Original Article

ANATOLIAN CURRENT MEDICAL

DOI: 10.38053/acmj.977881

Anatolian Curr Med J 2021; 3(4); 303-309

The validity and agreement of PI-RADS v2 in the diagnosis of prostate cancer

Şehnaz Tezcan, Ülkü Bekar, Müge Gürbüz Onbaşıoğlu, Giray Ergin

Koru Hospital, Ankara, Turkey

Cite this article as: Tezcan Ş, Bekar Ü, Gürbüz Onbaşıoğlu M, Ergin G. The validity and agreement of PI-RADS v2 in the diagnosis of prostate cancer. Anatolian Curr Med J 2021; 3(4); 303-309.

ABSTRACT

Aim: The purpose of this study was to evaluate accuracy of multi-parametric MRI (mpMRI) in detection of clinically significant (CS) prostate cancer (PC) and determine agreement of Prostate Imaging Reporting and Data Systems version2 (PI-RADS v2) among three readers.

Material and Method: The study included 65 (32 malignancy, 33 benign) patients with clinically suspected PC who were underwent mpMRI between January 2017 and January 2020 followed by biopsy or prostatectomy. The images were evaluated by three readers who were blinded to patient data. The inter-observer agreement was analyzed with Cohen's weighted kappa statistics.

Results: 74 lesions were detected in 46 patients among 65 patients. When a PI-RADS assessment category ≥3 (K value, 0.406-0.632) was considered positive for CS PC for readers, higher sensitivity, lower specificity and lower agreement was found than PI-RADS ≥4 (K value, 0.545-0.667). The sensitivity and specificity of index lesion detection ranged from 71.8%-90.6%, 60.6%-72.7%, respectively. We found moderate to substantial agreement for index lesion detection. The agreement of PZ lesions was higher than TZ lesions. The agreement in DWI scores was higher than the agreement in T2 scores between readers.

Conclusion: By using PI-RADS v2, high sensitivity but moderate specificity was found in detection of index lesion. The agreement in PI-RADS category assignment was moderate among readers. The agreement and sensitivity in threshold of PI-RADS 4 was higher than PI-RADS 3. TZ lesions showed more variability among radiologists than PZ lesions by using PI-RADS v2.

Keywords: The prostateimaging reporting and data systems version 2, prostate cancer, inter-observer agreement

INTRODUCTION

The use blood prostatic specific antigen (PSA) is the main screening method to detect prostate cancer (PC). However, low specificity and false positive results of PSA may result in unnecessary biopsy procedures (1). Hence, in recent years, multi-parametric magnetic resonance imaging (mpMRI) has become a widely used modality for diagnosis of clinically significant (CS) PC prior to biopsy (2,3). European Society of Urogenital Radiology (ESUR) has developed the Prostate Imaging Reporting and Data Systems version 1 (PI-RADS v1) to provide a global standardization of diagnosis of PC in 2012 (4). In PI-RADS v1, lesions were scored 1 to 5 in each individual pulse sequence. However, this categorization caused variability in assessing PC among radiologists due to lack of strength in determination of final overall score. Subsequently, PI-RADS version 2 (v2) was published in 2015 to improve inter-observer agreement (IOA) of prior PI-RADS system (5). In PI-RADS v2, the dominant sequence was determined for each zone which was diffusion-weighted images (DWI) in peripheral zone (PZ) and T2-weighted images (T2WI) in transition zone (TZ) (5,6). If a lesion score cannot be defined with dominant sequence, contrast enhancement in PZ and diffusion restriction in TZ is used to specify PI-RADS score (5).

Previous studies revealed that PI-RADS v2 had high sensitivity rates (%70-90) but low to moderate reproducibility to detect CS PC (2,3,5-9). In previous reports, IOA of PI-RADS v2 has been studied with preselected lesion which was determined by study coordinator (3,7-9). In the studies analyzing preselected lesions, the diagnostic performance of mpMRI to determine malignancy cannot be evaluated properly due to bias. In the literature, the reproducibility among readers

Corresponding Author: Şehnaz Tezcan, sehnazce@yahoo.com

Received: 02.08.2021 **Accepted:** 20.09.2021

in lesion detection and characterization as would be done in routine clinical practice was analyzed in limited reports (2,6,10). This study technique provides to analyze the ability of radiologists to differentiate malignancy from benign lesions with minimizing the bias. The aim of this study was to evaluate diagnostic performance of mpMRI for detection, localization and characterization of lesions among three readers in a routine clinical practice and determine the agreement of PI-RADS v2.

MATERIAL AND METHOD

The study was carried out with the permission of Health Science University, Dr. Abdurrahman Yurtarslan Oncology Health Application and Research Center Clinical Researchs Ethics Committee (Date: 10.03.2021, Decision No: 2021-03/1071). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Study Population

This retrospective study requirement for informed consent was waived. All patients underwent 1.5 T MRI. 146 patients with clinically suspected PC based on blood PSA or clinical examination with no prior biopsy or with prior negative biopsy who were underwent mpMRI between January 2017 and January 2020 were enrolled in this study. Of these patients, 41 patients who had not histopathologic evaluation in our hospital were excluded from this study. 105 patients that were followed by radical prostatectomy (RP), trans-vesical prostatectomy or systematic 12-core trans-rectal ultrasound (TRUS)-guided biopsy, were included in this study. 34 of the 105 patients included in this study were positive for PC by histopathologic analysis. Of these patients, two patients with PC were excluded from this study because of poor image quality of contrast enhanced images. The remaining 71 patients were negative for PC. Of these patients, 33 patients were randomly selected to reach a ratio of approximately 1: 1 cancer to non-cancer control group. 33 patients were chosen from the box included patients with negative for PC (N=71) by study coordinator due to simple random sampling method. The total study population was 65 patients (32 patients with PC, 33 control subjects). A flowchart of patients who participated in the study is shown in **Figure 1**. Characteristics of patients are demonstrated in **Table 1**.

Table 1. Patient characteristics

Characteristics	Cancer group	Control group	P value
No.	32	33	
Age (y)[a]	66.3±8.2	64.6±6	0.346
PSA value[a]	13.5±15.3	8.1±6.3	0.06
PSA density[a]	0.33±0.43	0.11±0.08	0.008
Prostate volume[a]	50.4±29.9	92.7±73.5	0.004
GS/ISUP (no.)			
6/1	8 (RP:6, TRUS: 2)[a]	-	
7/2	9 (RP:8, TRUS: 1)[b]	-	
7/3	7 (RP:5, TRUS: 2)[b]	-	
8/4	4 (RP:1, TRUS: 3)[b]	-	
9/5	4 (RP:4 TRUS: 0)[b]	-	

[a]Values are number or mean with standard deviation, [b]the method of obtaining histopathologic specimens. Dash (-) represents not applicable. GS, Gleason score; ISUP, The International Society of Urological Pathology classification; RP, radical prostatectomy; TRUS, trans-rectal ultrasound (TRUS)-guided biopsy

MRI Protocol

All MRI examinations were performed using 1.5 T MRI (GE Optima 360, USA®) with 8 channel body/torso array coil. All patients were examined in supine position. A routine protocol was performed including T2WI, DWI with ADC map, T2 fat-sat, T1WI and dynamic contrast-enhanced (DCE) images. **Table 2** indicates the MRI acquisition parameters and sequences in this study. The DCE images were obtained after administration of 0.1 mmol/kg of gadoteric acid. DWI was performed using b values of 50, 1000 s/mm².

Study Design

All MRI examinations were read by 3 radiologists (10, 5 and 8 years, respectively) in prostate MRI. The images were analyzed by readers who were blinded to each patient's data and clinical findings. All readers had experience with PI-RADS v2 prior to this study. The lesion localization was not given to readers. Readers were asked to detect lesion and determine the characteristics of lesion such as localization, measurement, shape, margin, capsule invasion, extra-prostatic extension (EPE) and contrast enhancement. Readers recorded the number of lesions and determine index lesion using PI-RADS v2. And also readers assigned T2 score, DWI score and a final overall score using PI-RADS v2 of each patient. Once readers detected a lesion, they marked it and recorded the number of slice and sequence. The recorded reports for each lesion were compared among readers to determine the agreement in detection.

Table 2. Multi-parametric MRI acquisition protocol

	Axial T2WI	Sagittal T2WI	Coronal T2WI	Axial DWI	Axial T2 fat-sat	Axial T1WI	Axial DCE
Sequence	FSE	FSE	FSE	EPI	FSE	FSE	3D FSPGR
TR (ms)	5594	4300	6200	5400	5357	486	5
TE (ms)	90	102	100	80	78	35	1.7
FOV (mm²)	20×20	24×24	22×22	20×20	20×20	20×20	30×30
Flip angle (˚)	160	160	160	-	160	160	45
Matrix	320×224	320×224	320×244	140×70	320×224	288×244	192×128
B Values	-	-	-	50, 1000	-	-	-
Slice thickness (mm)	3	3	3	3	3	3	3

TR: repetition time, TE: echo-time, FOV: field of view, FSE: fast spin echo, EPI: echo planar imaging; FSPGR, fast spoiled gradient-echo; DCE, dynamic contrast enhanced

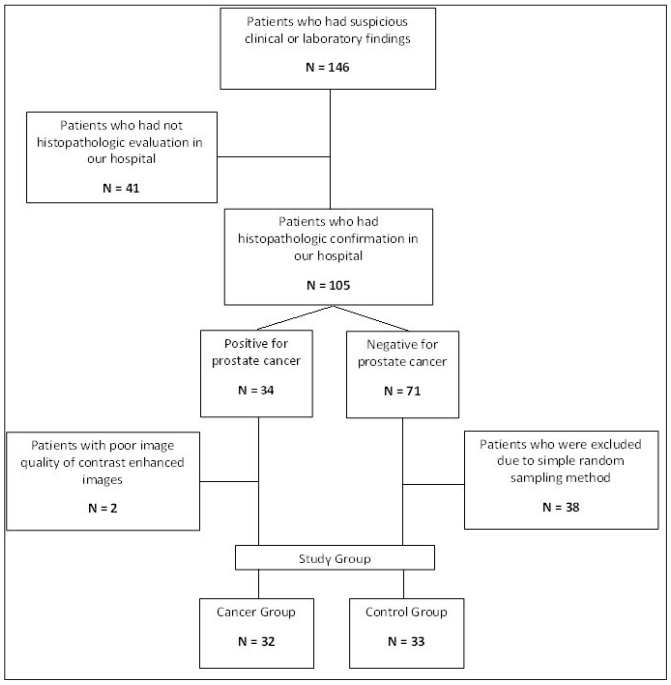

Figure 1. Flowchart of inclusion and exclusion criteria of study sample

Histopathologic Analysis

64 of 65 patients underwent a systemic 12 core TRUS-guided biopsy by 13-years experienced urologist. In cancer group (N=32), 25 of them had been performed with RP following TRUS-guided biopsy in our hospital. In remaining 7 patients with CS PC, RP had not been performed in our hospital, therefore only histopathologic results of TRUS-guided biopsy included in this study for those patients. In one participant (1/65), trans-vesical prostatectomy had been performed. The histopathologic results of TRUS-guided biopsy (39 patients), RP (25 patients) and trans-vesical prostatectomy (1 patient) were analyzed in this study. Gleason score (GS) ≥7, and/or volume ≥0.5 cc, and/or EPE were defined as CS PC. Index lesion was defined as the highest grade lesion on pathological specimens. The International Society of Urological Pathology (ISUP) classification was used to categorize the lesions.

Statistical Analysis

The Kolmogorov-Smirnov test was used to analyze the normal distribution of data. Descriptive statistics were applied to compare demographics, PSA levels and prostate volumes. The reader sensitivity, specificity and accuracy of lesions were analyzed at both patient and lesion level. The final overall PI-RADS category at patient level was defined as the PI-RADS v2 category of index lesion, was classified into two groups which were PI-RADS thresholds ≥3 and ≥4. The IOA was assessed to PI-RADS category, T2 score and DWI score, DCE positivity, lesion detection, index lesion detection and assignment of capsule invasion and EPE at patient level. The assignment and agreement of zone location of lesions were analyzed at lesion level. IOA between each pair of readers for lesions was evaluated by using Cohen's weighted kappa statistics, considering categories according to Landis and Koch recommendations (Kappa (K) value; <0 Poor; 0.00-0.20 Slight; 0.21-0.40 Fair; 0.41-0.60 Moderate; 0.61-0.80 Substantial; 0.81-1.00 Almost Perfect) with the 95% confidence intervals (CIs). Analyses were performed using SPSS (version 22). Statistical significance was accepted at a p-value of less than 0.05.

RESULTS

In 19 patients, no lesion was reported by all readers among 65 patients. In 16 of 19 patients, histopathologic workup showed no CS PC in specimens. In remaining 3 patients, CS PC was detected in PZ (ISUP 1 in two patients, ISUP 2 in 1 patient). Among 65 patients, 74 lesions were detected in 46 patients by at least one reader. Of these 74 lesions, 55 (74.3%) lesions in PZ, 19 (25.6%) lesions in TZ were labeled. Histopathologic analysis revealed 46 (39 in PZ, 7 in TZ) CS PC among these 74 lesions. In PZ lesions, ISUP 1 in 11 (28%), ISUP 2 in 10 (25.6%), ISUP 3 in 8 (20.5%), ISUP 4 in 5 (12.8%), ISUP 5 in 5 (12.8%) lesions were reported. In TZ lesions, ISUP 1 in 1 (14.2%), ISUP 2 in 2 (28.5%), ISUP 3 in 1 (14.2%), ISUP 5 in 3 (42.8%) lesions were reported. The sensitivity and specificity for all readers at patient-level was presented in **Table 3**. When a PI-RADS category ≥3 was considered positive for CS PC for all readers, the sensitivity was found to be higher than PI-RADS ≥4 for all lesions (p<0.000). The specificity decreased in PI-RADS ≥3 at versus PI-RADS ≥4 (p<0.000).

Reader agreement was defined as the agreement of PI-RADS category assessment at least two readers of three readers. While the sensitivity of reader agreement (at least 2/3 readers) was higher in PI-RADS ≥3 than PI-RADS ≥4 (84.3% vs 75%), the specificity was higher in PI-RADS ≥4 (72.7% vs 81.8%, **Table 3**). When a PI-RADS category ≥3 was considered positive for CS PC, all false positive cases were in category of ISUP 1. When a PI-RADS category ≥4 was considered positive for CS PC, the majority of false positive cases were in category of ISUP 1 (6/8). The sensitivity of reader agreement (at least 2/3 readers) was found to be similar to sensitivity of the average sensitivity of 3 readers in PI-RADS ≥3 (84.3% vs 82.2%, **Table 3**). The specificity of reader agreement (at least 2/3 readers) was found to be higher than the average specificity of 3 readers in PI-RADS ≥3 (72.7% vs 64.6%, **Table 3**). The reader agreement (at least 2/3 readers) had higher accuracy than did each readers in PI-RADS ≥3 (p<0.000, **Table 3**). While the average sensitivity of 3 readers (69.7%) was lower than that of the reader agreement (75%), the accuracy was higher in reader agreement (at least 2/3 readers) than accuracy of each readers in PI-RADS ≥4 (**Table 3**).

Table 3. Validity analysis of All lesions at patient-level

Category Assignment	Reader 1 (%)	Reader 2 (%)	Reader 3 (%)	Reader agreement* (%)
≥PI-RADS 3				
Sensitivity	90.6 (74.9-98)	84.3 (67.2-94.7)	71.8 (53.2-86.2)	84.3 (67.2-94.7)
Specificity	60.6 (42.1-77)	60.6 (42.1-77)	72.7 (54.4-86.7)	72.7 (54.4-86.7)
Accuracy	75.3 (63.1-85.2)	72.3 (59.8-82.6)	72.3 (59.8-82.6)	78.4 (66.5-87.6)
≥PI-RADS 4				
Sensitivity	68.7 (49.9-83.8)	78.1 (60-90.7)	62.5 (43.6-78.9)	75 (56.6-88.5)
Specificity	87.8 (71.8-96.6)	69.7 (51.2-84.4)	81.8 (64.5-93)	81.8 (64.5-93)
Accuracy	78.4 (66.5-87.6)	73.8 (61.4-83.9)	72.3 (59.8-82.6)	78.4 (66.5-87.6)

Values in parenthesis are 95% confidence intervals, *Reader agreement necessitated at least 2 of 3 readers assigned a lesion

Table 4 shows the sensitivity, specificity and accuracy for all readers at patient-level in the detection of index lesion.

The sensitivity and specificity of positive enhancement were 54.5% and 68.7% (reader 1), 42.4% and 87.5% (reader 2) and 45.4% and 62.5% (reader 3), respectively.

Table 5 demonstrates the sensitivity and specificity of all lesions, PZ lesions and TZ lesions for all readers at the lesion-level. The sensitivity of all lesions was higher than specificity in the majority of readers (**Table 5**). The average sensitivity of PZ lesions was higher than TZ lesions (PZ vs TZ; 71.3% vs 48.1%, respectively), but the difference wasn't significant (p=0.361). The TZ lesions had higher average specificity than did PZ lesions, however, it wasn't significant (p=0.415). The sensitivity and specificity of index lesions were higher than all remaining lesions (**Table 4, 5**).

Table 6 shows agreement for all readers in assessing lesions with PI-RADS v2. While K value of the IOA was higher in PI-RADS ≥4 than PI-RADS ≥3, the agreement between the readers was moderate to substantial in both thresholds of PI-RADS ≥3 and PI-RADS ≥4 for all lesions. In the lesion based analysis, the agreement of PZ lesions which was in moderate agreement category was higher than the agreement of TZ lesions which was in poor to fair agreement category. And also, the agreement of TZ lesions between readers wasn't significant (p >0.05). We found moderate to substantial agreement for index lesion detection and slight to moderate agreement for all lesions. The slight to fair agreement was found in T2 scores. The agreement in DWI scores which was in substantial to almost perfect agreement categories, was higher than the agreement in T2 scores between readers. In the threshold of DWI score ≥4, the agreement was higher than the threshold of DWI score ≥3. The agreement in DCE positivity was found to be fair to moderate among readers. While the agreement in capsule invasion and EPE were substantial between reader 1 and 2, the agreement between the other readers was fair to moderate (**Table 6**). Representative images were featured in **Figure 2** and **Figure 3**.

Table 4. Validity analysis of ındex lesions at patient-level

	Reader 1 (%)	Reader 2 (%)	Reader 3 (%)
Sensitivity	90.6 (74.9-98)	84.3 (67.2-94.7)	71.8 (53.2-86.2)
Specificity	60.6 (42.1-77)	60.6 (42.1-77)	72.7 (54.4-86.7)
Accuracy	75.3 (63.1-85.2)	72.3 (59.8-82.6)	72.3 (59.8-82.6)

Values in parenthesis are 95% confidence intervals

Table 5. Validity analysis of all lesions at lesion-level

	Reader 1 (%)	Reader 2 (%)	Reader 3 (%)
All lesions			
Sensitivity	83.6 (70.3-92.6)	71.4 (56.7-83.4)	51 (36.3-65.5)
Specificity	65.9 (50-79.5)	65.9 (50-79.5)	79.5 (64.7-90.2)
PZ lesions			
Sensitivity	80.9 (65.8-91.4)	76.1 (60.5-87.9)	57.1 (40.9-72.2)
Specificity	88.6 (75.4-96.2)	65.9 (50-79.5)	86.3 (72.6-94.8)
TZ lesions			
Sensitivity	87.5 (42.1-99.6)	42.8 (9.9-81.5)	14.2 (0.36-57.8)
Specificity	75.5 (60.4-87.1)	100 (92.1-100)	93.3 (81.7-98.6)

Values in parenthesis are 95% confidence intervals; PZ, peripheral zone; TZ, transitional zone

Table 6. Inter-reader Agreement in Prostate Imaging Reporting and Data Systems version 2

	Reader 1-2 K value (p value)	Reader 1-3 K value (p value)	Reader 2-3 K value (p value)
PI-RADS Category			
≥PI-RADS 3	0.406 (0.001)	0.449 (<0.000)	0.632 (<0.000)
≥PI-RADS 4	0.545 (<0.000)	0.615 (<0.000)	0.667 (<0.000)
T2 score			
≥T2 score 3	0.400 (0.001)	0.299 (0.016)	0.212 (0.078)
≥T2 score 4	0.277 (0.014)	0.149 (0.208)	0.256 (0.008)
DWI score			
≥DWI score 3	0.746 (<0.000)	0.810 (<0.000)	0.935 (<0.000)
≥DWI score 4	0.954 (<0.000)	0.915 (<0.000)	0.970 (<0.000)
DCE positivity	0.344 (0.003)	0.464 (<0.000)	0.368 (0.002)
Lesion Localization			
All lesions	0.170 (0.09)	0.144 (0.12)	0.494 (<0.000)
PZ lesion	0.493 (<0.000)	0.450 (<0.000)	0.570 (<0.000)
TZ lesions	0.113 (0.196)	-0.033 (0.733)	0.235 (0.08)
Index lesion detection	0.406 (0.001)	0.449 (<0.000)	0.632 (<0.000)
Capsule invasion	0.789 (<0.000)	0.380 (0.006)	0.412 (0.008)
EPE	0.728 (<0.000)	0.380 (0.006)	0.343 (0.033)

* K value; Kappa value of Cohen's weighted kappa statistics, CI; confidence interval; DWI, diffusion-weighted imaging; DCE, dynamic contrast enhancement, PZ, peripheral zone; TZ, transitional zone; EPE, extra-prostatic extension

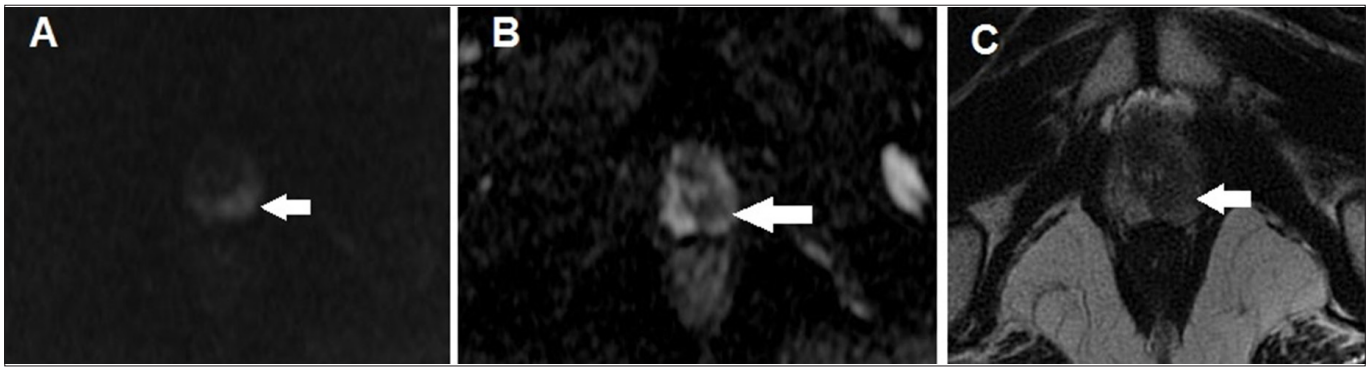

Figure 2. 70-year-old man with prostate cancer (group 3). A. Diffusion-weighted image (DWI). B. Apparent diffusion coefficient (ADC). C. Axial-T2 image. The lesion in left posterolateral segment of apex is hyperintense on DWI, hypointense on ADC and T2. PI-RADS 4 category was assigned by all readers for this patient.

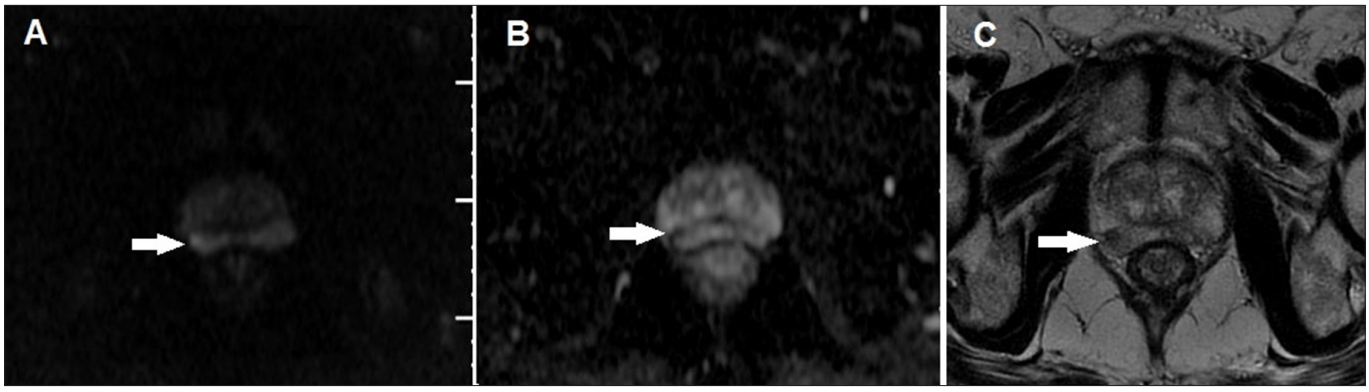

Figure 3. 70-year-old man with prostate cancer (group 1). A. Diffusion-weighted image (DWI). B. Apparent diffusion coefficient (ADC). C. Axial-T2 image. The lesion in the posterolateral segment of right midgland is hyperintense on DWI, hypointense on ADC and T2. PI-RADS 3 category was assigned by two readers in this patient. One reader assigned PI-RADS4 category.

DISCUSSION

In this study, we evaluated the agreement among three readers using PI-RADS v2 and analyzed the validity of mpMRI to detect the CS PC. The mpMRI provides additional information for the decision of biopsy besides the clinical findings. The readers evaluated the images without knowing the data of patients to minimize the bias. The determination of optimal PI-RADS category threshold for the decision of biopsy is still a confusing issue. In our study, when PI-RADS 4 was used as threshold value for biopsy indication, we observed that an increase in specificity and decrease in sensitivity than threshold of PI-RADS 3. The preference of PI-RADS 4 category for biopsy indication provided the diagnosis of benign patients more accurately and reduced unnecessary biopsy procedures. However, using PI-RADS 4 as a threshold also resulted in missing some malignant patients. When PI-RADS 3 was used as threshold value for biopsy, the unnecessary biopsy ratios increased, but the risk of misdiagnosis of malignancy has been reduced. The diagnostic accuracy of thresholds of PI-RADS 4 and PI-RADS 3 were similar to each other in this study. Previous studies also reported higher sensitivity and lower specificity for ≥PI-RADS 3 than for ≥PI-RADS 4 similar to our study (2,3,11). And also, the agreement of ≥PI-RADS 4 was higher than ≥PI-RADS 3 in this study similar to previous studies (2,3,7,11). Rosenkrantz et al. (11) found a moderate agreement among 6 readers (k values of 0.509-0.593 for ≥PI-RADS4 and 0.386-0.534 for ≥PI-RADS3) and Purysko et al. (3) reported substantial and almost perfect agreement among 2 readers (k values of 0.91 for ≥PI-RADS4 and 0.63 for ≥PI-RADS3) from different medical centers, evaluating the preselected lesions. Although, readers from different centers may improve the results due to eliminating similar approaches of readers from single center, the study design with evaluating the preselected lesions may lead to bias in evaluating reproducibility and accuracy of the results. The agreement of the both PI-RADS 3 and 4 thresholds were moderate to substantial among 3 readers in our study. We believe that the definition of PIRADS 3 is inadequate for differentiation of malignancy from benign lesions. In the description of PI-RADS 3, the subjective term of mildly or moderately signal intensity may result in variability among readers due to lack of clear definition of assessment in PI-RADS 3. In TZ, some benign nodules may show hyper-intensity on DWI and hypo-intensity on ADC, thus the morphologic features of TZ lesions on T2 predominates for the assessment of PI-RADS category. When heterogeneous signal intensity with obscured margins is detected in TZ on T2, PI-RADS category assigned as 3 due to PI-RADS v2. However, in

PI-RADS category assessment of TZ lesions, the greater amount of benign prostatic nodules may lead to difficulty in evaluating the margin and morphology of lesions on T2. The majority of the previous studies reported poor agreement in TZ than PZ among readers due to the uncertainty definition which may lead to variability in PI-RADs v2 (2,3,7,8,11). In current study, slight agreement was found in TZ lesion that was lower than PZ lesion among readers.

DCE provides information to discriminate the PI-RADS 4 from PI-RADS 3 due to the principle of early enhancement of malignancy as compared to adjacent normal prostatic tissue. However, direct visual assessment of enhancement without any qualitative evaluation such as kinetic curves or semi-quantitative methods may lower the agreement among readers. Kim et al. (12) found a limited efficiency of time-intensity curves to predict the malignancy. Rosenkrantz et al. (13) reported higher sensitivity of semi-quantitative model than qualitative model with no association of both models with GS. In the literature, the impact of DCE on PI-RADS v2 is still controversial (2,7,11-13). In this study we found slight to moderate agreement and moderate sensitivity and specificity in positivity of early enhancement of lesions similar to previous studies (2,7,11). Although, previous studies reported various validity and reproducibility results of DCE, the impact of the usefulness of mpMRI as compared to bi-parametric MRI was emphasized in the literature (14,15). Nevertheless, further studies which analyze the qualitative evaluation or quantitative and semi-quantitative methods in predicting the strength of DCE besides the direct visual evaluation on PI-RADS categorization with larger patient group are required to decide whether contrast agent is needed for the diagnosis of CS PC in MRI.

Double reading of MRI may be used in training to increase the experience of radiologists and also may improve the diagnostic performance of work-up. It is widely used in screening mammography to increase the accuracy (16). In mpMRI, double reading is not a common method in interpretation of MRI which has a moderate reproducibility among readers, in particular for low-experienced or nonspecialized radiologists (2,3,7,8,17). In this study, the sensitivity, specificity and accuracy were mildly higher in double reading than the average of 3 readers in both threshold of PI-RADS 3 and 4. In double reading, the majority of false positive cases had low grade PC in the current study. Previous studies also reported lower accuracy results in low grade tumors than high grade tumors in mpMRI (18). Although we found a mild increase in the validity of double reading than readers individually, it cannot be an advice for using the double reading as a method in interpretation of mpMRI due to our results.

In PI-RADS v2, the index lesion is defined as a lesion which has the highest PI-RADS assessment category. Our results showed high sensitivity, moderate specificity and moderate to substantial agreement in detecting the index lesions similar to previous studies (2,3,6-8). We found higher sensitivity, specificity and reproducibility in index lesions than all remaining lesions for all readers. Reporting the index lesion provides convenience to determine the overall PI-RADS category and to guide subsequent biopsy for cognitive biopsy technique. Although, biopsy is performed to multiple cores to improve the diagnostic performance, predicting the index lesion with mpMRI prior to procedure may be helpful to focus on the highest suspicious core for multiple tissue sampling.

Our study had some limitations. First, the study design was retrospective and sample size was small. Second, this study evaluated agreement among three readers without considering the experience levels of readers which may have an influence on the agreement. Third, as previously noted, all examinations were performed at a single center with using same protocol by readers from single center which could induce similar approaches. Nevertheless, we established the study method including the evaluation as it should be in routine clinical practice without analyzing preselected lesions to minimize this bias. Even though, studies evaluating the preselected lesions may ensure that all readers analyzing same lesion, in current study the lesions were marked by readers to avoid misinterpretation. In the current study, we included patients who had been performed TRUS-guided biopsy besides patients subjected to radical prostatectomy which would induce a bias toward high-risk PC. However, TRUS-guided biopsy may lower the accuracy of results due to the lack of evaluation of all segments of prostate on specimens which was the fourth limitation of this report.

CONCLUSION

By using PI-RADS v2, radiologist can detect the malignant lesions in particular for index lesions with high sensitivity rates that enable to make decision on biopsy beside blood PSA levels and physical examination. And also, the determination of index lesion prior to biopsy using mpMRI forms an advantage to focus on the most suspicious region while tissue sampling. Specificity was found to be moderate that may result in unnecessary biopsy procedures in some cases. The moderate agreement in PI-RADS category assignment has confirmed the results of previously reported studies. PZ lesions showed lesser variability among radiologists than TZ lesions by using PI-RADS v2. The agreement in threshold of PI-RADS 4 was higher than PI-RADS 3 that can be resulted due to the inadequate definition of PI-RADS3 in PI-RADS v2.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Health Science University, Dr. Abdurrahman Yurtarslan Oncology Health Application and Researchs Center Clinical Research Ethics Committee (Date: 10.03.2021, Decision No: 2021-03/1071).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

REFERENCES

1. Kohestani K, Wallström J, Dehlfors N, et al. Performance and inter-observer variability of prostate MRI (PI-RADS version 2) outside high-volume centres. Scand J Urol 2019; 53: 304-11.
2. Greer MD, Shih JH, Lay N, et al. Interreader variability of prostate imaging reporting and data system version 2 in detecting and assessing prostate cancer lesions at prostate MRI. AJR Am J Roentgenol 2019; 1-8.
3. Purysko AS, Bittencourt LK, Bullen JA, Mostardeiro TR, Herts BR, Klein EA. Accuracy and interobserver agreement for prostate imaging reporting and data system, version 2, for the characterization of lesions identified on multiparametric MRI of the prostate. AJR Am J Roentgenol 2017; 209: 339-49.
4. Barentsz JO, Richenberg J, Clements R, et al. European Society of Urogenital Radiology. ESUR prostate MR guidelines 2012. Eur Radiol 2012; 22: 746-57.
5. American College of Radiology. Prostate imaging reporting and data system version 2. www.acr.org/Quality-Safety/Resources/PIRADS.Published 2015.
6. Greer MD, Brown AM, Shih JH, et al. Accuracy and agreement of PIRADSv2 for prostate cancer mpMRI: a multireader study. Comparative Study J Magn Reson Imaging 2017; 45: 579-85.
7. Mussi TC, Yamauchi FI, Tridente CF, et al. Interobserver agreement of PI-RADS v. 2 lexicon among radiologists with different levels of experience. J Magn Reson Imaging 2020; 51: 593-602.
8. Mussi TC, Yamauchi FI, Tridente CF, et al. Interobserver agreement and positivity of PI-RADS version 2 among radiologists with different levels of experience. Acad Radiol 2019; 26: 1017-22.
9. Seibert MK, Lehmann T, Aschenbach R, et al. Assessment of PI-RADS v2 for the detection of prostate cancer. Eur J Radiol 2016; 85: 726-31.
10. Popita C, Popita A, Andrei A, et al. Interobserver agreement in prostate cancer detection using multiparametric MRI. J BUON 2018; 23: 1061-9.
11. Rosenkrantz AB, Ginocchio LA, Cornfeld D, et al. Interobserver reproducibility of the PI-RADS version 2 lexicon: a multicenter study of six experienced prostate radiologists. Radiology 2016; 280: 793-804.
12. Kim SH, Choi MS, Kim MJ, et al. Role of semi-quantitative dynamic contrast-enhanced MR imaging in characterization and grading of prostate cancer. Eur J Radiol 2017; 94: 154-9.
13. Rosenkrantz AB, Sabach A, Babb JS, et al. Prostate cancer: comparison of dynamic contrast-enhanced MRI techniques for localization of peripheral zone tumor. AJR Am J Roentgenol 2013; 201: W471-8.
14. Franco FB, Fennessy FM. Arguments against using an abbreviated or biparametric prostate MRI protocol. Abdom Radiol (NY) 2020; 45: 3982-9.
15. Xu L, Zhang G, Shi B, et al. Comparison of biparametric and multiparametric MRI in the diagnosis of prostate cancer. Cancer Imaging 2019; 19: 90.
16. Trimboli RM, Verardi N, Cartia F, Carbonaro LA, Sardanelli F. Breast cancer detection using double reading of unenhanced MRI including T1-weighted, T2-weighted STIR, and diffusion-weighted imaging: a proof of concept study. AJR Am J Roentgenol 2014; 203: 674-81.
17. Puech P, Randazzo M, Ouzzane A, et al. How are we going to train a generation of radiologists (and urologists) to read prostate MRI? Curr Opin Urol 2015; 25: 522-35.
18. Holtz JN, Silverman RK, Tay KJ, et al. New prostate cancer prognostic grade group (PGG): can multiparametric MRI (mpMRI) accurately separate patients with low-, intermediate-, and high-grade cancer? Abdom Radiol (NY) 2018; 43: 702-12.