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ARTICLE

Value of clinical parameters and MRI with PI-RADS$_{V2}$ in predicting seminal vesicle invasion of prostate cancer

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ABSTRACT

Objective: To investigate the usefulness of magnetic resonance imaging (MRI) with Prostate Imaging Reporting and Data System version 2 (PI-RADS$_{V2}$) and clinical parameters in predicting seminal vesicle invasion (SVI).

Material and methods: In this retrospective study, we identified 569 prostate cancer patients who underwent radical prostatectomy with MRI before surgery. SVI was interpreted with PI-RADS$_{V2}$. Clinical parameters such as the prostate-specific antigen (PSA) and Gleason score (GS) were analyzed for the prediction of SVI. Logistic regression models and receiver operating characteristic (ROC) curves were used to evaluate SVI based on clinical parameters and MRI with PI-RADS$_{V2}$.

Results: The median age at presentation was 67 years (43–85 years). The median PSA level was 6.1 ng/mL (2.2–72.8 ng/mL). There were 113 patients with a biopsy GS of $\geq$ 8. A total of 34 patients (6.0%) were interpreted to have SVI by MRI of which 20 were true positive, and 52 patients (9.1%) had true SVI in the final pathologic analysis. In multivariable analysis, PSA (HR: 1.03, 95% CI: 1.00–1.07), biopsy GS $\geq$ 8 (HR: 4.14, 95% CI: 2.12–8.09), and MRI with PI-RADS$_{V2}$ (HR: 14.67, 95% CI: 6.34–33.93) were significantly associated with pathologic SVI. The area under the curve of the model based on the clinical parameters PSA and GS plus MRI (0.862) was significantly larger than that of the model based on clinical parameters alone (0.777, $p < 0.001$).

Conclusions: MRI with PI-RADS$_{V2}$ using the clinical parameters PSA and GS was effective in predicting SVI.

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MRI; PI-RADSv2; seminal vesicle invasion

Introduction

Magnetic resonance imaging (MRI) is one of the most important diagnostic modalities for preoperative staging in prostate cancer as it can accurately determine the extent of the lesion compared with other tests [1,2]. The development of multi-parametric MRI (mp-MRI) can be obtained to clinically stage more accurately [3]. The prediction of prostate cancer staging is important in determining the treatment plan. In particular, seminal vesicle invasion (SVI) is associated with a very poor prognosis. The accurate evaluation of SVI is important for treatment decision-making [4]. According to the NCCN guidelines, patients with SVI are classified as a very-high-risk group, and the use of external beam radiation therapy (EBRT) with androgen deprivation therapy (ADT) is recommended as a treatment option [5].

However, predicting SVI accurately is difficult before radical prostatectomy (RP). The accurate prediction of SVI preoperatively remains a major challenge. Although digital rectal examination can identify SVI, it is useful only in a palpable stage and is less accurate. On DRE an enlarged seminal vesicle is usually not palpable [6–8]. The possibility of diagnosis using transrectal ultrasonography (TRUS) with seminal vesicle biopsies has been investigated; however, this method is invasive and has low sensitivity (47.4 ~ 66.7%) [9,10]. MRI fusion biopsy is also an invasive method and has low sensitivity [11].

Therefore, mp-MRI with anatomical and functional sequences has emerged as an ideal method for staging prostate cancer [12]. mp-MRI not only provides imaging data on multiple adverse features but also has a high specificity, sensitivity, and negative predictive value (NPV) for detecting clinically significant prostate cancer [13]. In 2015, the Prostate Imaging Reporting and Data System (PI-RADS) steering committee developed an updated version (PI-RADS$_{V2}$) to overcome some of the limitations of PI-RADS$_{V1}$ [14]. The pretreatment risk of SVI based on the clinical stage, serum prostate-specific antigen (PSA) levels, and Gleason score (GS) of biopsy specimens can also be determined using tools such as the Kattan nomogram, Partin tables, and Roach formula [15–17].

Here, we investigated the efficacy of clinical parameters and MRI with PI-RADSv2 in predicting SVI.

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Materials and methods

Patient population

This study was approved by our institutional review board. Patients who were treated for clinically localized prostate cancer at our institution from January 2017 to December 2017 were eligible for analysis. All patients were diagnosed by systematic (12 or more) needle biopsies, and all core biopsies were available for review by the study pathologists. In addition, the patients underwent 3 T MRI with PI-RADS$_{V2}$ and RP [18].

Exclusion criteria included neoadjuvant hormone therapy or radiotherapy prior to RP and distant metastasis. A total of 569 patients were included in the analysis. In 31 patients (5.5%) MRI was performed for MRI fusion biopsy.

In this retrospective chart review, preoperative clinicopathologic data including patient characteristics, the results of MRI with PI-RADSv2, surgical techniques, and pathologic findings were assessed.

MRI protocol and pathological evaluation

MRI was performed using a 3-T Achieva unit (Philips Medical Systems, Best, The Netherlands) and a 32-channel external phased array coil. Transverse T1-weighted images, transverse, coronal, and sagittal T2-weighted fast spin-echo images, dynamic contrast-enhanced images, and diffusion-weighted images of the prostate and seminal vesicles were obtained. Dynamic contrast-enhanced imaging was gained after intravenous injection of 0.1 mmol/kg gadopentetate dimeglumine (Magnevist; Schering, Berlin, Germany) and diffusion-weighted imaging was gained using a single spin-echo echoplanar imaging sequence at 3400/117 with b values of 0, 1000, and 1500 s/mm2, as reported previously [19]. MRI was performed at least 2 months after biopsy to prevent interference. PI-RADS$_{V2}$ has been used at our institution since 2017. Four experienced radiologists analyzed the images using PI-RADS$_{V2}$. They have at least 10 years of experience in genitourinary radiology.

In PI-RADS$_{V2}$, the features of SVI are defined as follows: focal or diffuse T2 hypointense signal and/or abnormal contrast enhancement within and/or along the seminal vesicle, restricted diffusion, obliteration of the angle between the base of the prostate and the seminal vesicle, and demonstration of direct tumor extension from the base of the prostate into and around the seminal vesicle [14].

The RP specimens were fixed in 10% formalin and examined microscopically at 5 mm intervals perpendicular to the apico-basal axis. SVI was confirmed when we observed the invasion of malignant cells into the muscular layer of the seminal vesicle. The total cancer was assessed according to the pathology report, and each specimen was pathologically staged according to the 2018 TNM classification. The specimen is analyzed by two genitourinary pathologists, who have at least 10 years of experience in this field.

Statistical analysis

Quantitative data are expressed as the median (range) or mean (standard deviation), and categorical variables are expressed as the absolute value (percentage). Univariate and multivariable logistic regression and receiver operating characteristic (ROC) curve analyses were performed for all clinical and imaging variables to predict SVI. The area under the curve (AUC) was evaluated for models of SVI prediction based on clinical parameters alone and MRI alone. In addition, a model was constructed for the prediction of SVI based on the combined data of clinical parameters and MRI.

All statistical analyses were performed using IBM SPSS Statistics Version 21 (IBM Corporation, Somers, NY, USA) and the R statistical package (R Foundation for Statistical Computing, Vienna, Austria).

Results

Clinical and pathological characteristics are summarized in Table 1. The median age in this study was 67 years (interquartile range (IQR): 62–71), and the median preoperative PSA was 6.1 ng/mL (IQR: 4.5–9.4 ng/mL). All patients underwent 12 core prostate biopsies, and additional targeted

Table 1. Clinical characteristics of the patients.

Clinical characteristics	$N = 569$ N (IQR or %)
Median age (years)	67 (62–71)
Height (cm)	169.3 ± 6.13
Weight (kg)	68.7 ± 9.0
BMI	25.0 ± 2.7
Median preoperative PSA	6.1 (4.5–9.4)
Biopsy core	
12	541 (95.1%)
13	18 (3.2%)
14	7 (1.2%)
15	3 (0.5%)
Biopsy GS	
6	152 (26.7%)
7 (3 + 4)	210 (36.9%)
7 (4 + 3)	94 (16.5%)
8 (3 + 5, 4 + 4, 5 + 3)	76 (13.3%)
9 (4 + 5, 5 + 4)	34 (6.0%)
10 (5 + 5)	3 (0.6%)
MR T stage	
<mT2c	391 (68.7%)
mT3a	144 (25.3%)
mT3b	34 (6.0%)
D'Amico risk group	
Low	66 (11.6%)
Intermediate	263 (46.2%)
High	240 (42.2%)
OP method	
Open RP	102 (18%)
Robotic RP	467 (82%)
Pathologic characteristics	
Pathologic GS	
6	66 (11.6%)
7 (3 + 4)	260 (45.6%)
7 (4 + 3)	165 (28.9%)
8 (3 + 5, 4 + 4, 5 + 3)	32 (5.6%)
9 (4 + 5, 5 + 4)	46 (8.1%)
10 (5 + 5)	1 (0.2%)
Pathologic T stage	
<T2c	346 (60.8%)
T3a	168 (30.0%)
T3b	52 (9.1%)
T4	3 (0.5%)
Pathologic N stage	
N0 or Nx	552 (97.0%)
N1	17 (3.0%)
Resection margin +	204 (36.0%)

biopsies were performed for 28 patients. The biopsy GS was 6 in 152 patients (26.7%), 7(3 + 4) in 304 patients (36.9%), 7(4 + 3) in 304 patients (16.5%) and ≥8 in 113 patients (19.9%). In MRI staging, 391 patients (68.7%) were ≤T2. A total of 144 patients (25.3%) had an extracapsular extension on MRI, and 34 patients (6.0%) had SVI on MRI. Of 569 patients, 462 patients (82.0%) underwent robot-assisted laparoscopic RP, and the remainder underwent open retropubic RP.

In the final pathological analysis, the GS was 6 in 66 patients (11.6%), 7(3 + 4) in 260 patients (45.6%), 7(4 + 3) in 165 patients (28.9%) and ≥8 in 79 patients (13.9%). A total of 52 patients (9.1%) had SVI based on prostatectomy pathology. Surgical margins were positive in 204 patients (36.0%). Lymphadenectomy were performed in 505 patients (88.7%) but only 17 patients (3.0%) were found lymph node metastases.

In multivariable logistic regression analysis of clinical parameters, independent predictors of SVI were as follows: preoperative PSA (HR: 1.05, 95% CI: 1.02–1.08); biopsy GS ≥ 8 (HR: 4.97, 95% CI: 2.70–9.15; Table 2).

We analyzed the efficacy of MRI with PI-RADSv2 in detecting SVI and found that the sensitivity, specificity, PPV, and NPV of MRI were 38.4%, 97.2%, 58.8%, and 94.0%, respectively (Table 3).

We investigated the prediction of SVI with and without MRI using clinical parameters such as age, grade, and PSA according to systematic biopsy results. When clinical parameters were combined with MRI information, the independent predictors of SVI were preoperative PSA (HR: 1.03, 95% CI: 1.00–1.07), biopsy GS ≥ 8 (HR: 4.14, 95% CI: 2.70–9.15), and MRI (HR: 14.67, 95% CI: 6.34–33.93) in multivariable logistic regression analysis (Table 2). Therefore, we used MRI with PI-RADSv2 and clinical parameters to improve the detection of SVI. We predict SVI prediction based on a multivariable linear regression model.

Figure 1 shows a comparison of the AUCs before and after integrating the results of MRI with PI-RADSv2. The AUC of clinical parameters combined MRI (0.862) was significantly larger than that of the model based on clinical parameters alone (0.777, $p < 0.001$; Table 4). Moreover, we found that the best prediction of SVI was achieved when MRI information was combined with the clinical parameters PSA and biopsy GS ≥ 8. The sensitivity and specificity of our SVI prediction model were measured as 75.0% and 74.9%, respectively.

Discussion

Accurate staging in cancer treatment is one of the most important factors in determining the treatment strategy for prostate cancer patients. A prediction of high-stage disease may be helpful in determining therapy and prognosis. Notably, SVI indicates high-risk pathological stage of pT3b in prostate cancer, thus an important prognostic factor for prostate cancer patients. Moreover, SVI is related with high recurrence rates showing only 20% biochemical disease-free survival rate in 10 years after RP, 56–76% 10-year metastasis-free survival rate after RP, and 84% cancer-specific survival rate [20].

In cases of suspected SVI, EBRT may be preferred over RP and brachytherapy due to the risks of incomplete resection and under-dosing, respectively. According to the NCCN guidelines, the presence of SVI is an indication for adjuvant radiation therapy after RP, and EBRT is recommended rather than prostatectomy.

Table 3. Correlation of MRI with pathology results in detecting SVI.

	Pathology +	Pathology−	Total
MRI+	20	14	34
MRI−	32	503	535
Total	52	517	569

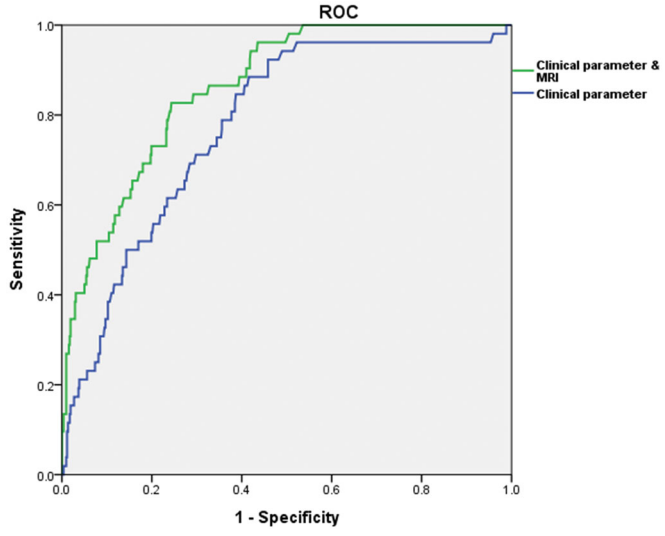

Figure 1. AUC of models for predicting SVI.

Table 4. Comparison of AUC values for predicting SVI.

	AUC value (95% CI)	*p* Value (compared with MRI)	*p* Value (compared with clinical parameter)
Clinical parameter	0.777 (0.715–0.838)	<0.001	
Clinical parameter combined MRI	0.862 (0.818–0.906)	<0.001	<0.001

Table 2. Univariate and multivariate logistic regression analyses for predicting seminal vesicle invasion.

	Univariate		Multivariate			
			Clinical		Clinical + MRI	
	HR (95% CI)	*p* Value	HR (95% CI)	*p* Value	HR (95% CI)	*p* Value
Age	1.04 (0.99–1.09)	0.092				
BMI	0.94 (0.85–1.05)	0.943				
Preoperative PSA	1.06 (1.04–1.09)	<0.001	1.05 (1.02–1.08)	<0.001	1.03 (1.00–1.07)	0.039
Biopsy GS ≥ 8	5.93 (3.28–10.73)	<0.001	4.97 (2.70–9.15)	<0.001	4.14 (2.12–8.09)	<0.001
MRI	22.46 (10.39–48.54)	<0.001			14.67 (6.34–33.93)	<0.001

However, it is difficult to accurately predict SVI before pathologic analysis. The risk of SVI is usually determined according to preoperative information [21]. There have been several studies on the prediction of SVI before surgery [22,23]. Although transrectal ultrasound-guided seminal vesicle biopsy has been suggested [10,24], this method is invasive and difficult for many patients. Sometimes it is difficult to distinguish between SVI and intraprostatic ejaculatory duct invasion as the lining epithelium has the same histological appearance in core needle biopsied tissues. Moreover, the limited efficacy of seminal vesicle biopsies is due to low incidence of SVI, occasional false positives, and its low sensitivity. These methods are also recommended for high-risk groups but do not provide more accurate information than standard clinical information. Therefore, the clinical risk of SVI is currently based on clinical parameters such as the clinical stage, serum PSA levels, and GS of biopsy specimens and tools such as the Kattan nomogram, Partin tables, and Roach formula [15–17].

However, early studies have shown that MRI can be helpful in the detection and staging of prostate cancer [24–26]. Wang et al. [27] performed endorectal imaging using 1.5 T MRI and analyzed 573 patients prior to prostate cancer surgery. They demonstrated that endorectal MRI findings are a significant presurgical predictor of SVI. In recent years, the increasing use of mpMRI has led to an improvement in tumor evaluation, with better comprehension of the prostate and cancer anatomy and its relationship with periprostatic fascia. Moreover, functional imaging (DWI and DCE) and the use of 3 T MRI found to improve sensitivity for both ECE and SVI [28,29]. 3 T MRI increased signal-to-noise ratio, can be obtained increased spatial resolution [30]. In a meta-analysis of detecting PCa, de Rooij et al. [13] reported high sensitivity (0.74) and specificity (0.88) of mpMRI using T2WI, DWI, and DCE. The use of the PI-RADS scoring system for PCa detection on mpMRI results in good diagnostic accuracy [31]. Currently, 3 T, mp-MRI and PI-RADS improve prediction of stage.

Grivas et al. [32] evaluated the staging accuracy of 3 T mp-MRI for 527 patients. They reported that the sensitivity, specificity, PPV, and NPV for SVI detection were 75.9%, 94.7%, 62%, and 97%, respectively. Therefore, 3 T mp-MRI can be used to predict SVI. High accuracy can be attributed to the fact that MRI was performed at a high field strength of 3 T using endorectal coils that could reduce interference. Endorectal coil might have improved the accuracy for SVI in the study by Grivas et al. In addition, Rayn et al. [33] showed that when mp-MRI findings were added to the systematic biopsy-based MSKCC nomogram, the AUC was increased by 0.10 for organ-confined disease. We analyzed the sensitivity and specificity of MRI with PI-RADSv2 in detecting SVI and found that the sensitivity and specificity of MRI were 38.4% and 97.2%. This result was measured to have a lower sensitivity compared to the result of Grivas et al. It is thought that this difference appeared because the patient group of this study contains more patients with lower risk than the previous study. Recent meta-analysis results showed that the mp-MRI in detecting SVI has low sensitivity (58%) [34].

To make a guideline for standardized evaluation and reporting of mp-MRI comprising T2-weighted, diffusion-weighted, and dynamic contrast-enhanced sequences, the European Society of Urogenital Radiology (ESUR) published the first version of the PI-RADS (PI-RADSV1) on year 2012. The PI-RADSV1 had five-point scale that assigned an individual score to each of the MRI sequences but it did not include any recommendations on how to translate the derived scores from 1 to 15 into an easily understandable cancer probability. To address the issues of PI-RADS$_{V1}$, PI-RADSv2 was developed upon the foundation set by PI-RADS$_{V1}$. PI-RADS$_{V1}$ uses the dominant sequences for determining the category of PI-RADSv2 depending on the location of the specific lesion rather than the sum of each component score [35].

SVI can be categorized into 3 types in PI-RADSV2: 1 – tumor extension along the ejaculatory ducts into the seminal vesicle above the base of the prostate, focal T2 hypointense signal within and/or along the seminal vesicle, enlargement and T2 hypointensity within the lumen of the seminal vesicle, restricted diffusion within the lumen of the seminal vesicle, enhancement along or within the lumen of the seminal vesicle, and obliteration of the prostate-seminal vesicle angle; 2 – direct extraglandular tumor extension from the base of the prostate into and around the seminal vesicle; 3 – metachronous tumor deposit with separate focal T2 hypointense signal and enhancing mass in the distal seminal vesicle [14].

We evaluated the efficacy of MRI with PI-RADS$_{V2}$ and clinical parameters. In our patient population, 34 patients (6.0%) had suspected SVI as determined by MRI, and 52 patients (9.1%) had evidence of SVI based on surgical histopathologic analysis. However, 20 patients were confirmed by both MRI and histopathologic analysis. In univariate and multivariable analyses, MRI was found to be a significant predictor of SVI. PSA and biopsy GS $\geq$ 8 were also important parameters for predicting SVI, and the addition of MRI information would be helpful. The AUC values of the predictive models based on clinical parameters alone, and clinical parameters plus MRI were 0.777, and 0.862, respectively. When MRI information was combined with clinical parameters, the prediction of SVI was improved. Therefore, MRI with PI-RADS$_{V2}$ and clinical parameters could provide the best predictive value for SVI. Our findings are consistent with those of previous studies, which have suggested that mp-MRI can help predict SVI preoperatively. If we explain to the patient with information using clinical parameters plus MRI, we can explain the risk of recurrence after RP and explain the other treatment methods in addition to RP.

The present study was a single-institution, retrospective analysis with some limitations. We analyzed 569 patients, all of whom underwent more than 12 systematic core biopsies and 3 T MRI. Additionally, PI-RADS$_{V2}$ was uniformly used to assess mp-MRI. Strength of this study is that it is one of the largest studies to demonstrate the value of mp-MRI with PI-RADS$_{V2}$ and clinical parameters in predicting SVI for prostate cancer patients.

Conclusions

MRI with PI-RADS v2 criteria for SVI showed quite poor sensitivity and only moderate specificity. However, MRI information provides a better predictive value for SVI when combined with clinical parameters. With this approach, urologists can better advise their patients regarding the appropriate treatment and explain the need for additional treatment using this MRI information.

Ethical approval

This article does not contain any studies with human participants or animals performed by any of the authors.

Informed consent

Informed consent is waived by IRB.

Disclosure statement

The authors declare that they have no conflict of interest.

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