surgery, which is the type of surgery performed in most of Latin America, are expected to demonstrate similar AUCs for PRECE.

Conclusion

PRECE shows high discrimination for the prediction of extraprostatic disease in an independent Latin American cohort. Further external validation studies, from different geographical settings, are awaited to confirm the reliability and reproducibility of PRECE in other clinical settings.

Acknowledgments

None.

Conflicts of interest

The authors declares that there is no conflicts of interest.

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