Original Article

Assessment of the performance of Partin's nomogram (2007) in contemporary Indian cohort

Rajiv Yadav, Sohrab Arora, Manish Sachdeva, Narmada Prasad Gupta

Department of Urology, Institute of Kidney and Urology, Medanta - The Medicity, Gurgaon, Haryana, India

ABSTRACT

Introduction: Partin's nomogram is an important prognostic tool to predict adverse pathological features for clinically localized prostate carcinoma. This tool is widely used by both radiation and surgical oncologists for pre-intervention counseling, treatment planning, and predicting the possible need for adjuvant treatment. However, the model is derived from a Western population with typical characteristics of prostate cancer in a prostate-specific antigen (PSA) screened population. Therefore, this study was conducted to assess the performance of the Partin's nomogram as applied to an Indian cohort by assessing the discrimination and calibration properties.

Methods: A retrospective review of 282 patients treated with robotic radical prostatectomy from 2010 to 2015 was conducted. Partin tables (year 2007) were used to calculate the predicted probabilities for lymph node invasion (LNI), seminal vesicle invasion (SVI), and extraprostatic extension (EPE). The discrimination properties were assessed using the receiver operating characteristic (ROC) curves. Calibration of the model was done to show the relationship between predicted and observed values.

Results: The mean age of the patients was 64.3 years. Most (59.4%) were clinical T2 disease. Patients with PSA >10 ng/ml comprised 60% of the population. ECE, SVI, and LNI were present in 39.2%, 22%, and 11% of cases, respectively. ROC analysis revealed area under curve values for EPE, SVI, and LNI of 68%, 67.5%, and 71.2%, respectively. Calibration plot suggested that the Partin tables under-predicted the risk whenever the values of predicted risk were more than 26%, 3%, and 1% for EPE, SVI, and LNI, respectively, and over predicted when the risk was lower.

Conclusion: Our data show that Partin's tables, despite having fair discrimination properties, do not accurately predict LNI, SVI, and ECE across the entire range of predicted values in a contemporary Indian cohort.

Key words: India, nomogram, Partin's nomogram, prostate cancer, radical prostatectomy, robotic prostatectomy

INTRODUCTION

Carcinoma prostate is the second most common cancer in India[1] and has the best chance of cure in situations where the disease is organ-confined. Therefore, it is important to identify patients with adverse prognostic factors so that appropriate pretreatment counseling can be done about the treatment modalities and potential need for adjuvant therapy. Partin's nomogram is one of the widely used prognostic models used by both the urologists and radiation oncologists for predicting the risk of pathological adverse factors, namely extraprostatic extension (EPE), seminal vesicle invasion (SVI), and lymph node invasion (LNI) in patients with clinically localized prostate cancer.[2]

The currently used Partin's nomogram was revised in the year 2007 to reflect the changes in patient population presenting at John Hopkins University.[3] Understandably, the population in the West (on which Partin's nomogram

For correspondence: Dr. Rajiv Yadav,
Senior Consultant, Urologic Oncology and Robotic Surgery,
Institute of Kidney and Urology, Medanta - The Medicity,
Sector 38, Gurgaon, Haryana, India.
E-mail: drrajivyadav@RoboticUroSurgery.com

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model is based) differs from the Indian population in terms of disease characteristics due to widespread screening and stage migration in the United States, which has not happened in India. Therefore, this study was conducted to assess the performance of the Partin's nomogram as applied to Indian cohort by assessing the discrimination and calibration properties. The aim was to assess the discrimination power of Partin nomogram to identify patients with high risk of EPE, SVI, and LVI; and also to assess the calibration of the nomogram across the entire range of predicted risk.

METHODS

A retrospective review was performed of 282 consecutive patients treated with robotic radical prostatectomy from 2010 to 2015 at a tertiary care center in India. All patients had systematic ultrasound-guided biopsy. Details about initial prostate-specific antigen (PSA), systematic biopsy, and clinical staging were collected from electronic hospital records. Staging was done according to American Joint Committee for Cancer 2004. Patients without biopsy details or missing values of any of the preoperative predictor variables were excluded from the analysis. Patients who had neoadjuvant hormonal or radiation therapy were also excluded. The grade used for the biopsy was the Gleason score of the core with the highest grade in cases with multiple cores having different grades. Extended lymph node dissection was done, except in low-risk cases. The decision to do a limited lymphadenectomy was taken by the operating surgeon based on clinical features. All radical prostatectomy specimens were mounted whole and sectioned at 5 mm intervals. Histopathology was reported by dedicated uropathologists. EPE was defined as extension outside the prostate capsule without SVI and LNI. SVI was defined as extension in the seminal vesicle without LNI.

The final statistical analysis was done on 253 patients using the SPSS® version 22. Revised (2007) Partin tables were used to define the predictive probabilities for LNI, SVI, and EPE.[3] The discrimination properties of Partin tables (ability to discriminate between those who had the outcome and those who had not) were assessed using the receiver operating characteristic (ROC) curves for these three outcomes. Calibration of the model was done to show the relationship between predicted and observed rates of EPE, SVI, and LNI of the Partin tables. Agreement between predicted and actual probability of each pathological stage was assessed graphically with calibration plots. The curve is compared to the ideal fit (45° line), where predicted values equal the actual values.

RESULTS

A total of 282 patients underwent robot-assisted laparoscopic prostatectomy during the study period, of which 253 patients qualified for analysis. The clinical and pathological properties of our cohort in comparison with Partin cohorts[3] are shown in Table 1. Our cohort was older than the Partin's cohorts and most (59.4%) were clinically T2 as compared to 22.9% of the Partin's cohorts. Patients with PSA >10 ng/ml comprised 60% of our patients, again significantly higher than comparative group (11.6%). About 16% of our patients were Gleason 8–9 compared to 3% in the Partin cohorts. These preoperative differences reflected in the pathological stage as well, with SVI and LNI present in 22% and 11% of our patients and only 2.9% and 1.2% of the comparative group, respectively.

ROC analysis of EPE, SVI, and LNI is shown in Figure 1a–c, respectively. Area under curve (AUC) values for EPE, SVI, and LNI were 68%, 67.5%, and 71.2%, respectively. This implies that Partin's tables incorrectly classified 32%, 32.5%, and 28.8% of the patients with respect to the risk of EPE, SVI, and LNI, respectively. Interestingly, the AUC values for the higher predicted risk were not very different from the mean predicted values in their ability to discriminate between the presence or absence of end points. The values were 69.4%, 68.4%, and 69.9% for EPE, SVI, and LNI, respectively.

Table 1: The clinical and pathological properties of our cohort in comparison with Partin cohorts

Characteristics	Study cohort	Partin's 2007 cohort
Number of patients	253	5730
Age		
Mean (in years)	64.3	57.4
Range	44–84	34–75
Clinical stage		
T1c	98 (37.69)	4419 (77.1)
T2a	104 (40)	998 (17.4)
T2b		313 (5.5)
T2c	51 (19.62)	
PSA (ng/ml)		
Mean	17.3±17.18	Not available
Range	0.9–130	Not available
0-4	7 (2.69)	1398 (24.4)
4-10	97 (37.3)	3665 (64)
>10	156 (60)	667 (11.6)
Preoperative biopsy Gleason score		
5-6	127 (48.85)	4402 (76.8)
7=3+4	69 (26.54)	816 (14.2)
7=4+3	22 (8.46)	348 (6.1)
>7	42 (16.15)	164 (3)
Pathological stage		
EPE	102 (39.23)	1276 (22)
SVI	58 (22.3)	180 (2.9)
LNI	28 (10.77)	70 (1.2)

PSA=Prostate-specific antigen, EPE=Extracapsular extension, SVI=Seminal vesicle invasion, LNI=Lymph node invasion

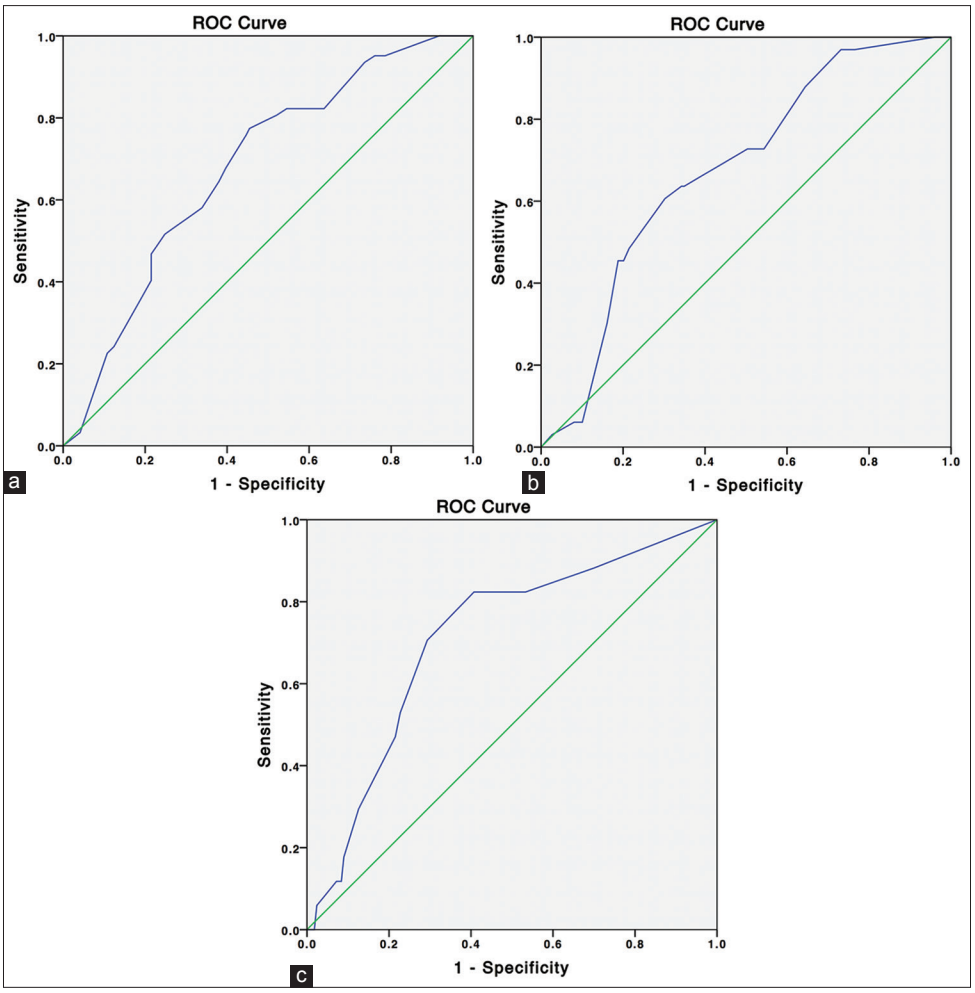

Figure 1: (a) Receiver operating characteristic curve for extraprostatic extension. Area under curve = 68%. (b) Receiver operating characteristic curve for seminal vesicle invasion. Area under curve = 67.5%. (c) Receiver operating characteristic curve for lymph node invasion. Area under curve = 71.2%

To compare Partin's predicted probabilities to the actual proportions of EPE, SVI, and LNI across the entire range of predictions, calibration curves were plotted which are shown in Figure 2a–c, respectively. Partin's tables were most accurate for EPE when the predicted risk was around 26% and for all predictions above this, the tables underpredicted the risk. For the values below this, the tables overpredicted the risk. The calibration plots for SVI and LNI showed a similar trend with Partin's tables underpredicting the risk when the chances of SVI and LNI were above 3% and 1%, respectively, and overpredicting the risk when the predicted risk according to the nomogram was <3% and 1%, respectively.

DISCUSSION

Partin's nomogram remains one of the most commonly used predictive tools and have been validated in various populations.[4,5] These tables were first validated for the patients at John Hopkins University and have been revised in the year 2007 to reflect the stage migration that has occurred in the US.[2,3] External validation of a predictive model is important before its clinical application in a certain population. Simply because, the predictions based on a model cannot be expected to perform well if the development cohort is drastically different from the validation cohort. The clinical characteristic of contemporary Indian prostate cancer patient cohort is expected to be different compared to the US population due to difference in PSA screening practice, patient selection, and treatment protocols.[6,7] Therefore, it is important to do external validation of Partin's nomogram in Indian patients before its clinical use. To the best of our knowledge, our study is the first of this kind in an Indian population.

The accuracy of a nomogram can be measured in two terms – discrimination and calibration. Discrimination is the ability of the nomogram to correctly categorize patients according to the presence or absence of predicted end point. For example, a nomogram with a good discrimination ability would categorize 80% of patients correctly. This is measured by the ROC analysis with an AUC of >70–80%, indicating good discrimination. Calibration properties of a nomogram are more important than the discrimination properties.

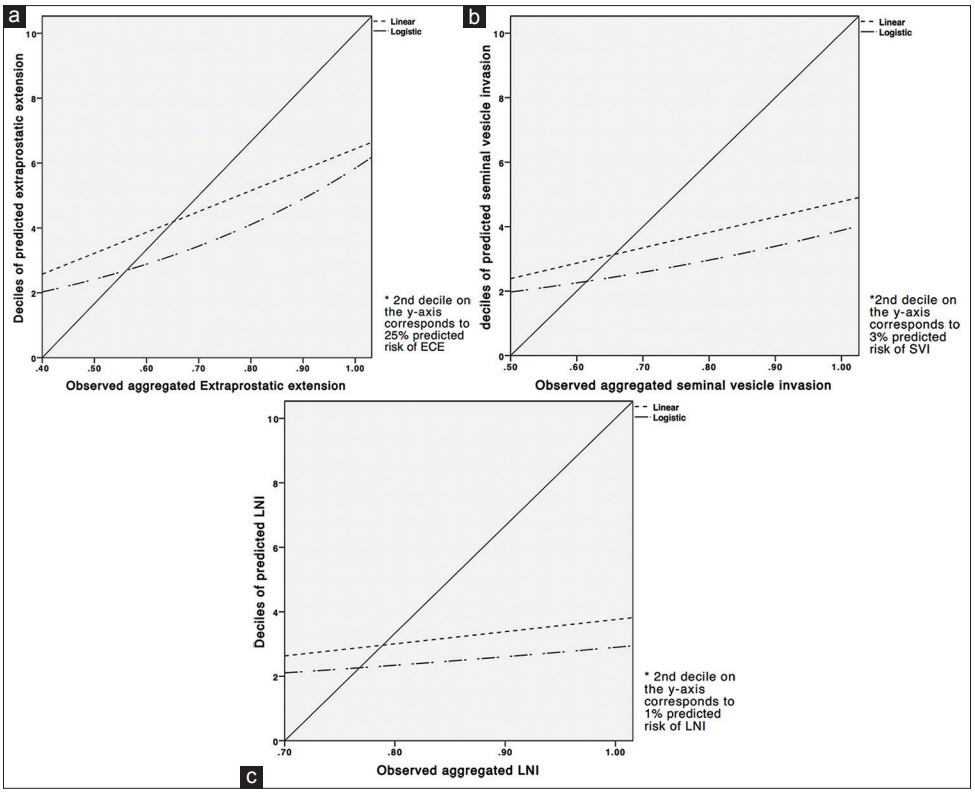

Figure 2: (a) Calibration plot for extraprostatic extension. (b) Calibration plot for seminal vesicle invasion. (c) Calibration plot for lymph node invasion

Calibration measures the performance of the nomogram across the entire range of predicted values. A nomogram may not perform well in a specific range of predicted probabilities even though it may have good discrimination abilities. A well-calibrated nomogram would give accurate predictions even for the patients at the extremes of risk.

We found that the updated Partin's nomogram had fair discrimination properties, but was poorly calibrated to our cohort. It performed well in a very small window of predicted risk, but for either extremes of predicted risk, the nomogram had a poor accuracy. For example, for predicted risk of EPE below 26%, the nomogram overpredicted the risk, whereas above 26%, it underpredicted. The nomogram predicted well only in a small window close to 26% predicted risk of EPE. The reason for this could be that our cohort had significant demographic differences when compared to the Partin's cohort with a higher number of patients having ECE, SVI, and LNI [Table 1].

There are clinical implications of "under" and "over" prediction. If there is a significant underprediction in a model, many patients may undergo limited node dissection and preservation of neurovascular bundles when the chances of them being positive were actually high. With overprediction, some patients may have more extensive surgery than required, or may not undergo surgery at all and be pushed toward radiotherapy or adjuvant treatment. Therefore, calibration of a clinical model is very important before its clinical application in decision making.

It is interesting to note that in the Partin's cohort, patients had limited lymph node dissection. The chances of positive nodes increase if more nodes are harvested,[8] which helps in better staging and prognostication. In our cohort, an extended lymph node dissection was done for intermediate- and high-risk patients. Lymph nodes were positive in 10.8% of the cases, which is much higher than the Partin's cohort. The ROC curves showed a 71.2% accuracy of the Partin's tables to predict LNI, comparable to 71.4% reported by another study from the Indian subcontinent,[7] but significantly lower than 89% reported by Partin's 2007 cohort.[3] The calibration curves expectedly showed that if the predicted lymph node positivity is more than 1%, the Partin's tables performed poorly, underestimating the outcome.

The implication of the extent of LN dissection was addressed by Briganti *et al*. who proposed a nomogram based on the extent of pelvic lymphadenectomy in localized prostate cancer, which was further updated in 2012 to include the percentage of positive cores.[9,10] In populations different from Partin's cohort in terms of higher risk of lymph node positivity and when extended LN dissection is often needed (such as in our cohort), it might be more appropriate to use the nomograms proposed by Briganti instead of

Partin's. Similarly, for SVI, other nomograms like the ones proposed by Koh *et al*.[11] and Gallina *et al*.[12] have further improved the predictive accuracy (over the Partin's model) by including presence and percentage cancer in the biopsy cores taken from the base of prostate.

EPE risk prediction has also undergone further refinement with other nomograms. Nomogram proposed by Graefen *et al*.[13] gives side-specific risk of EPE as well. Side-specific risk prediction is especially helpful in surgical planning and deciding about the option of side-specific aggressive nerve sparing surgery versus wide excision.

Our study has several limitations, being a single-center study with a relatively small number of patients. Extended lymph node dissection was not done in all the cases thus potentially missing some of the lymph node positive cases. Another important limitation was that the review of biopsies was done only in case of doubtful biopsy reporting (or with incomplete reporting) done outside our institution. The histopathology was not reported by a single pathologist. On the flip side, this assumed disadvantage may in fact represent more real-life situation, closer to clinical practice where patient's biopsy is done by referring urologists, and histopathology reporting is done by multiple pathologists.

The use of the 2007 Partin table instead of the latest version published in 2013 may be interpreted as another limitation. However, we have a different view point regarding this. Although one would expect that this new version would work better than the older versions, we found that our cohort more closely resembled the older Partin cohorts, and therefore older predictive models are a better fit for our patients. This is because our patient cohort represents a nonscreened referral population whereas the population in Western countries have shown stage shift over the years.

CONCLUSION

Our data show that Partin's tables, despite having fair discrimination properties, do not accurately predict LNI, SVI, and ECE across the entire range of predicted values in the contemporary Indian cohort of clinically localized prostate cancer.

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Conflicts of interest
There are no conflicts of interest.

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