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Original Research Article

A Retrospective Single-Center Study in Development a New Indian Nomogram to Estimate Pathologic Extracapsular Extension (ECE) Risk in Prostate Cancer

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Abstract

Aim: The aim of the present study was to develop a new Indian nomogram to estimate pathologic extracapsular extension (ECE) risk in prostate cancer.

Methods: This was a retrospective single-institution study of patients who underwent primary RP at department of General surgery. The data of 200 patients were analyzed. The collected data included prebiopsy serum prostate-specific antigen (PSA) levels, clinical T-stage (cT) determined by digital rectal examination (DRE), Gleason score (GS) from transrectal ultrasound (TRUS)-guided prostate biopsy, MRI data, and histopathologic findings from the RP specimens of all patients.

Results: Out of 200 patients, 100 patients had ECE on MRI, whereas 100 patients had ECE on final pathology. All variables except age demonstrated a statistically significant difference in detecting ECE on final pathology on univariate analyses. Based on multivariate logistic regression analyses, cT, GS and MRI ECE risk score remained significant predictors of ECE.

Conclusion: MRI adds incremental value to the existing validated risk stratification tool and provides significant additional ability for predicting ECE in prostate cancer staging. We constructed a nomogram for predicting ECE based on the results of cT, PSA, GS, and MRI ECE risk score in Indian patients. The nomogram provides a good prediction of ECE.

Keywords: extracapsular extension, prostate cancer, magnetic resonance imaging, Partin nomogram

Introduction

Prostate cancer (PCa) is the second most common cancer diagnosed in men and fifth most common oncologic cause of mortality among men. As per GLOBOCON 2020 data, approximately 1.4 million men were diagnosed with PCa worldwide. [1] The incidence of PCa is higher in Western countries than in Eastern and South Central Asia. [2] Mortality rates of PCa vary worldwide and high rates are found in African decent populations and very low rates in Asia. [3] PCa is a disease of older people with a median age of 68 years. It has been estimated that in Europe and the United States, the diagnosis of PCa in men over 65 years of age will cause a 70% increase in annual diagnosis by 2030. [4,5] Men with intermediate- and high-risk PCa benefit the most from active treatment while advanced age and poor performance status decreases the benefit of intervention with curative treatment. [6]

Nomogram are predictive tools for clinical outcomes based on a set of variables. They assist in making predictions for individual patients rather than for population risk groups and are thus more applicable while assessing a single patient. Nomograms aid in risk assessment and decision making by predicting outcomes with different treatment modalities. PCa is a diagnosis particularly suited to the use of nomograms since there are a multitude of treatment options with extremely varying outcomes and nomograms have become an essential part of decision making in these men.

Digital rectal examination (DRE) and transrectal ultrasound (TRUS) are traditionally used for clinical staging of prostate cancer (PCa), but both are lacking in sensitivity and specificity, and TRUS often underestimates the size and stage of the tumour. [7] Thus, prediction of extracapsular tumour

extension (ECE) by DRE and TRUS has low accuracy. [8,9] Radical prostatectomy (RP) provides great disease control for patients with localised PCa (cT1-T2), while RP for locally advanced disease (cT3) remains controversial. [7,10] Recovery of erectile function and continence after RP is related to surgical technique and preservation of the neurovascular bundles (NVB). Accurate preoperative knowledge of tumour stage and possible ECE are crucial in achieving the best surgical, oncological, and functional result with total tumour resection, while trying to preserve both potency and continence.

The aim of the present study was to develop a new Indian nomogram to estimate pathologic extracapsular extension (ECE) risk in prostate cancer, by including PI-RADS v1-based magnetic resonance imaging (MRI) ECE risk score to the clinical variables used in the Partin nomogram (PN).

Materials and Methods

This was a retrospective single-institution study of patients who underwent primary RP at department of General surgery, Government Medical College and Hospital, Bettiah, Bihar, India for one year The data of 200 patients were analyzed. The collected data included prebiopsy serum prostate-specific antigen (PSA) levels, clinical T-stage (cT) determined by digital rectal examination (DRE), Gleason score (GS) from transrectal ultrasound (TRUS)-guided prostate biopsy, MRI data, and histopathologic findings from the RP specimens of all patients. Currently, the widely used PN considers clinical T stage as per AJCC guidelines. Hence, in our nomogram, clinical T stage was considered purely on DRE findings. MRI findings were added to the existing variables of PN.

Based on Harrell's guidelines, when we planned to set a nomogram for binary situations (i.e., presence or absence of ECE), the minimum value of cases needed in either group is 10 times the number of variables used for predicting. In this study the number of patients in the groups were 100 with ECE and 100 without ECE, above the required number.

Magnetic resonance imaging technique MRI information in most cases was obtained before biopsy or at least 4 weeks after biopsy to reduce the biopsy artifacts. All patients underwent multiparametric MRI (mpMRI) and biparametric MRI using a 1.5 T or 3.0 T MRI scanner without endorectal coil. The MRI characteristics of the ECE of the tumor were assessed as follows at par with the ESUR prostate MR guidelines 2012 [11] Score 0 – no sign of ECE, Score 1 – capsular abutment; Score 3 – capsular irregularity, retraction, or thickening; Score 4 – neurovascular bundle thickening and capsular signal loss or bulging; and Score 5 – direct sign of tumor tissue in the extra prostatic tissues.

MRI images of some patients done at outside centers were re-interpreted by radiologists at our institution in the absence of adequate details in the reports; certain MRI images were retrospectively analyzed for characterizing ECE risk score. In case of any discrepancy, an intradepartmental discussion was done to arrive at a unified consensus on the final report.

Pathology Analysis and Staging

All biopsy and surgical specimens were evaluated by two dedicated uropathologists. The location, primary and secondary GS, and the percentage of positive cores were recorded for every core of the TRUS-guided biopsy specimens. In case of any discrepancy, an intradepartmental discussion was done to arrive at the final report.

In the literature, two distinct definitions were considered for EPE – pT3a: the presence of tumor beyond the confines of the prostate without invasion of the seminal vesicles and whole EPE (wEPE): the presence of tumor beyond the confines of the prostate regardless of the status of seminal vesicles. [12] In our study, we have considered wEPE.

Statistical Analysis

Baseline descriptive statistics were used to present demographics, tumor, and MRI data. The sensitivity, specificity, positive predictive value, and negative predictive value of MRI (index test) for the diagnosis of histological ECE (reference standard) were calculated. The 2013 Partin nomogram (PN) was used to define the predictive probability of ECE. Univariate and multivariate logistic regression analyses were performed to identify predictors of ECE. The area under the receiver operating characteristic curve (AUC) values were calculated for PSA, cT, GS, and MRI ECE risk score. A New nomogram was created by binary logistic regression analysis using 300 bootstrap resamples to decrease the overfitting bias. Univariate and multivariate logistic regression analyses were used to arrive at relative significance of variables, and the nomogram was built based on R statistical package version 3.4 (R Foundation for Statistical Computing, Vienna, Austria).

Results

Table 1: Summary of the patients' characteristics

Variables	Total	ECE group	Non-ECE group
Number of patients	200	100	100
Age, mean±SD (years)	65.5±6.54	63.7±6.44	62.68±5.65
PSA, mean±SD (ng/mL)	18.6±26.4	24.26±32.08	13.70±12.74
cT (DRE), *n* (%)			
cT1	60	20	40
cT2a	125	60	65
>cT2a	15	13	2
Final RP pT, *n* (%)			
pT2		48	
pT3a		28	
pT3b		22	
pT4		2	
Biopsy GS, *n* (%)			
3+3	48	32	14
3+4	64	38	26
4+3	40	17	24
>7	48	12	36
Final RP GS, *n* (%)			
3+3	22	17	4
3+4	64	45	23
4+3	62	26	36
>7	52	12	37
pLN, *n* (%)			
N0	160	65	95
N1	40	35	5

Out of 200 patients, 100 patients had ECE on MRI, whereas 100 patients had ECE on final pathology.

Table 2: Factors that predict extracapsular extension based on univariate and multivariate analysis

Variables	TNM ECE		Univariate *P-value*
	Yes	No	
Age, mean±SD (years)	63.7±6.44	62.68±5.65	0.515
MRI ECE risk score, *n* (%)			
0	26	80	<0.001
1	2	3	
3	4	7	
4	28	4	
5	40	6	
Partin ECE score, mean±SD	34.86±9.33	28.07±12.51	<0.001
PSA, mean±SD (ng/mL)	25.28±31.07	14.71±12.73	<0.001
cT, *n* (%)			
T1c	28	40	<0.001
T2a	52	58	
>T2a	20	2	
Biopsy GS, *n* (%)			
3+3	30	15	<0.001
3+4	45	30	
4+3	15	25	
>7	10	30	

All variables except age demonstrated a statistically significant difference in detecting ECE on final pathology on univariate analyses.

Discussion

Carcinoma prostate (PCa) is the second most common cancer in men in India, and a large number of patients are diagnosed at a locally advanced stage unlike in other developed countries. [13-15] Guidelines emphasize radical prostatectomy (RP) or, more recently, nerve-sparing radical prostatectomy (NSRP) as the surgery of choice for patients with localized disease, age less than 65 years, and with a mean life expectancy of at least 10

years, for better functional and oncological outcomes. [16,17] PCa with extracapsular extension (ECE) is associated with decreased overall and cancer-specific survival following RP compared to organ-confined disease. [18,19] Clinical staging based on physical examination has limited accuracy with 25-30% patients, with ECE being under staged preoperatively. [20]

Several studies have focused on exploring the incremental value of magnetic resonance imaging (MRI) parameters to these predictive tools to improve the predictability of tumor staging. Prostatic MRI reporting is standardized at present with the introduction of a structured uniform reporting and scoring system (PI-RADS) and ECE risk scoring. [21] In 2015, Boesen et al. verified the ECE risk score in predicting ECE with relatively high accuracy. [22] However, the cumulative effect or benefit of MRI parameters among different population groups is questionable. Out of 200 patients, 100 patients had ECE on MRI, whereas 100 patients had ECE on final pathology. All variables except age demonstrated a statistically significant difference in detecting ECE on final pathology on univariate analyses. Based on multivariate logistic regression analyses, cT, GS and MRI ECE risk score remained significant predictors of ECE. As the causative factors of prostate cancer differ epidemiologically and biologically from more developed nations, [13] the predictions based on the nomograms plotted for the population in these countries may be different for an Indian cohort. [23] The adaptability of such models to other geographic areas was poor. [24] This led us to develop a new nomogram based on the data of prostate cancer in the Indian population by adding the MRI-based ECE risk score to clinical variables.

Nomograms, in the form of user-friendly graphical interfaces, assist in clinical decision making by transforming statistical predictive models into a single numerical estimate tailored to the individual patient. [25] Several authors have developed various statistical tools to predict the pathological stage, especially after the use of PN. Advantages of mpMRI, widely used in these days, as an efficient imaging tool for prostate cancer staging were discussed by Sciara et al [26] and were supported by Gupta et al [27] who argued that mpMRI is better for staging prostate cancer than the Partin table. In 2015, Boesen et al. analyzed the diagnostic performance of preoperative mpMRI ECE risk score, and it showed an AUC of 0.86 with moderate inter-reader agreement (K = 0.45). [22]

Conclusion

MRI adds incremental value to the existing validated risk stratification tool and provides significant additional ability for predicting ECE in prostate cancer staging. We constructed a nomogram for predicting ECE based on the results of cT, PSA, GS, and MRI ECE risk score in Indian patients. The nomogram provides a good prediction of ECE.

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