PI-RADS v2 Findings of MRI and Positive Biopsy Core Percentage would Predict Pathological Extraprostatic Extension in Patients who Underwent Robot Assisted Radical Prostatectomy: A Retrospective Study

Shimpei Yamashita[1], Yasuo Kohjimoto[1], Hirotatsu Sato[2], Kazuro Kikkawa[1], Tetsuo Sonomura[2], Isao Hara[1]*

Purpose: This study aimed to examine whether preoperative Prostate Imaging Reporting and Data System v2 (PI-RADS v2) can predict pathological extracapsular extension (EPE) after radical prostatectomy. We also studied the preoperative factors which can predict EPE.

Materials and Methods: In our institute, 294 patients underwent robot assisted radical prostatectomy (RARP) between December 2012 and August 2016. In this era, we performed MRI after biopsy to determine clinical stage before surgery. PI-RADS v2 scores were retrospectively reviewed using biparametric MRI and EPE in pathological mapping of resected specimens for each lobe.

Results: In the excised specimen, EPE was observed in 73 lobes (12%). The percentage of EPE by PI-RADS v2 score was score '1': 6% (17/297 lobes), '2': 3% (1/33 lobes), '3': 12% (8/67 lobes), '4': 19% (27/139 lobes), and '5': 38% (20/52 lobes). The higher the PI-RADS score, the higher the percentage of EPE (P <0.01). When classified as PI-RADS score ≥ 4 and < 4, the positive predictive value (PPV) was 24.6% (47/191 lobes, 95%CI: 0.187 – 0.313) and negative predictive value (NPV) was 93.5% (371/397 lobes, 95%CI: 0.906 – 0.957). By multivariate analysis, positive biopsy core percentage ≥ 60%, and PI-RADS score ≥ 4 were independent factors for predicting EPE. The positive rate of EPE in lobes with zero, one and two factors (PI-RADS ≥ 4 and positive biopsy core percentage ≥ 60%) was 4%, 19%, and 38%, respectively.

Conclusion: PPV and NPV of PI-RADS ≥ 4 for predicting pathologic EPE were 24.6% and 93.5%, respectively. PI-RADS ≥ 4 and positive biopsy core percentage ≥ 60% were independent risk factors for predicting EPE. The positive rate of EPE in lobes with zero, one and two factors (PI-RADS ≥ 4 and positive biopsy core percentage ≥ 60%) was 4%, 19%, and 38%, respectively.

Keywords: radical prostatectomy; positive biopsy core percentage; PI-RADS v2; extraprostatic extension; prostate cancer

INTRODUCTION

According to the Cancer Information Service, the number of incidences of prostate cancer in Japan in 2020 was 95,6000, which has the highest incidence among types of cancer in men, overtaking gastric cancer[(1)]. Radical prostatectomy and radiation as radical treatments have become increasingly important for patients with prostate cancer without metastasis. Determining the extent of disease spread is crucial for not only the choice of treatment (surgery or radiation), but also the surgical approach of radical prostatectomy (preserving the neurovascular bundle or wide resection). Accurate prediction of extra prostatic extension (EPE) is especially highly anticipated.

Magnetic resonance imaging (MRI) is currently a standard examination for prostate cancer. Establishment of multiparametric MRI (mpMRI) including diffusion-weighted imaging (DWI) and dynamic contrast enhancement (DCE) has dramatically improved the quality of image diagnosis compared with T2 weighted imaging (T2W) only[(2)]. Prostate Imaging Reporting and Data System version 2 (PI-RADS v2) assessment is also thought to be a major improvement in reporting of prostate MRI[(3)]. Since the superiority of MRI-targeted biopsy over standard systematic biopsy was demonstrated[(4)], it is becoming standard to perform MRI before biopsy. However, MRI was used to be performed after biopsy for determining clinical stage in the era when we performed this study. Therefore, the initial PI-RADS was designed mainly for the purpose of detection[(5)], many studies on PI-RADS v2 have demonstrated various applications beyond that. PI-RADS v2-based scoring system has shown not only improved diagnostic accuracy for EPE[(6)], it is also considered to be a good predictive factor for PSA (prostate-specific antigen) recurrence after surgery[(7)].

mpMRI may therefore play a central role for the diagnosis of prostate cancer, although there are potential drawbacks to performing DCE. Intravenous administration of gadolinium incurs higher financial costs and longer scanning time. Moreover, gadolinium is a heavy

[1]Department of Urology, Wakayama Medical University, Wakayama, Japan.
[2]Department of Radiology, Wakayama Medical University, Wakayama, Japan.
*Correspondence: Department of Urology, Wakayama Medical University
Tel: +81 73 441 0637. Fax: +81 73 444 8085. E-mail: isaohara@me.com.
Received July 2021 & Accepted February 2022

Table 1. Sequence parameters for bi-parametric MRI of the prostate protocol performed at 3 Tesla[a]

	Field of view	Matrix size	Slice thickness/gap (mm)	TR (msec)	TE (msec)	Echo train length	Flip angle	Receiver bandwidth (Hz/Voxel)	Number of signals averaged
Axial T1 TSEb	200 × 200	512 × 512	3/0.3	716.5	9	3	90	365	1
Axial T1 Dual Echo GREc	230 × 230	384 × 384	4/0.4	317.6	1.2/2.3	2	70	1142	1
Axial T2 TSE	200 × 200	512 × 512	3/0.3	6000	110	9	90	438	1
Axial FatSAT T2 TSE	230 × 230	512 × 512	4/0.4	6000	90	19	90	238	1
Coronal T2 TSE	230 × 230	512 × 512	3/0.3	6000	110	9	90	2031	1
Sagittal T2 TSE	250 × 250	512 × 512	3/0.3	5361	95.7	59	90	436	1
Axial DWId	250 × 250	160 × 160	3/0.3	11000	59.6	35	90	3520	2

[a] Clinical 3 Tesla systems: Ingenia (Philips, Amsterdam, Netherlands; Coil: Torso coil linked to posterior spine elements), b Turbo spin echo, c Gradient recalled echo, d DWI = Diffusion weight imaging performed with spectral fat suppresion echo planar imaging with tridirecional motion probing gradients and b values of 0, 1000, 2000 mm^2 /s with automatic apparent diffusion coefficient map generation

metal, which causes accumulation in multiple organs such as renal glomeruli, the brain, and bones, with possible clinical sequelae, such as nephrogenic systemic fibrosis, when administered in patients with renal dysfunction[8]. Regarding diagnostic accuracy, the role of DCE is weakened in PI-RADS v2 compared with PI-RADS v1[3,5]. Biparametric MRI (bpMRI) without DCE has been shown to have similar rates of tumor detection to mpMRI[9,10]. Conversely, DCE has been shown to be useful for detecting cancer, and predicting tumor aggressiveness[11,12]. Further evidence is therefore required to elucidate the optimum method of detection.
Here, we studied the incidence of EPE according to the PI-RADS v2 score using bpMRI, which can be more easily applied to patients than mpMRI. We also studied the factors for predicting EPE before operation.

PATIENTS AND METHODS

Patients

Between December 2012 and August 2016, 305 patients underwent robot assisted radical prostatectomy (RARP) at Wakayama Medical University Hospital. Among them, 294 patients underwent preoperative MRI and could be evaluated for pathological extra prostatic extension (EPE) by resected specimens. This study was approved by the Wakayama Medical University Institutional Review Board (No. 1670) in accordance with the principles of the Declaration of Helsinki. For NCCN high risk patients, we present radical prostatectomy as well as radiation therapy combined with androgen deprivation therapy. RARP was performed according to the standard techniques, as previously described[13].

Evaluation of preoperative MRI

Preoperative MRI were performed with a 3T MRI system without use of endorectal coils. Since we did not adopt MRI-targeted biopsy, we performed MRI for determining clinical stage after standard systematic biopsy. The bpMRI (T2W+ DWI) protocol used for prostate cancer imaging is shown in Table 1. T2-weighted images and diffusion-weighted images (DWI) with b = 2000 were used. Apparent diffusion coefficient (ADC) were generated from the DWI data. Radiologists evaluated MRI according to PI-RADS v2[3]. Briefly, PI-RADS v2 uses a five-point scale on the likelihood (probability) that a combination of multi parametric MRI (mpMRI) findings on T2W, DWI, and ADC correlate with the presence of a clinically significant cancer for each lesion in the prostate gland. Left and right lobes of the prostate were independently evaluated, so 588 lobes from 294 patients were scored in this study.

Statistical analyses

A receiver operating characteristic (ROC) curve with an area under the curve (AUC) was generated to analyze the predictive accuracy of age, preoperative PSA, biopsy Gleason score, biopsy positive rate, and PI-RADS score for pathologic EPE. Optimal thresholds were then determined by maximizing the Youden index. Logistic regression models were conducted for univariate and multivariate analyses. The discriminatory power of the multivariable model was quantified using C-statistic, and the internal validity of the multivariable model was assessed using K-fold cross-validation.
The comparison of EPE rate according to PI-RADS score and risk number was performed by chi square test and Fisher's exact test. Data analyses were conducted using the statistical software JMP Pro 12 (SAS Institute, Cary, USA). All *P* values were two-tailed, and $P<0.05$ was considered to be statistically significant.
This study was a retrospective evaluation of archival material, and the data extracted would be of significance in the pre-operative evaluation of patients with prostate cancer.

RESULTS

Patient demographics

Patient demographics of all 294 patients are shown in Table 2. Mean age and PSA level were 67.3 years and 9.8 ng/ml, respectively. Regarding NCCN risk groups, 56 patients (19%) were categorized as high risk.
Distribution of PI-RADS score
In total, 588 lobes from 294 patients were evaluated according to PI-RADS scores. Distribution of PI-RADS scores is shown in Table 3. Almost half of the overall lobes were scored as PI-RADS 1, but 191 lobes (33%) were scored as PI-RADS 4 or 5.
Rate of EPE according to PI-RADS score
Figure 1 shows the percentage of EPE according to PI-RADS scores. Total percentage of EPE was 73 out of 588 lobes (12%). While 18 out of 330 lobes (5.4%) showed EPE in patients with PI-RADS score 1 or 2, 27 out of 139 lobes (19%) and 20 out of 52 lobes (38%) showed EPE in patients with PI-RADS score 4 and 5, respectively. In ROC analysis, the optimal cutoff value for the PI-RADS score for detecting EPE was PI-RADS 4 (AUC: 0.716, 95%CI: 0.652 – 0.780). When classified as PI-RADS score 4 or 5 group and <4 group,

Table 2. Patient demographics

No. Patients	294
Age, years	67.3 ± 5.4
PSA, ng/mL	9.8 ± 5.5
ISUP grading group, n (%)	
1	77 (26)
2	78 (27)
3	55 (19)
4	71 (24)
5	13 (4)
cT stage, n (%)	
T1c	96 (33)
T2	185 (63)
T3a	13 (4)
NCCN risk groups	
Low	98 (33)
Intermediate	140 (48)
High	56 (19)

Continuous variables are shown in "mean ± standaed deviation" form.
PSA prostate specific antigen, ISUP International Society of Urological Pathology, NCCN National Comprehensive Cancer Network

the positive predictive value (PPV) and negative predictive values were 24.6% (47/191 lobes, 95%CI: 0.187 – 0.313) and 93.5% (371/397 lobes, 95%CI: 0.906 – 0.957), respectively. Sensitivity and specificity were 64.4% (47/73 lobes, 95%CI: 0.523 – 0.753) and 72.0% (371/515 leaves, 95%CI: 0.679 – 0.759), respectively.

Factors contributing EPE

Table 4 shows univariate and multivariate analysis of the association between various parameters and EPE.

Table 3. Destribution of PI-RADS score

PI-RADS score, n (%)	
1 Very low (clinically significant cancer highly unlikely)	297 (51)
2 Low (clinically significant cancer unlikely)	33 (6)
3 Intermediate (clinically significant cancer equivocal)	67 (11)
4 High (clinically significant cancer likely)	139 (24)
5 Very high (clinically significant cancer highly likely)	52 (9)
Total, n (%)	588 (100)

According to univariate analysis, preoperative PSA level, positive biopsy core percentage ≥ 60%, digital rectal examination (DRE) positivity, and PI-RADS score ≥ 4 were factors influencing EPE. Among these factors, positive biopsy core percentage ≥ 60%, and PI-RADS score 4 or 5 were independent factors influencing EPE by multivariate analysis.

EPE positive rate according to the number of risk factors

We defined two factors (positive biopsy core percentage ≥ 60%, and PI-RADS score 4 or 5) as risk factors predicting EPE according to multivariate analysis (**Table 4**). Figure 2 shows the EPE rate according to the number of risk factors. While only 12 out of 332 lobes without risk factors showed EPE (4%), 34 out of 183 (19%) lobes with one factor, and 27 out of 71 (38%) lobes with two factors showed EPE, respectively ($P <$ 0.01). The discriminatory power of the multivariable model was quantified using C-statistic and AUC was 0.784 (95%CI: 0.729 – 0.840). The internal validity of the multivariable model was assessed using K-fold

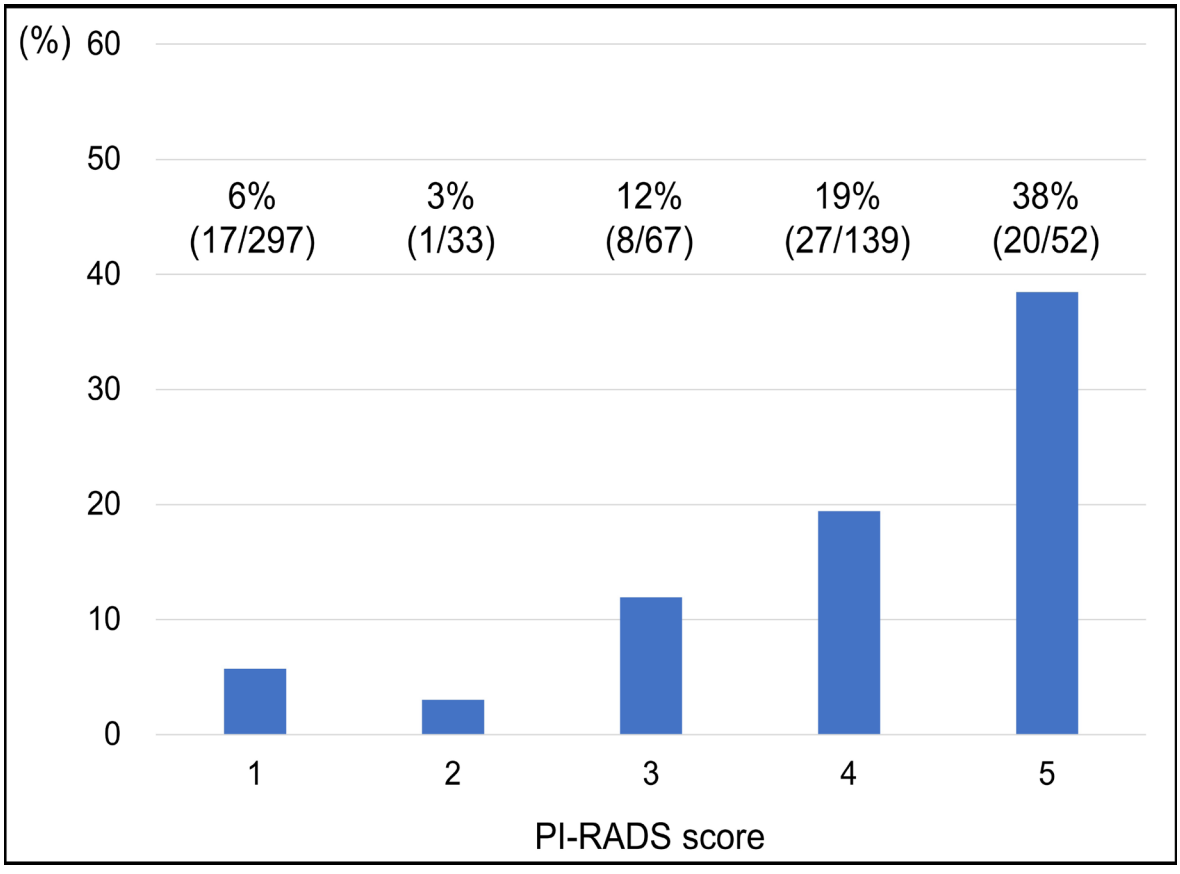

Figure 1. Distribution of PI-RADS score of 588 lobes in 294 patients

cross-validation, and AUC was 0.749 (95%CI: 0.689 – 0.809). **Table 5** shows sensitivity, specificity, PPV and NPV of each factor (positive biopsy core percentage ≥ 60%, PI-RADS score 4 or 5) and combined these 2 factors for predicting EPE.

DISCUSSION

Imaging diagnosis including endoscopy is the mainstay for not only cancer detection, but also for tumor staging in most kinds of cancers. In prostate cancer, PSA and systematic biopsy have been key for detection, with imaging tools such as MRI and CT in an auxiliary role. However, the introduction of mpMRI caused dramatic changes in the detection of prostate cancer. MRI targeted biopsy was shown to be better at detecting clinically significant cancer than the traditional systematic biopsy by systematic review and meta-analysis[14]. Another improvement regarding prostate MRI was the establishment of a scoring system, PI-RADS. Although the most recent version of PI-RADS is v2.1[15], PI-RADS v2 is still relevant in daily clinical settings[3].

Surgery and radiation therapy are the gold standard treatment for clinically significant cancer without metastasis. Some studies showed better oncological outcomes of radical prostatectomy for locally advanced prostate cancer compared with radiation therapy[16, 17]. Accurate preoperative diagnosis of EPE and complete resection are crucial for surgery in locally advanced prostate cancer treatment. Consequently, many people have sought to further develop MRI imaging for EPE prediction. In PI-RADS v1, irregularity (score 3), NVB thickening (score 4), bulge or loss of capsule (score 4), and measurable extra-capsular disease (score 5) were defined as criteria for EPE extension. Schieda et al. demonstrated that AUC of ROC for EPE using PI-RADS v1 was 0.62 and optimal sensitivity/specificity was achieved with PI-RADS ≥ 3[18]. Compared with the previous staging method, sensitivity for EPE improved with PI-RADS v1(59.5% [49.1 – 68.2] vs 24.5% [16.7 – 31.2], P = 0.01), but there was no difference in specificity (62.7% [49.6 – 73.6] vs 42.0% [31.7 – 50.7], P = 0.06). Conversely, Lim et al. reported that the tumor volume calculated from MRI and percentage of positive core biopsies were good predictive factors for EPE. They also suggested that qualitative assessment of T2W-MRI according to PI-RADS v1was limited for the diagnosis of EPE. The AUC of two radiologists for detecting EPE of PI-RADS v1 was 0.51 and 0.46[19]. The scoring system for EPE was changed in PI-RADS v2 to improve diagnostic accuracy[3]. In PI-RADS v2, the prediction of EPE was dichotomized into either organ-confined disease or EPE disease. Morphologic features such as asymmetry or invasion of the NVB, bulging prostatic contour, obliteration of the rectoprostatic angle, and breach of the capsule with evidence of direct tumor extension or bladder wall invasion, are thought to be EPE findings. These features correspond to risk score of ≥ 3 in PI-RADS v1. In addition to these morphologic features, tumor-capsule contact length >10 mm was newly added to EPE criteria. Matsuoka et al. verified the usefulness of newly added criteria in PI-RADS v2[20];

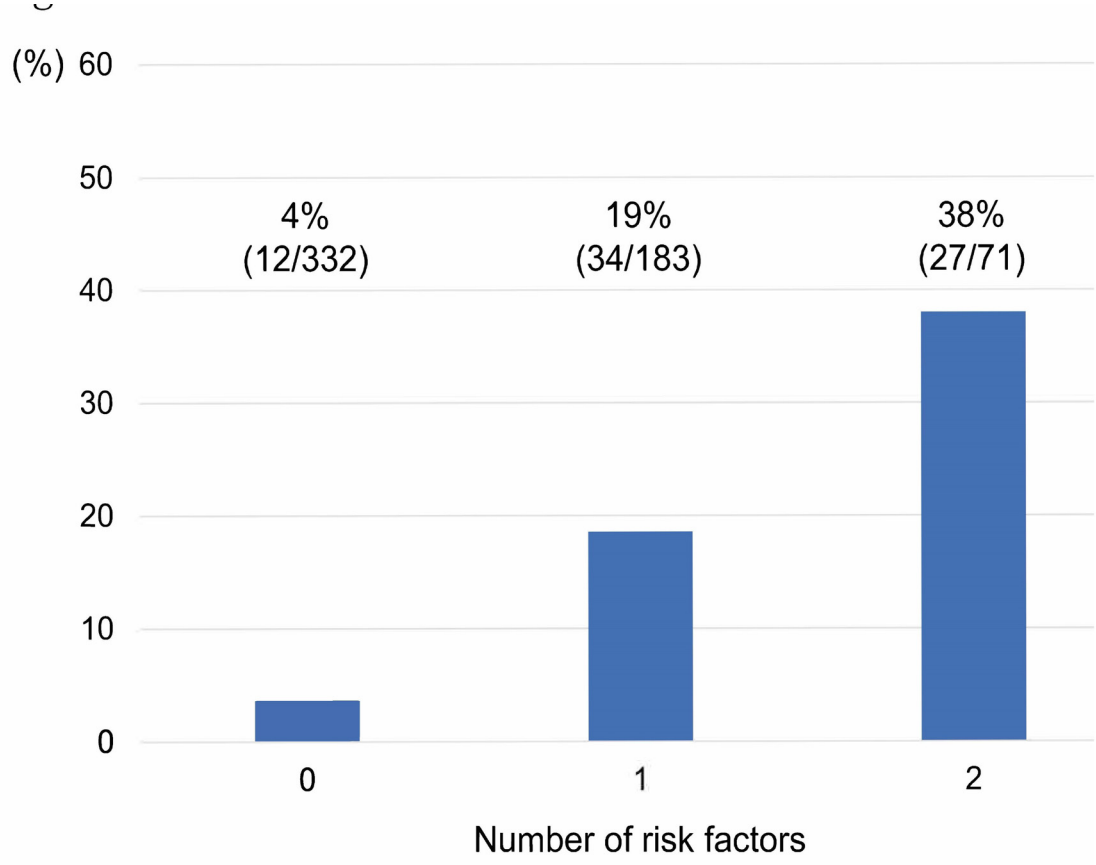

Figure 2. Positive extra prostatic extension (EPE) rate according to the number of risk factors

Table 4. Univariable and multivariable analyses of associations between various parameters and extraprostatic extension positive

	Univariable analysis			Multivariable analysis		
	OR	95% CI	*P* value	OR	95% CI	*P* value
Age ≥ 64 years	1.79	0.92 – 3.81	0.08	1.50	0.73 – 3.34	0.27
Pre operative PSA ≥ 8.9 ng/mL	1.94	1.18 – 3.19	< 0.01	1.54	0.89 - 2.63	0.11
Biopsy ISUP grading group ≥ 4	1.67	0.99 – 2.76	0.05	1.00	0.55 - 1.76	0.99
Biopsy positive rate ≥ 60%	5.79	3.47 – 9.73	< 0.01	3.87	2.21 - 6.82	< 0.01
DRE positive	2.79	1.50 – 5.03	< 0.01	1.51	0.74 – 2.94	0.24
PI-RADS score ≥ 4	4.66	2.80 – 7.89	< 0.01	3.28	1.91 – 5.71	< 0.01

PSA prostate specific antigen, ISUP International Society of Urological Pathology, DRE digital rectal examination, PI-RADS Prostate Imaging Reporting and Data System

PI-RADS v2 had higher negative predictive values than from PI-RADS v1 (96.3 – 97.1% vs 84.9 – 89.1%, p = 0.003 and 0.021, for each reader). PI-RADS v1 and PI-RADS v2 had positive predictive values of 56.9 – 70.5%, 49.1 – 50.5%, respectively (p=0.025 and 0.300, for each reader). PI-RADS v2 was concluded to reduce under-staging, but over-staging remained a concern because PPV was around 50%. They also demonstrated that between 73.3 and 74.1% of the patients with a biopsy Gleason score of ≤ 7 and between 35.7 and 44.4% of the patients with a biopsy Gleason score of ≥ 8 were overstaged in the patients judged to be EPE positive by PI-RADS v2, but not by PI-RADS v1. Accurate prediction of microscopic EPE on MRI images seems to be difficult, but attempting to increase the correctness of EPE by combining some complementary factors similarly to Matsuoka et al. seems to be logical.

Our study evaluated the incidence of EPE according to PI-RADS v2 category. At first, we tried to investigate the relationship between the description of EPE in PI-RADS v2 and EPE pathology. Many vague descriptions about EPE were found, however, and interpretation was often difficult. In comparison, the scoring for categories was clearly stated and easy for urologists to understand. A score of 5 in PI-RADS v2 was defined as lesion ≥ 1.5 cm or definite EPE behavior, so a certain percentage of EPE tumors are expected to be judged as score 5. EPE was diagnosed in 38% of the lesions with a score of 5 in our study. The probability of EPE increased as the PI-RADS score increased. When we set the cut off value of score ≥ 4 for prediction of EPE, the percentage of EPE was 24.6% (47/191). To improve diagnostic accuracy, we tried to find other factors influencing EPE. We picked five factors including age, preoperative PSA, biopsy Gleason score ≥ 8, biopsy positive rate ≥ 60%, and DRE positivity. Among them, only biopsy positive rate ≥60% remained as an independent predictive factor by multivariable analysis (**Table 4**). Finally, PI-RADS ≥ 4 and biopsy positive rate ≥ 60% were chosen as risk factors for predicting EPE. EPE was shown in 27 out of 71 lobes (38%) with these two factors.

Complementary factors of PI-RADS v2 to predict EPE have been investigated in several studies, and tumor volumes have been reported to be representative factors[6,19,21]. Lim et al. reported that tumor diameter was an excellent marker to predict EPE and cut off value was 15 mm[6], which coincidentally corresponded to the size of score 5 in PI-RADS v2. Lim et al. also demonstrated that tumor volume and biopsy positive rate were significant predictive markers for EPE[19]. In our study, biopsy positive rate was a good predictive marker for EPE. Positive biopsy rate is associated with tumor volume and it could be a surrogate tumor volume marker which cannot be detected by MRI. Another concern is biopsy Gleason grade, which was pointed out by Matsuoka et al[20]. Although biopsy Gleason score was marginally associated with EPE by univariable analysis, it could not be considered as prognostic factor in multivariable analysis in our study (**Table 4**).

This study has several limitations. First, MRI and PI-RADS v2 are used to detect clinically significant cancer before prostate biopsy these days, but MRI was performed for determining clinical staging after biopsy in this study. Therefore, not target biopsy but only systematic biopsy has been performed. Since it is very important to determine whether NVB is sacrificed or preserved in radical prostatectomy, we studied whether PI-RADS v2 could predict EPE, which was different from the original purpose. In fact, there are some papers similar to our study. I believe that the PI-RADS v2 score is significant in EPE prediction. However, analysis of the pathological findings of targeted biopsies will be conducted in the future.

Second, bpMRI, not mpMRI, was used in our study, and it remains controversial whether bpMRI can completely replace mpMRI[9-12]. DCE is becoming less important in PI-RADS v2 and owing to patient convenience, bpMRI was adopted in this study.

Third, this study was a retrospective evaluation of archival material, and the data extracted would be of significance in the pre-operative evaluation of patients with prostate cancer.

Lastly, the sample number (294 patients, 588 lobes) was relatively low. We will continue to evaluate more patients by this method.

Table 5. Sensitivity, specificity, PPV and NPV of each factor prediciting extra prostatic extension

	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
PI-RADS score ≥ 4	0.644 (0.523 – 0.753)	0.720 (0.679 – 0.759)	0.246 (0.187 – 0.313)	0.935 (0.906 – 0.957)
Biopsy positive rate ≥ 60%	0.562 (0.441 – 0.678)	0.819 (0.783 – 0.851)	0.306 (0.229 – 0.391)	0.929 (0.902 – 0.951)
Both of above 2 factors	0.370 (0.523 – 0.753)	0.914 (0.679 – 0.759)	0.380 (0.187 – 0.313)	0.911 (0.906 – 0.957)

PPV positive predictive value, NPV negative predictive value

CONCLUSIONS

PPV and NPV of PI-RADS ≥ 4 for predicting pathologic EPE were 24.6% and 93.5%, respectively. PI-RADS ≥ 4 and positive biopsy core percentage ≥ 60% were independent risk factors for predicting EPE. The positive rate of EPE in lobes with zero, one and two factors (PI-RADS ≥ 4 and positive biopsy core percentage ≥ 60%) was 4%, 19%, and 38%, respectively.

ACKNOWLEDGEMENT

We acknowledge proofreading and editing by Benjamin Phillis at the Clinical Study Support Center, Wakayama Medical University. We also appreciate Prof. Toshio Shimokawa at the Clinical Study Support Center, Wakayama Medical University, for critical support from the view of epidemiologist.

CONFLICT OF INTEREST

The authors report no conflict of interest.

REFERENCES

1. institute NC. Cancer information service: ganjoho.jp; [updated 2021/1/18. Available from: https://ganjoho.jp/en/public/statistics/short_pred.html.
2. Oberlin DT, Casalino DD, Miller FH, Meeks JJ. Dramatic increase in the utilization of multiparametric magnetic resonance imaging for detection and management of prostate cancer. Abdom Radiol (NY). 2017;42:1255-8.
3. Weinreb JC, Barentsz JO, Choyke PL, Cornud F, Haider MA, Macura KJ, et al. PI-RADS Prostate Imaging - Reporting and Data System: 2015, Version 2. Eur Urol. 2016;69:16-40.
4. Kasivisvanathan V, Rannikko AS, Borghi M, Panebianco V, Mynderse LA, Vaarala MH, et al. MRI-Targeted or Standard Biopsy for Prostate-Cancer Diagnosis. N Engl J Med. 2018;378:1767-77.
5. Barentsz JO, Richenberg J, Clements R, Choyke P, Verma S, Villeirs G, et al. ESUR prostate MR guidelines 2012. Eur Radiol. 2012;22:746-57.
6. Lim CS, McInnes MDF, Lim RS, Breau RH, Flood TA, Krishna S, et al. Prognostic value of Prostate Imaging and Data Reporting System (PI-RADS) v. 2 assessment categories 4 and 5 compared to histopathological outcomes after radical prostatectomy. J Magn Reson Imaging. 2017;46:257-66.
7. Kim R, Kim CK, Park JJ, Kim JH, Seo SI, Jeon SS, et al. Prognostic Significance for Long-Term Outcomes Following Radical Prostatectomy in Men with Prostate Cancer: Evaluation with Prostate Imaging Reporting and Data System Version 2. Korean J Radiol. 2019;20:256-64.
8. Idee JM, Fretellier N, Robic C, Corot C. The role of gadolinium chelates in the mechanism of nephrogenic systemic fibrosis: A critical update. Crit Rev Toxicol. 2014;44:895-913.
9. Choi MH, Kim CK, Lee YJ, Jung SE. Prebiopsy Biparametric MRI for Clinically Significant Prostate Cancer Detection With PI-RADS Version 2: A Multicenter Study. AJR Am J Roentgenol. 2019;212:839-46.
10. Jambor I, Bostrom PJ, Taimen P, Syvanen K, Kahkonen E, Kallajoki M, et al. Novel biparametric MRI and targeted biopsy improves risk stratification in men with a clinical suspicion of prostate cancer (IMPROD Trial). J Magn Reson Imaging. 2017;46:1089-95.
11. Druskin SC, Ward R, Purysko AS, Young A, Tosoian JJ, Ghabili K, et al. Dynamic Contrast Enhanced Magnetic Resonance Imaging Improves Classification of Prostate Lesions: A Study of Pathological Outcomes on Targeted Prostate Biopsy. J Urol. 2017;198:1301-8.
12. Greer MD, Shih JH, Lay N, Barrett T, Kayat Bittencourt L, Borofsky S, et al. Validation of the Dominant Sequence Paradigm and Role of Dynamic Contrast-enhanced Imaging in PI-RADS Version 2. Radiology. 2017;285:859-69.
13. Koike H, Kohjimoto Y, Iba A, Kikkawa K, Yamashita S, Iguchi T, et al. Health-related quality of life after robot-assisted radical prostatectomy compared with laparoscopic radical prostatectomy. J Robot Surg. 2017.
14. Kasivisvanathan V, Stabile A, Neves JB, Giganti F, Valerio M, Shanmugabavan Y, et al. Magnetic Resonance Imaging-targeted Biopsy Versus Systematic Biopsy in the Detection of Prostate Cancer: A Systematic Review and Meta-analysis. Eur Urol. 2019;76:284-303.
15. Turkbey B, Rosenkrantz AB, Haider MA, Padhani AR, Villeirs G, Macura KJ, et al. Prostate Imaging Reporting and Data System Version 2.1: 2019 Update of Prostate Imaging Reporting and Data System Version 2. Eur Urol. 2019;76:340-51.
16. Cooperberg MR, Vickers AJ, Broering JM, Carroll PR. Comparative risk-adjusted mortality outcomes after primary surgery, radiotherapy, or androgen-deprivation therapy for localized prostate cancer. Cancer. 2010;116:5226-34.
17. Feldman AS, Meyer CP, Sanchez A, Krasnova A, Reznor G, Menon M, et al. Morbidity and Mortality of Locally Advanced Prostate Cancer: A Population Based Analysis Comparing Radical Prostatectomy versus External Beam Radiation. J Urol. 2017;198:1061-8.
18. Schieda N, Quon JS, Lim C, El-Khodary M, Shabana W, Singh V, et al. Evaluation of the European Society of Urogenital Radiology (ESUR) PI-RADS scoring system for assessment of extra-prostatic extension in prostatic carcinoma. Eur J Radiol. 2015;84:1843-8.
19. Lim C, Flood TA, Hakim SW, Shabana WM, Quon JS, El-Khodary M, et al. Evaluation of apparent diffusion coefficient and MR volumetry as independent associative factors for extra-prostatic extension (EPE) in prostatic carcinoma. J Magn Reson Imaging. 2016;43:726-36.
20. Matsuoka Y, Ishioka J, Tanaka H, Kimura T, Yoshida S, Saito K, et al. Impact of

the Prostate Imaging Reporting and Data System, Version 2, on MRI Diagnosis for Extracapsular Extension of Prostate Cancer. AJR Am J Roentgenol. 2017;209:W76-W84.

21. Abreu-Gomez J, Walker D, Alotaibi T, McInnes MDF, Flood TA, Schieda N. Effect of observation size and apparent diffusion coefficient (ADC) value in PI-RADS v2.1 assessment category 4 and 5 observations compared to adverse pathological outcomes. Eur Radiol. 2020;30:4251-61.