Predicting the Probability of Lymph Node Involvement with Prostate Cancer Nomograms: Can We Trust the Prediction Models?

Predicción de la probabilidad de compromiso ganglionar con nomogramas para cáncer de próstata. ¿Podemos confiar en los modelos de predicción?

Julian Chavarriaga[1] Catalina Barco-Castillo[2] Jessica Santander[2] Laura Zuluaga[2] Camilo Medina[2] Carlos Trujillo[2] Mauricio Plata[2] Juan Ignacio Caicedo[2]

[1] Division of Urology, Facultad de Medicina, Pontificia Universidad Javeriana, Bogotá, Colombia
[2] Department of Urology, Hospital Universitario, Fundación Santa Fe de Bogotá, Bogotá, Colombia

Address for correspondence Julian Chavarriaga, MD, Facultad de Medicina, Pontificia Universidad JaverianaBogota, Colombia (e-mail: chavarriagajulian@gmail.com).

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Abstract

Introduction Prediction of lymph node involvement (LNI) is of paramount importance for patients with prostate cancer (PCa) undergoing radical prostatectomy (RP). Multiple statistical models predicting LNI have been developed to support clinical decision-making regarding the need of extended pelvic lymph node dissection (ePLND). Our aim is to evaluate the prediction ability of the best-performing prediction tools for LNI in PCa in a Latin-American population.

Methods Clinicopathological data of 830 patients with PCa who underwent RP and ePLND between 2007 and 2018 was obtained. Only data from patients who had ≥ 10 lymph nodes (LNs) harvested were included ($n = 576$ patients). Four prediction models were validated using this cohort: The Memorial Sloan Kettering Cancer Center (MSKCC) web calculator, Briganti v.2017, Yale formula and Partin tables v.2016. The performance of the prediction tools was assessed using the area under the receiver operating characteristic (ROC) curve (AUC).

Results The median age was 61 years old (interquartile range [IQR] 56–66), the median Prostate specific antigen (PSA) was 6,81 ng/mL (IQR 4,8–10,1) and the median of LNs harvested was 17 (IQR 13–23), and LNI was identified in 53 patients (9.3%). Predictions from the 2017 Briganti nomogram AUC (0.85) and the Yale formula AUC (0.85) were the most accurate; MSKCC and 2016 Partin tables AUC were both 0,84.

Conclusion There was no significant difference in the performance of the four validated prediction tools in a Latin-American population compared with the European or North American patients in whom these tools have been validated. Among the 4 models, the Briganti v.2017 and Yale formula yielded the best results, but the AUC overlapped with the other validated models.

Keywords
- prostate cancer
- lymph node
- nomogram
- partin tables
- surgical pathology

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Resumen

Introducción La predicción del compromiso ganglionar es de suma importancia en pacientes con cáncer de próstata (CaP) que se van a someter a prostatectomía radical (PR). Múltiples modelos estadísticos se han desarrollado para predecir el riesgo de compromiso ganglionar y facilitar las decisiones clínicas de realizar o no linfadenectomía pélvica ampliada (LPA). Nuestro objetivo es evaluar la habilidad de predicción de las mejores herramientas de predicción de compromiso ganglionar en CaP en una población latinoamericana.

Métodos Se evaluaron los datos clínico-patológicos de 830 pacientes con CaP sometidos a PR y LPA entre el 2007–2018. Solo se analizaron os pacientes con 10 o más ganglios extraídos ($n = 576$). Cuatro modelos de predicción fueron validados en esta cohorte: el modelo de la calculadora *online* del Memorial Sloan Kettering Cancer Center (MSKCC), el Briganti v.2017, la fórmula de Yale, y tablas de Partin v.2016. Se evaluó el desempeño de los modelos con curvas de características operativas del receptor (COR) y el área bajo la curva (ABC).

Resultados La mediana de edad fue 61 años (rango intercuartílico [RI]: 56–66), mediana de Prostate specific antigen (PSA) 6,81 ng/mL (RI: 4,8–10,1), y mediana de ganglios extraídos 17 (RI: 13–23); se documentó compromiso ganglionar en 53 pacientes (9.3%). La habilidad de predicción del nomograma de Briganti v.2017 ABC (0,85) y la fórmula de Yale ABC (0,85) fueron las más precisas. El modelo del MSKCC y las tablas de Partin v.2016 mostraron AUC de 0,84 ambos.

Conclusiones No encontramos diferencia estadisticamente significativa en el desempeño de los cuatro modelos de predicción validados en esta población latinoamericana comparada con pacientes norteamericanos o europeos en los que estas herramientas fueron desarrolladas. Entre los 4 modelos, el nomograma de Briganti v.2017 y la fórmula de Yale mostraron los mejores resultados; sin embargo, el AUC se sobrepone con los otros modelos validados.

Palabras clave

- neoplasias de la próstata
- escisión del ganglio linfático
- prostatectomía
- patología quirúrgica

Introduction

Prostate cancer (PCa) is the second most frequently diagnosed cancer among males worldwide and in Colombia, being the fifth most common cause of death by cancer among males worldwide and the leading cause of death by cancer in Colombia.[1,2] Radical prostatectomy (RP) and radiotherapy are the standard of care for patients with PCa and aims to cure the patient, being most effective when the disease is confined to the organ. Currently, 12 to 16% of patients with PCa in the United States of America (USA) are managed with RP.[3–5] Extended pelvic lymph node dissection (ePLND) remains the most accurate method to detect lymph node (LN) metastases despite its invasive nature and the non-negligible risk of complications.

In the PSA era, the fraction of lymph node involvement (LNI) in localized PCa patients has decreased to $< 4\%$; only 0.87% of low-risk, 2% of intermediate risk and 7.1% of high-risk patients have LNI. Despite ePLND being considered a safe procedure, complications may occur, and their severity may vary considerably. Lymphocele rates range between 22 and 54%, thromboembolic events range between 0 and 8%, ureteral injury in $< 1\%$ of ePLND, the most frequent neurologic structure injured is to the obturator nerve with a rate between 0 and 5.1%, which represents a landmark of the ePLND template in retropubic RP versus 1.8% in laparoscopic or robot assisted RP. It is of paramount importance to recognize that both the LN yield and the risk of complications are dependent on the extent of the dissection.[6–12]

To facilitate the selection of PCa patients who would benefit from ePLND, prediction tools (nomograms, formulas, web calculators) have been designed to predict the probability of LNI preoperatively. These tools have been designed and calculated with logistic regression models, classification and regression trees (CART), artificial neural networks and simple linear formulas. More than 20 models are available to this date to predict LNI in patients with PCa. Some of the models are the nomograms reported by Briganti, 2006, 2006 (# harvested LN), 2007, 2007 (# positive cores), 2012, and 2017, Yonsei and Winter nomograms, linear formulas, such as the Roach formula, the Nguyen Formula and the Yale formula; Partin tables that have been validated multiple times, the last one in 2016, and the prediction models proposed by the MSKCC, Godoy prediction model and their web calculators,[13–27] Our aim is to evaluate the prediction ability of the most commonly used and best-performing prediction tools for LNI in PCa (MSKCC web calculator, Briganti v.2017, Yale formula and Partin tables v.2016) in a Latin-American population for the first time.

Methods

Patient data were collected retrospectively from our institution PCa database; clinicopathological data of 830 patients

with PCa who underwent RP and ePLND between 2007 and 2018 were obtained. Patient anonymity was guaranteed. Internal Review Board (IRB) approval was obtained before collecting data. Only data from patients who had $\geq$ 10 LNs harvested to guarantee that only data for adequate ePLNDs were collected according to previous validation studies.[14,16,19,27] The following histopathological results were available: PSA, cT-stage (assessed by Digital rectal examination [DRE]), Gleason score, number of biopsy cores, number of harvested LNs and positive LNs. Patients for whom data on biopsy cores taken were missing were excluded from the study. A total of 576 patients fulfilled all of these criteria and were included in the study ($n = 576$ patients).

The ePLND template applied included harvesting nodes overlying the obturator fossa; the external iliac vessels, the internal iliac artery and the common iliac vessels and the presacral stations may be removed, which would allow for clearing $\sim$ 75% of all anatomical landing sites of LN metastases.[28,29] All the LNs harvested were centrally reviewed by a uropathologist at our institution.

Four prediction models were validated, the MSKCC web calculator, (https://www.mskcc.org/nomograms/

Table 1 Comparison between positive and negative lymph nodes groups and global characteristics

	Negative LN n = 513	Positive LN n = 53	Global n = 566	*p-value*
Preoperative characteristics				
Age (years old)¥	61 [56–66]	64 [59–68]	61 [56–66]	0.013
PSA (ng/mL)¥	6.5 [4.79–9.1]	13 [7.1–20]	6.81 [4.8–10.11]	< 0.001
Clinical stage□				
T1a	1 (0.2)	0 (0)	1 (0.2)	< 0.001
T1b	9 (1.9)	1 (2)	10 (1.9)	
T1c	262 (54.8)	16 (32)	279 (52.7)	
T2a	142 (29.7)	14 (28)	156 (29.5)	
T2b	44 (9.2)	7 (14)	51 (9.6)	
T2c	8 (1.7)	2 (4)	10 (1.9)	
T3a	8 (1.7)	4 (8)	12 (2.3)	
T3b	4 (0.8)	6 (12)	10 (1.9)	
Biopsy				
Total biopsy cores¥	13 [12–15]	13 [12–15.25]	13 [12–15]	0.244
Positive biopsy cores¥	1 [0–2]	7 [6–11]	4 [2–7]	< 0.001
Gleason score¥	7 [6.75–7]	8 [7–8]	7 [7–7]	< 0.001
Gleason Grade, Group□				
1	125 (24.5)	2 (3.8)	127 (22.5)	< 0.001
2	203 (39.8)	6 (11.3)	210 (37.5)	
3	102 (20)	12 (22.6)	114 (20.2)	
4	68 (13.3)	24 (45.3)	92 (16.3)	
5	9 (1.8)	8 (15.1)	17 (3)	
Predicted risk according to the nomograms				
MSKCC nomogram (%)¥	4 [2–11.25]	20 [15.5–24.5]	5 [2–14]	< 0.001
Briganti nomogram (%)¥	3 [1–15]	36 [15–58]	3 [1–20]	< 0.001
Yale formula (%)¥	5 [3–8]	15 [10.25–23]	6 [3–10]	< 0.001
Partin tables (%)¥	1 [1–4]	11 [5–13.25]	2 [1–5]	< 0.001
Postoperative findings				
Resected lymph nodes¥	17 [13–22.5]	18 [14.5–24.5]	17 [13–23]	0.316
Positive lymph nodes¥	.	2 [1–2.5]	.	.
pN□	.	.	53 (9.4)	.

Abbreviations: LN, lymph node; MSKCC, Memorial Sloan Kettering Cancer Center; pN, Pathologic Nodes.
¥Reported as Median [IQR].
¥Reported as Median [IQR].
□Reported as n (%).

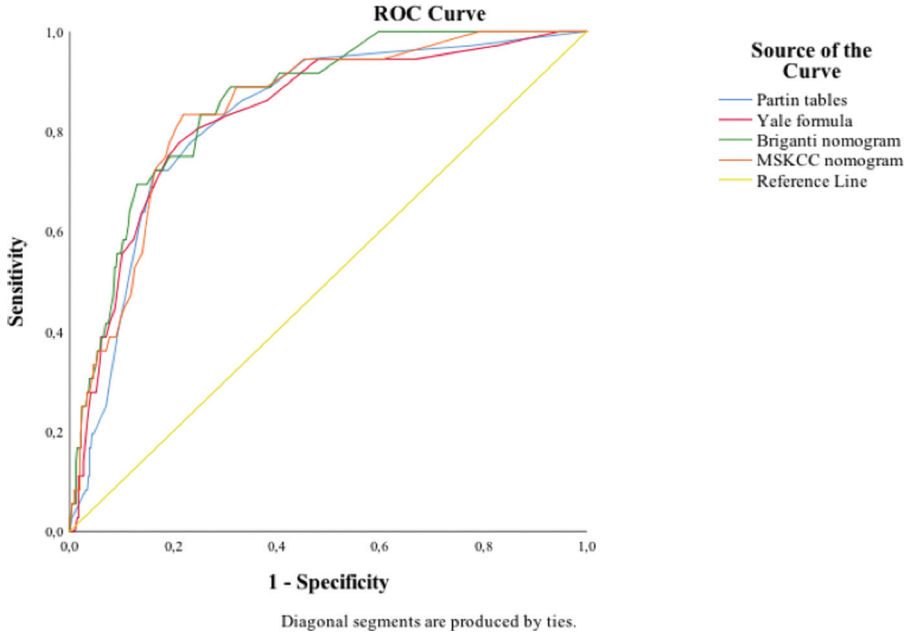

Fig. 1 Receiving operator characteristic curve for the four prediction models assessed. MSKCC = Memorial Sloan Kettering Cancer Center.

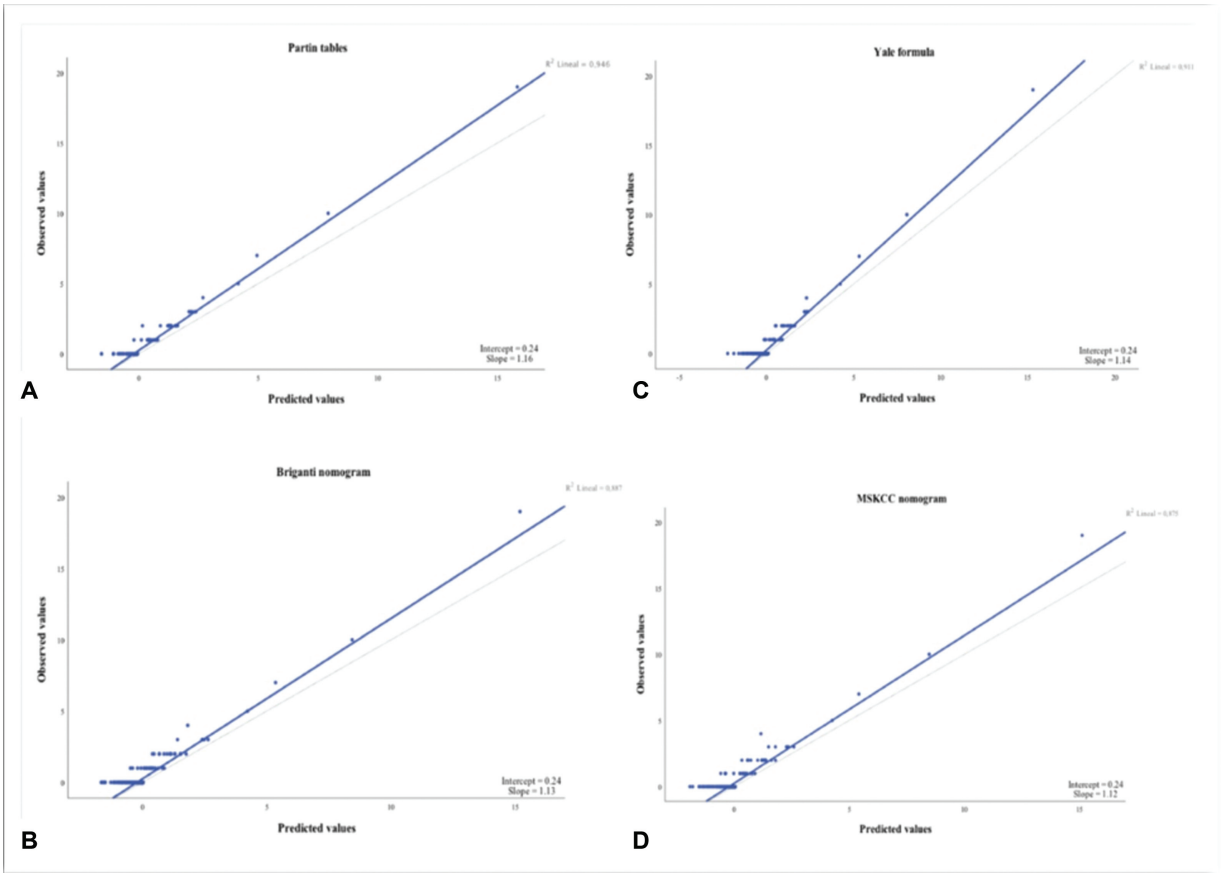

Fig. 2 Logistic regression of the four models with calibration plots. (**A**) Partin tables v.2016 showed a calibration-in-the-large (Interception) a = 0.24 and a slope b = 1.16. (**B**) Briganti v.2017 nomogram showed an interception a= 0.24 and a slope b = 1.13. (**C**) Yale formula showed an interception a= 0.24 and a slope b = 1.14. (**D**) MSKCC web calculator showed an interception a = 0.24 and a slope b = 1.12. MSKCC = Memorial Sloan Kettering Cancer Center.

prostate/pre_op), Briganti v.2017, Yale formula and Partin tables v.2016. Model coefficients were derived and made available at www.evidencio.com for validation purposes. Evidencio is an online platform that allows researchers to translate prediction models into user-friendly online calculators, facilitating the application of prediction models. Cutoff values for each model were 2% (Partin), 7% (Briganti), 20% (MSKCC) and 15% (Yale formula), those were taken from the internal validation study of each prediction model as the best performing cutoff value to predict LNI.[13,15,16,18,22,23,26,27,30]

Descriptive statistics were reported in terms of the frequency for categorical variables, the median with interquartile range (IQR) for continuous variables that did not follow a normal distribution. Significant differences ($p < 0.05$) between groups were assessed using the Fisher exact test for categorical variables and a Mann-Whitney U test for continuous variables in the comparison of positive LN (LN +) and negative LN (LN-) groups (►**Table 1**). Prediction tools performance was assessed using the area under the receiver operating characteristic (ROC) curve (AUC). Logistic regression statistics were used to evaluate models under- and overestimation showing the agreement between predicted and harvested LNI. Characteristics of the logistic regression were described in terms of calibration slope and intercept. The calibration slope reflects whether predicted risks are appropriately scaled with respect to each other over the entire range of predicted probabilities and is ideally equal to 1. The intercept (calibration-in-the-large) is a measure that quantifies whether the average of predictions corresponds to the average outcome frequency and ideally equals 0. The c-statistic represents the probability that individuals with the outcome receive a higher predicted probability than those without. It corresponds to the AUC of the ROC for binary outcomes and can range from 0.5 (no discrimination) to 1.0 (perfect discrimination).[31]

Results

Baseline characteristics of the cohort are shown on ►**Table 1**. A total of 830 patients with PCa who underwent RP and ePLND between 2007 and 2018 at the University Hospital, Fundación Santa Fe de Bogotá are described. Only data from patients who had ≥10 LNs harvested were included; A total of 576 patients were analyzed. The median age was 61 years old (IQR 56–66), the median PSA was 6.81 ng/mL (IQR 4.8–10.1), the median of biopsy cores taken was 13 (IQR 12–15), and the median LN harvested were 17 LNs (IQR 13–23), LNI was identified in 53 patients (9.3%). There were significant statistical differences between patients with LN+ and LN- in PSA value, primary Gleason score, positive biopsy cores and clinical stage.

All prediction models were statistically significant, and their AUCs were between the confidence intervals (CIs). Predictions from the 2017 Briganti nomogram AUC (0,85) and the Yale formula AUC (0,85) were the most accurate; the MSKCC AUC and 2016 Partin tables AUCs were 0.84. Because of overlapping confidence intervals (CIs) for the AUCs, logistic regression models were necessary to predict the best performing models. Receiver operating characteristic plots showing the AUC for the four prediction models are presented in ►**Fig. 1** and ►**Table 2**.

Table 2 Receiver operating characteristic curves regression

	Area	95%CI	*p-value*
MSKCC nomogram	0.844	(0.764–0.891)	0.032
Briganti nomogram	0.859	(0.764–0.901)	0.035
Yale formula	0.859	(0.804–0.913)	0.028
Partin tables	0.844	(0.785–0.904)	0.03

Abbreviation: MSKCC, Memorial Sloan Kettering Cancer Center.

Calibration plots with logistic regression statistics were used to evaluate models under- and overestimation showing the agreement between predicted and harvested LNI. Calibration plots are shown on ►**Fig. 2**; Partin tables v.2016 showed a calibration-in-the-large (interception) a = 0.24 and a slope b = 1.16, the Briganti v.2017 nomogram showed an interception a = 0.24 and a slope b = 1.13, the Yale formula showed an interception a = 0.24 and a slope b =1.14, and the MSKCC web calculator showed an interception a = 0.24 and a slope b =1.12; calibration-in-the-large or interception were the same for all prediction models, although the slope varied between prediction models, the closest to 1 were the Briganti v.2017 and the MSKCC web calculator.

Discussion

There is still controversy regarding the utility and the ability of most of the prediction models validated to predict LNI in PCa in Latin-American patients; given that these prediction tools have been developed and validated with North-American and European patients with different genotypic and phenotypic traits. Our study is the first of its kind, we externally validated the four most accurate prediction tools in a Latin-American (Colombian) population.[14,19] The 2017 Briganti nomogram and the Yale formula showed the highest AUC (0.859;, however, the 95% CIs for the other two prediction models overlap with the CIs of the aforementioned prediction tools, hence, it remains uncertain if either of these two models truly predicts LNI better than the other validated models, but solve the question of whether or not these models are able to predict LNI with the same accuracy in Latin-American patients.

Partin was the first to published an LNI prediction tool in 1993, where he used PSA, cT and Gleason score to predict LNI in patients with PCa who underwent RP + PLND. In 2016, the last series of Partin tables were published and it included 4,459 patients treated between 2010 and 2015 with an update of the World Health Organization – International Society of Urological Pathology (WHO-ISUP) classification published in 2016 (Grade, Group) and found an AUC of 0.8 to predict LNI.[23–25] Briganti was another of the pioneers developing prediction nomograms in PCa patients. He published his first nomogram in 2006, but the difference with the Partin tables was that at the time it was the only nomogram based on the results of ePLND. Gacci et al reported an

external validation of Briganti nomograms with a predictive accuracy of 79% with the 2012 model.[32] In 2017, Briganti published his last version of the prediction model including patients treated with open, laparoscopic and laparoscopic-robot-assisted RP; The main advantage of this model is the inclusion of the number of cores taken on the biopsy and the number of positive cores to the prediction variables, confirming that the percentage of positive cores involved with PCa was the most reliable predictor of LNI, the AUC of LNI prediction was 0.876, which overlaps with ours.[15,22,26,27,30]

Godoy et al, in 2011, published an update of the MSKCC nomogram, they assessed 3,721 patients with PCa managed with RP + ePLND, including only the patients with at least 10 LNs harvested. They found 5.2% of LNI in the whole cohort. The AUC for prediction of LNI was 0.862, resembling our findings.[13,16] Regarding statistical and mathematical formulas to predict LNI, there has been quite an evolution to finally develop the Yale formula, the latter was developed with data of The National Cancer Institute Surveillance, Epidemiology, and End Results (SEER) database. Only data of patients with at least 10 LNs harvested was included; they found a specificity of 94.9% with a 15% cut-off value.[18,20,21]

Two external validations of LNI prediction models in PCa patients have taken place in Bulgarian and Dutch patients. In Bulgaria, Hinev et al externally validated Briganti nomograms from 2006 up to 2012 and the MSKCC prediction tool, developed in 2011 by Godoy et al. They found that Briganti's nomograms showed a higher predictive accuracy as compared with the MSKCC prediction model, reporting a calculated AUC of 0.875 for the 2012 Briganti nomogram, and 0.770 for the MSKCC prediction model.[19] Hueting et al validated in the Netherlands 16 prediction models for LNI in PCa patients.[14] They found that the most recent update of the Briganti model (v2012) and of the MSKCC (v2011) showed the highest AUC (0.76) and (0.75), respectively, which is lower than in the Briganti and Godoy validation studies and in our study. In this study, 27.6% of the patients had LNI, contrary to previous validation studies such as Partin Tables (8%), Godoy-MSKCC (5.2%) and our study, in which the percentage of LNI was 9.4%.[16,23–25]

The limitations of our study were that despite the percentage of positive cores involved with PCa was the most reliable predictor of LNI; Godoy and Briganti did not describe a standardized method for taking the biopsy cores. In recent years, Multiparametric magnetic resonance imaging (mpMRI) and fusion-guided biopsies of the prostate are becoming the standard of care for patients with suspicion of PCa.[33] Despite this trend, not all of our patients underwent mpMRI, and external validation of nomograms using data from mpMRI were not feasible.[31,33] Data from the technique and equipment used in the prostate biopsy was not available in our database, so this could represent a bias.[31–33] Laparoscopic-robotic-assisted surgery has been increasingly used to perform RP and ePLND in our institution in recent years, mostly since 2016. The methods for harvesting LNs may have been different in the whole series (Open ePLND, Laparoscopic ePLND, Robot-assisted ePLND) and the templates may variate from one technique to the other; we were not able to discriminate the surgical modality in our database.[14,16,22,23,26,30]

Conclusion

Prediction models for LNI in PCa patients undergoing RP play an important role supporting clinical decision-making. Most of these models have been developed in North American or European patients and have never been validated or assessed in Latin-American patients. We found that the 2017 Briganti nomogram AUC (0,85) and the Yale formula AUC (0,85) were the most accurate prediction models in our population, overlapping CIs for the AUCs of the four models were found and calibration plots showed that Briganti v.2017 nomogram (slope = 1.13) and the MSKCC web calculator (slope = 1.12) were the prediction tools with the lowest prediction variability. We recommend using the Briganti v.2017 nomogram and the MSKCC, given their overlapping AUCs and their lower variability. The present study confirms that PCa prediction models for LNI are accurate and could be used with confidence in Latin-American patients.

Conflict of Interests

The authors have no conflict of interests to declare.

References

1 Ramírez-Barbosa P, Acuña Merchán L. Cancer risk management in Colombia, 2016. Colomb Med (Cali) 2018;49(01):128–134
2 Stewart BW, Wild CP. International Agency for Research on cancer. Wfile:///Users/yumenghan/Downloads/Cancer immunology and canine malignant melanoma.pdforld Health Organizarion. World cancer refile:///Users/yumenghan/Downloads/Cancer immunology and canine malignant melanoma.p. 2014 [Internet]. 2014;(1):630. Available from: http://www.iarc.fr/
3 Dinan MA, Robinson TJ, Zagar TM, et al. Changes in initial treatment for prostate cancer among Medicare beneficiaries, 1999-2007. Int J Radiat Oncol Biol Phys 2012;82(05):e781–e786
4 Dalela D, Menon M. Contemporary Trends in Radical Prostatectomy in the United States: Open vs Minimally Invasive Surgery. Mayo Clin Proc 2016;91(01):1–2. Doi: 10.1016/j.mayocp.2015.11.009
5 Kowalczyk KJ, Levy JM, Caplan CF, et al. Temporal national trends of minimally invasive and retropubic radical prostatectomy outcomes from 2003 to 2007: results from the 100% Medicare sample. Eur Urol 2012;61(04):803–809
6 Loeb S, Partin AW, Schaeffer EM. Complications of pelvic lymphadenectomy: do the risks outweigh the benefits? Rev Urol 2010;12(01):20–24
7 Kawakami J, Meng MV, Sadetsky N, Latini DM, Duchane J, Carroll PR; CaPSURE Investigators. Changing patterns of pelvic lymphadenectomy for prostate cancer: results from CaPSURE. J Urol 2006;176 (4 Pt 1):1382–1386
8 Spring DB, Schroeder D, Babu S, Agee R, Gooding GA. Ultrasonic evaluation of lymphocele formation after staging lymphadenectomy for prostatic carcinoma. Radiology 1981;141(02):479–483
9 Briganti A, Chun FKH, Salonia A, et al. Complications and other surgical outcomes associated with extended pelvic lymphadenectomy in men with localized prostate cancer. Eur Urol 2006;50 (05):1006–1013
10 Stone NN, Stock RG, Unger P. Laparoscopic pelvic lymph node dissection for prostate cancer: comparison of the extended and modified techniques. J Urol 1997;158(05):1891–1894
11 Kavoussi LR, Sosa E, Chandhoke P, et al. Complications of laparoscopic pelvic lymph node dissection. J Urol 1993;149(02):322–325

12 Clark T, Parekh DJ, Cookson MS, et al. Randomized prospective evaluation of extended versus limited lymph node dissection in patients with clinically localized prostate cancer. J Urol 2003;169 (01):145–147, discussion 147–148
13 Kim KH, Lim SK, Kim HY, et al. Yonsei nomogram to predict lymph node invasion in Asian men with prostate cancer during robotic era. BJU Int 2014;113(04):598–604
14 Hueting TA, Cornel EB, Somford DM, et al. External Validation of Models Predicting the Probability of Lymph Node Involvement in Prostate Cancer Patients. Eur Urol Oncol 2018;1(05):411–417. Doi: 10.1016/j.euo.2018.04.016
15 Gandaglia G, Fossati N, Zaffuto E, et al. Development and Internal Validation of a Novel Model to Identify the Candidates for Extended Pelvic Lymph Node Dissection in Prostate Cancer. Eur Urol 2017;72(04):632–640. Doi: 10.1016/j.eururo.2017.03.049
16 Godoy G, Chong KT, Cronin A, et al. Extent of pelvic lymph node dissection and the impact of standard template dissection on nomogram prediction of lymph node involvement. Eur Urol 2011; 60(02):195–201
17 Karnes RJ. To what extent can we predict prostate cancer lymph node involvement? Eur Urol 2011;60(02):202–203, discussion 204
18 Yu JB, Makarov DV, Gross C. A new formula for prostate cancer lymph node risk. Int J Radiat Oncol Biol Phys 2011;80(01):69–75
19 Hinev AI, Anakievski D, Kolev NH, Hadjiev VI. Validation of nomograms predicting lymph node involvement in patients with prostate cancer undergoing extended pelvic lymph node dissection. Urol Int 2014;92(03):300–305
20 Nguyen PL, Chen MH, Hoffman KE, Katz MS, D'Amico AV. Predicting the risk of pelvic node involvement among men with prostate cancer in the contemporary era. Int J Radiat Oncol Biol Phys 2009; 74(01):104–109
21 Roach M III, Marquez C, Yuo HS, et al. Predicting the risk of lymph node involvement using the pre-treatment prostate specific antigen and Gleason score in men with clinically localized prostate cancer. Int J Radiat Oncol Biol Phys 1994;28(01):33–37
22 Briganti A, Karakiewicz PI, Chun FKH, et al. Percentage of positive biopsy cores can improve the ability to predict lymph node invasion in patients undergoing radical prostatectomy and extended pelvic lymph node dissection. Eur Urol 2007;51(06):1573–1581
23 Tosoian JJ, Chappidi M, Feng Z, et al. Prediction of pathological stage based on clinical stage, serum prostate-specific antigen, and biopsy Gleason score: Partin Tables in the contemporary era. BJU Int 2017;119(05):676–683
24 Makarov DV, Trock BJ, Humphreys EB, et al. Updated nomogram to predict pathologic stage of prostate cancer given prostate-specific antigen level, clinical stage, and biopsy Gleason score (Partin tables) based on cases from 2000 to 2005. Urology 2007;69(06): 1095–1101
25 Eifler JB, Feng Z, Lin BM, et al. An updated prostate cancer staging nomogram (Partin tables) based on cases from 2006 to 2011. BJU Int 2013;111(01):22–29
26 Briganti A, Chun FKH, Salonia A, et al. Validation of a nomogram predicting the probability of lymph node invasion based on the extent of pelvic lymphadenectomy in patients with clinically localized prostate cancer. BJU Int 2006;98(04):788–793
27 Briganti A, Larcher A, Abdollah F, et al. Updated nomogram predicting lymph node invasion in patients with prostate cancer undergoing extended pelvic lymph node dissection: the essential importance of percentage of positive cores. Eur Urol 2012;61(03): 480–487
28 Bianchi L, Gandaglia G, Fossati N, et al. Pelvic lymph node dissection in prostate cancer: indications, extent and tailored approaches. Urologia 2017;84(01):9–19
29 Ramos JG, Caicedo JI, Cataño JG, et al. Extended pelvic lymphadenectomy in patients with clinically localized prostate cancer: A prospective observational study. Actas Urológicas Españolas (English Ed.) 2016;40(07):446–452
30 Briganti A, Chun FKH, Salonia A, et al. Validation of a nomogram predicting the probability of lymph node invasion among patients undergoing radical prostatectomy and an extended pelvic lymphadenectomy. Eur Urol 2006;49(06):1019–1026, discussion 1026–1027
31 Debray TPA, Vergouwe Y, Koffijberg H, Nieboer D, Steyerberg EW, Moons KGM. A new framework to enhance the interpretation of external validation studies of clinical prediction models. J Clin Epidemiol 2015;68(03):279–289
32 Gacci M, Schiavina R, Lanciotti M, et al. External validation of the updated nomogram predicting lymph node invasion in patients with prostate cancer undergoing extended pelvic lymph node dissection. Urol Int 2013;90(03):277–282
33 Oglio PD, Stabile A, Hermenigildo B, et al. Impact of multiparametric MRI and MRI - targeted biopsy on pre - therapeutic risk assessment in prostate cancer patients candidate for radical prostatectomy. World J Urol 2018(0123456789):. Doi: 10.1007/s00345-018-2360-1