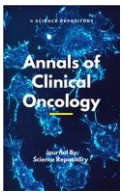

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Research Article

Validation of PI-RADS v2 Scores at Various Non-University Radiology Practices

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ABSTRACT

Purpose: The purpose of this study was to validate the second version of the Prostate Imaging Reporting and Data System (PI-RADSv2) scores in predicting positive in-bore MRI-guided targeted prostate biopsy results across different non-university related institutions. The study focuses on PI-RADS v2 scoring because during the study period, PI-RADS v2.1 had not been released.

Materials and Methods: This was a retrospective review of 147 patients who underwent multiparametric magnetic resonance imaging (mpMRI) of the pelvis followed by in-bore MRI-guided targeted prostate biopsy from December 2014 to May 2018. All lesions on mpMRI were rated according to PI-RADS v2 criteria. PI-RADS v2 scores were then compared to MR-guided biopsy results and pre-biopsy PSA values.

Results: Prostate Cancer (PCa) was detected in 54% (80/147) of patients, with more prostate cancer being detected with each subsequent increase in PI-RADS scores. Specifically, biopsy results in patients with PI-RADS 3, 4, and 5 lesions resulted in PCa in 25.6% (10/39), 58.1% (33/55), and 86.0% (37/43) respectively. Clinically significant PCa (Gleason score ≥7) was detected in 17.9% (7/39), 52.7% (29/55), and 72% (31/43) of cases for PI-RADS 3, 4, and 5 lesions respectively. When the PI-RADS scoring and biopsy results were compared across different institutions, there was no difference in the PI-RADS scoring of lesions or in the positive biopsy rates of the lesions. The sensitivity, specificity, PPV, and NPV for PI-RADS 3-4 lesions were also not statistically different across the institutions for detecting Gleason 7 or greater lesions.

Conclusion: Our results agree with prior studies that higher PI-RADS scores are associated with the presence of clinically significant PCa and suggest prostate lesions with PI-RADS scores 3-5 have sufficient evidence to warrant targeted biopsy. The comparison of PI-RADS score across different types of non-university practices revealed no difference in scoring and biopsy outcome, suggesting that PI-RADS v2 can be easily applied outside of the university medical center setting.

Clinical Relevance: PI-RADS v2 can be applied homogeneously in the non-university setting without significant difference in outcome.

Introduction

Improvements in MRI technology have led to increased utilization of multiparametric MRI (mpMRI) in detecting and characterization of prostate lesions [1]. Recently published results from the PRECISION trial found that mpMRI followed by MRI-targeted biopsy diagnosed more clinically significant prostate cancer than standard transrectal ultrasonography-guided (TRUS) biopsy in men at risk for prostate cancer who have not undergone a previous biopsy [2]. Additional benefits of MR-guided biopsy discovered from other trials include

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avoiding clinically insignificant prostate cancer and needing fewer core samples for the diagnosis of clinically significant cancer [3]. Although it is known that mpMRI will miss much of the low-grade (Gleason Score 6 or less) cancers, the clinical impact is likely low [4]. Furthermore, genetic and epigenetic evidence continues to accumulate demonstrating how Gleason 6 disease is a distinct entity in comparison to higher grade disease [5]. The benefits of MR-guided prostate biopsy over the risks of the biopsy complication and the unnecessary procedures performed for clinically insignificant cancer has led the American Urological Association (AUA) and Society of Abdominal Radiology (SAR) to recommend that patients who have had negative TRUS biopsy to undergo mpMRI followed by targeted biopsy if a lesion is present [6].

In order to standardize the reporting of mpMRI, the European Society of Urogenital Radiology (ESUR) introduced the Prostate Imaging Reporting and Data System (PI-RADS) in 2012 [7]. The update in 2015 to PI-RADS v2 simplified the analysis and implementation so that it can be more widely accepted [8, 9]. This simplified scoring system combines T2 appearance of the lesion, apparent diffusion coefficient and diffusion-weighted signal intensity, and early dynamic contrast enhancement to estimate the level of probability that a lesion harbors cancer without significantly altering the predictive capability from version 1 [9, 10]. The PI-RADS scores range from 1 to 5 with a PI-RADS 1 lesion indicating a clinically significant cancer is highly unlikely to be present whereas a PI-RADS 5 lesion indicates a clinically significant cancer is highly likely to be present. PI-RADS v2 is a consensus statement of the experts for reporting mpMRI, but its ability to predict the presence of clinically significant cancer still requires validation for research and clinical applications [9, 11]. While there has been validation of PI-RADS v2 for initial diagnosis, these results have been obtained predominantly in university-associated major academic centers [12-18]. Validation of PI-RADS v2 for initial diagnosis have not been reported in non-university associated academic or private practice setting.

In the present report, we retrospectively evaluated the efficacy of PI-RADS v2 scoring at predicting positive biopsy rates for in-bore MRI-guided targeted biopsy. Our goal is to assess the validity of PI-RADS v2 in a non-university practice setting where the practitioners and the referring urologists and radiologists are not associated with university academic center. This is one of the areas that had been suggested for further validation [11].

Materials and Methods

I Patient Selection

This study is a retrospective review of urological patients at Banner MD Anderson Cancer Center (Gilbert, AZ) who underwent mpMRI of the prostate followed by in-bore MR-guided targeted prostate biopsy from December 2014 to May 2018. The subjects were identified from the list of patients who had undergone in-bore MRI-guided prostate biopsy at Banner MD Anderson Cancer Center. The biopsies were performed by JC. The indications for biopsy include those with elevated PSA with or without prior negative biopsies, established prostate cancer patients on active surveillance who had developed new lesions, or subjects previously treated with ablation or prostatectomy who had developed new nodules. Inclusion criteria for this study included urology subjects at BMDACC aged 18-89 years old whose biopsy indications included those with elevated PSA with or without prior negative biopsies and active surveillance patients who had developed new lesions. Any previously treated subjects undergoing biopsy for recurrence assessment were excluded from the analysis. Additional exclusion criteria included subjects that underwent freehand biopsies secondary to an absent rectum or anus. Finally, subjects were excluded if radiographic images were not diagnostic due to severe motion or susceptibility artifact or if subjects do not have accessible medical records. This single institution study was approved by the Institutional Review Board at Banner MD Anderson Cancer Center in Gilbert, AZ, and informed consent was waived.

II MRI Scanning Sequences and Procedure

Multiparametric MR Pelvis imaging was obtained at BMDACC as well as outside institutions. All MR-guided biopsies occurred at BMDACC. The MR Pelvis imaging performed at BMDACC were obtained using a 32-channel body coil and a 3T whole body scanner (GE Discovery 750, Waukesha, WI) before and following intravenous contrast administration with and without fat suppression. All MR Pelvis images obtained at outside institutions, were obtained using 3T whole body scanners with and without intravenous contrast administration following a prostate cancer protocol at each institution. This included obtaining T1 weighted, T2 weighted, DWI, ADC, and post-contrast dynamic perfusion images.

MR-Guided biopsies were performed with 3T whole body scanners using the *In Vivo* DynaTrim system (*In Vivo* Corp, Gainesville, FL). Patients were placed in the MR scanner in a prone position and Lidocaine gel was injected into the rectum followed by placing an *In Vivo* needle guide that was connected into a guidance device. Following this, T2 weighted images were obtained in multiple planes for guidance. These images were then transferred to a DynaCad workstation which was used to calibrate and guide the trajectory of the biopsy. Once the trajectory was confirmed, an 18-gauge biopsy gun was inserted through the needle guide and core biopsies were obtained from the target lesion (2-4 cores per lesion). Post biopsy images with the needle in place were taken to demonstrate the needle through the intended lesion.

III Imaging and Pathology Correlation

Cerner Millennium PowerChart medical records and the Synapse v4 PACS system were used to identify and review charts/images. Searches through subject's electronic medical records allowed for acquisition of demographic, laboratory, diagnostic imaging, and histopathological information for each subject. Specific data obtained by researchers included subject prostate-specific antigen (PSA) values, indications for work-up, prior prostate biopsy results (if any), MRI imaging reports, and histopathologic results of the MR-guided biopsies. If not already performed on the initial read by outside board-certified radiologists, PI-RADS scores were assigned to each image based on the dominant sequence by JC in accordance with the PI-RADS v2 criteria [9].

PI-RADS scores were then compared to MR-guided biopsy results to determine if certain PI-RADS scores are predictive of more benign or malignant pathology. Although active surveillance patients had prior biopsy results, only the most recent MR-guided biopsy results obtained

at BMDACC were used for comparison between images and pathology. To maintain consistency for this study, prostate lesions that were found to demonstrate PIN (1 lesion), ASAP (1 lesion), atypical glands (1 lesion), or only a minute focus of prostatic adenocarcinoma (1 lesion) were excluded from this study.

IV Statistical Analysis

Data were tabulated for statistical analysis using T-test, Chi-squared test, and regression analysis. Descriptive statistics were tabulated for analysis via a Kruskal Wallis one way ANOVA. PI-RADS scoring and MR-guided biopsy result comparisons were tabulated via logistic regression and ROC curve analysis. Age, race, and lesion location were controlled for in our analysis. The programme used for statistical analysis was STATA version 14 (STATA Corp., College Station, TX).

Results

I Patient Demographics

After exclusion, 147 patients were left for analysis. Our study population demonstrated an average age of 67.2 years with a mean PSA value of 18.2 at time of biopsy. 10 lesions were scored as PI-RADS 2, 39 lesions as PI-RADS 3, 55 lesions as PI-RADS 4, and 43 lesions as PI-RADS 5. 80 (54.4%) of the lesions biopsied were located in the peripheral zone and 35 (23.8%) were located in the transitional zone. The remaining lesions involved both the peripheral and transitional zone or were located in areas of the prostate not amenable to a strict definition of transitional vs peripheral zone. Complete descriptive characteristics for our patient population are presented in (Table 1).

Table 1: Patient characteristics.

Variables	Values N=147
Age, Years (mean, SD)	67.2 (6.29)
Race (Caucasian, %)	127 (86.4)
PSA (mean, SD)	18.2 (41.5)
Lesion Location (N, %)	
Peripheral	80 (54.4)
Central	35 (23.8)
Other	32 (21.8)
PI-RADS (N, %)	
2	10 (6.80)
3	39 (26.5)
4	55 (37.4)
5	43 (29.3)
Lesion Size, cm	
$\leq$0.5	5 (3.40)
>0.5 - $\leq$ 1	33 (22.5)
>1 – $\leq$ 1.5	31 (21.1)
>1.5	78 (53.1)

II PI-RADS v2 Validation Overall

We first examined the accuracy of PI-RADS in detecting prostate cancer, regardless of Gleason score. Prostate cancer was detected in 54.4% (80/147) of patients. Biopsy results in patients with PI-RADS 3, 4, and 5 lesions resulted in prostate cancer in 25.6% (10/39), 58.1% (33/55), and 86.0% (37/43) respectively. Notably, PI-RADS 4 lesions demonstrated an odds ratio of 23.4 (2.08, 263.6) and PI-RADS 5 lesions demonstrated an odds ratio of 79.8 (6.45, 987.2) using PI RADS 2 as the reference. Neither age, race, PSA at time of biopsy, lesion location, nor lesion size alone had any significant impact on whether or not a lesion would be prostate cancer. Detailed findings regarding prostate cancer detection for PI-RADS scores can be found in (Table 2). For clinically significant cancers, PI-RADS 4 lesions demonstrate an odds ratio of 12.5 (1.23, 127.9) and PI-RADS 5 lesions demonstrated an odds ratio of 21.6 (2.07, 224.8) using PI RADS 2 as reference. The sensitivity of PI-RADS lesions demonstrates an inverse relationship as PI-RADS score increases, with a sensitivity of 98.8 (93.2, 100.0) for PI-RADS 3 or greater lesions which decrease to 46.3 (35.0, 57.8) for PI-RADS 5 lesions. This trend is maintained for clinically significant prostate cancer with a sensitivity of 100.0 (94.6, 100.0) for PI-RADS 3 or greater lesions and 46.3 (34.0, 58.9) for PI-RADS 5 lesions. Specificity increases with higher PI-RADS scores, with a specificity of 13.4 (6.33, 24.0) for PI-RADS 3 or greater lesions which increases to 91.0 (81.5, 96.6) for PI-RADS 5 lesions. For clinically significant prostate cancer, the specificity is 12.5 (6.16, 21.8) for PI-RADS 3 or greater lesions and 85.0 (75.3, 92.0) for PI-RADS 5 lesions.

III PI-RADS v2 Scoring by Institutions

We compared the differences in PI-RADS v2 scoring across different institutions for the cases that were referred for targeted biopsy. When categorized by the specific institution type (BMDACC, non-university academic radiology practice, N=90; local non-university, employed radiology practice, N=42; other private practice radiology groups, non-university non-academic radiology practice, N=15), the distribution of scores is just statistically significant when tested with Kruskal-Willis test ($p=0.045$, Table 3). This may be related to the increased PI-RADS 3 score from the local, non-university, employed radiology group. However, when both non-university, non-academic radiology groups are grouped, the scoring between the academic and non-academic groups did not differ ($p=0.18$, Table 3). These findings together suggest that application of PI-RADS v2 results in similar scoring distribution of lesions between the academic and non-academic radiology groups, although institutional scoring and management of PI-RADS 3 lesion can be a prominent source of variation.

IV PI-RADS v2 Validation by Institution

We compared the positive biopsy rate of the PI-RADS v2 scored lesions across different institutions. When evaluated by institution, the positive biopsy outcomes of PI-RADS scored lesions did not differ statistically (Table 3). When the non-academic radiology institutions are grouped together and compared against the academic radiology group, there is no difference in biopsy outcome between the types of institutions ($0.57 < p < 1$, Table 3). There is also little variation in sensitivity and specificity amongst institution type. When statistical testing is applied with

Bonferroni correction, the difference existed only in the specificities of the PI-RADS 3 (8.16% academic; 16.0% local, non-university, employed group; 33.3%, other centers) and 4 (44.9% academic; 72.0% local, non-university, employed group; 33.3% other centers) lesions. There was no difference in the sensitivities between the various institutions. The specificity difference existed between the academic group and other private practice groups for PI-RADS 3 scores ($p = 0.005$) and between the local, non-university, employed radiology group and the other two radiology practice types studied for PI-RADS 4 score. ($p = 0.004$ for academic vs local, non-university employed group; $p = 0.008$ for local non-university employed group vs other centers). No difference existed for PI-RADS 5 score across the institution types. The PPV and NPV of the PI-RADS scores across various institutions also did not show any difference. This data suggests that PI-RADS v2 can be applied across different institutions without differences in biopsy outcome.

Table 2: Prostate cancer detection.

Variables	Benign N=67	Positive N=80	OR (95% CI)	P-value
PI-RADS (N, %)				
2	9 (13.4)	1 (1.25)	REF	
3	29 (43.3)	10 (12.5)	4.30 (0.39, 46.6)	0.23
4	23 (34.3)	32 (40.0)	23.4 (2.08, 263.6)	0.011
5	6 (8.96)	37 (46.3)	79.8 (6.45, 987.2)	0.001
Age, Years (mean, SD)	66.1 (6.36)	68.0 (6.15)	1.08 (1.01, 1.16)	0.023
Race (Caucasian, %)	59 (88.1)	68 (85.0)	0.56 (0.16, 1.93)	0.36
PSA (mean, SD)	15.6 (43.1)	20.4 (40.3)	0.99 (0.98, 1.01)	0.52
Lesion Location (N, %)				
Peripheral	42 (62.7)	38 (47.5)	REF	
Central	14 (20.9)	21 (26.3)	1.90 (0.55, 6.58)	0.31
Other	11 (16.4)	21 (26.3)	2.09 (0.72, 6.06)	0.17
Lesion Size, cm				
$\leq$0.5	4 (5.97)	1 (1.25)	REF	
>0.5 - $\leq$ 1	22 (32.8)	11 (13.8)	1.39 (0.10, 19.1)	0.80
>1 – $\leq$ 1.5	15 (22.4)	16 (20.0)	2.49 (0.18, 34.3)	0.49
$\geq$1.5	26 (38.8)	52 (65.0)	1.97 (0.15, 26.6)	0.61

Detection of Clinically Significant Prostate Cancer (GS 3+4 or greater).

Variables	Benign+Gleason 6 N=80	Gleason >3+4 or greater N=67	OR (95% CI)	P-value
PI-RADS (N, %)				
2	10 (12.5)		REF	
3	32 (40.0)	7 (10.5)	2.17 (0.21, 22.8)	0.51
4	26 (32.5)	29 (43.3)	12.5 (1.23, 127.9)	0.033
5	12 (15.0)	31 (46.3)	21.6 (2.07, 224.8)	0.01
Age, Years (mean, SD)	66.8 (6.59)	67.6 (5.94)	1.04 (0.98, 1.10)	0.21
Race (Caucasian, %)	71 (88.8)	56 (83.6)	0.58 (0.18, 1.83)	0.35
PSA (mean, SD)	14.9 (39.5)	22.2 (43.8)	0.99 (0.98, 1.01)	0.89
Lesion Location (N, %)				
Peripheral	48 (60.0)	32 (47.8)	REF	
Central	18 (22.5)	17 (25.4)	1.38 (0.44, 4.26)	0.58
Other	14 (17.5)	18 (26.9)	1.75 (0.66, 4.65)	0.26

Lesion Size, cm				
≤0.5	4 (5.00)	1 (1.49)	REF	
>0.5 - ≤ 1	24 (30.0)	9 (13.4)	1.25 (0.09, 15.6)	0.86
>1 – ≤ 1.5	19 (23.8)	12 (17.9)	1.52 (0.12, 19.1)	0.74
≥1.5	33 (41.3)	45 (67.2)	1.86 (0.15, 22.8)	0.62

OR (95% CI) calculated using Multiple logistic regression adjusting for all other variables in the model.

Table 3: Characteristics between institution types.

Lesion Classification				
Variables	Academic Center N=90	Local Employed Group N=42	Other N=15	p-value
PI-RADS (N, %)				
2	4 (4.44)	4 (9.52)	2 (13.3)	0.045
3	21 (23.3)	17 (40.48)	1 (6.67)	
4	38 (42.2)	12 (28.6)	5 (33.3)	
5	27 (30.0)	9 (21.4)	7 (46.7)	
	Academic Center N=90	Local Employed Group + Other N=57		
PI-RADS (N, %)				0.18
2	4 (4.44)	6 (10.5)		
3	21 (23.3)	18 (31.6)		
4	38 (42.2)	17 (29.8)		
5	27 (30.0)	16 (28.1)		
Biopsy Outcome (Gleason positive vs benign)				
Variables	Academic Center N=90	Local Employed Group N=42	Other N=15	p-value
PI-RADS (N, %)				
2 (n=10)	0	0	1 (50.0)	0.20
3 (n=39)	5 (23.8)	4 (23.5)	1 (100.0)	0.35
4 (n=55)	21 (55.3)	8 (66.7)	3 (60.0)	0.83
5 (n=43)	24 (88.9)	6 (66.7)	7 (100.0)	0.14
	Academic Center N=90	Local Employed Group + Other N=57		
PI-RADS (N, %)				
2 (n=10)	0	1 (16.7)		1.0
3 (n=39)	5 (23.8)	5 (27.8)		1.0
4 (n=55)	21 (55.3)	11 (64.7)		0.57
5 (n=43)	24 (88.9)	13 (81.3)		0.65

Kruskal – Wallis Test to compare PI-RADS between center types.

Discussion

The purpose of this study was to validate PI-RADS v2 for predicting positive biopsies using in-bore MRI-guided prostate biopsy in a non-university practice setting. As expected, prostate cancer detection increased with higher PI-RADS scoring (Table 2). Biopsy results in patients with PI-RADS 3, 4, and 5 lesions resulted in prostate cancer in 25.6% (10/39), 58.1% (33/55), and 86.0% (37/43) of cases respectively. Importantly, there is a steadily increasing trend in PPV and specificity across all lesions with each successive increase in PI-RADS v2 score with concurrent drop in sensitivity.

It is important to note that the majority of validation data obtained for PI-RADS has been obtained at university-associated academic medical centers, and there is still a need to validate its application to non-university practices. Jordan *et al.* reported PI-RADS v2 scores as a significant predictor of clinically significant prostate cancer in a community setting [19]. They reported a positive biopsy rate of 17.7, 50, and 54.5% for PI-RADS 3, 4, and 5 lesions in the peripheral zone; and

8.5, 27.5, and 58.3% for PI-RADS 3, 4, and 5 lesions in the transitional zone [19]. Our results are in line with Jordan *et al.*, with 25.6, 58.2, and 86% positive biopsy rate for PI-RADS 3, 4, and 5 lesions with combined peripheral and transitional zone lesions. The difference in our study is the diverse readers for mpMRI PI-RADS scoring as we applied the community practice reads to our PI-RADS scoring. This diversity may be more reflective of the general practice, although it is also less well controlled in terms of the reading style. Another study by Kohestani *et al.* investigated performance and inter-observer variability of PI-RADS outside high-volume centers [20]. Looking at index tumors which were initially scored as PI-RADS v1 and then converted to PI-RADS v2, they noted a detection rate ranging from 67-76% if PI-RADS 3-5 were considered positive and 54-66% if only PI-RADS 4-5 scores were included.

For aggressive tumors with GS $\geq$ 4+3, the detection rate was higher at 83.1% for PI-RADS 3-5, and 79.2% for PI-RADS 4-5. Perhaps more importantly, the study noted similar detection rates amongst readers with >200 reads of similar cases (average detection rate 76%) compared to readers with approximately 50 cases (average detection rate 67%), suggesting that only a moderate number of cases are required to reach this learning plateau [20]. This is supported by Rosenkrantz *et al.* who noted a plateau after approximately 40 cases [21]. While Kohestani *et al.* used index lesions for their study, we studied each lesion. We also did not re-score reads from outside institutions, instead applying the PI-RADS score as it was read. A number of other studies investigating concordance amongst scoring in single private institutions also noted moderate to high rates of inter-observer reliability [22, 23]. However, we believe our work is the first to investigate this across different institutions. Given how similar the range of positive biopsy rates are for PI-RADS scoring in the non-academic setting to that of the academic medical centers, the definition of PI-RADS v2 can be robustly applied both in the community and academic centers.

An important finding of our study as well as the findings from the literature was the PPV of PI-RADS 3 lesions. The low PPV of PI-RADS 3 lesion has raised significant discussion regarding the appropriateness of biopsy as well as methods to improve positive biopsy rate [24]. PI-RADS 3 lesions typically have lower specificity and greater discordance amongst radiologist reads [25]. This is due to the lack of distinct feature as PI-RADS 3 lesions have been characterized as not belonging to either PI-RADS 1, 2, 4, or 5. This has resulted in the recently proposed upgrade to PI-RADS v2 to v2.1 which better defines some of the indeterminate lesions [26, 27]. The study from Tamada *et al.* showed that PI-RADS v2.1 improved the concordance and detection of lesion in the transitional zone, where most of the discrepancy amongst radiologists exists [28]. PI-RADS v2.1 improves the biopsy rates by shifting the indeterminate lesions to either higher or lower PI-RADS scoring [27, 28]. Schoots also suggested the possibility of biopsying only the PI-RADS 4 and 5 lesions, but based on literature review, this is not an acceptable method to improve positive biopsy rate as 30% of the PI-RADS 3 lesions are cancerous [24]. PI-RADS 3 lesions are present in approximately 30% of the mpMRI studies, and with approximately 20% of clinically significant prostate cancer in PI-RADS 3 lesions, which would delay diagnosis of 6% of clinically significant cancers [24].

Comparison with Breast Imaging Reporting and Data Systems (BI-RADS) may shed light as to the best methods for managing PI-RADS 3 lesions. In BI-RADS, the BI-RADS 3 lesion has only 3% chance of being malignant, which differs significantly from PI-RADS 3 lesion, where 10 to 30% of the lesion is malignant. BI-RADS manages the BI-RADS 3 lesions by recommending 6-month follow-up study. This short interim imaging allows the early changes to be detected but returns the stable lesions back to the screening pool. This interim look provides an alternative to immediate biopsy and could prevent significant number of unnecessary biopsies. This can be applicable to prostate cancer because of the generally slow-growing nature of prostate cancer [29]. In their study, Frye reported that even for intermediate risk lesions, the progression-free period on active surveillance is at least 1.2 years [29]. If surveillance took place at 6 to 12 months, this would provide ample opportunity for detecting progression. Therefore, one may consider more frequent surveillance as an alternative to immediate biopsy for managing PI-RADS 3 lesions.

Other methods incorporating serum marker studies have been evaluated to improve biopsy rates. A recent study by Gortz *et al.* demonstrated promising results in using PSA density as an adjunct towards PI-RADS 3 disease [30]. By using a PSA density threshold of 0.1 ng/ml/ml, 43% of the biopsy could be avoided at the cost of missing 2% of intermediate risk cancer in a biopsy naïve population [30]. Jordan *et al.* also support the use of PSA density, noting that PI-RADS v2 + PSAD is better than PI-RADSv2 alone [19]. Similar findings have been proposed by Schoots *et al.* in active surveillance population, by Baruah *et al.*, and by Maggi *et al.* who conducted a meta-analysis, although a threshold of 0.15 ng/ml/ml was used [24, 31-32]. There is also evidence that points to combining the 4K-score test or the European Randomized Study of Screening for Prostate Cancer risk calculator (ERSPC-RC) with mpMRI to better identify clinically significant disease [33]. A nomogram combining Free PSA, PIRADS, and neutrophil to lymphocyte ratio has also demonstrated positive results [34]. These findings all suggest the possibility of improving positive biopsy rates for PI-RADS 3 lesions. Clinical trial will be necessary to determine which option or combination of options is most optimal for managing PI-RADS 3 lesions.

Despite its findings, our study also has some limitations. Most importantly, the retrospective nature of our study carries inherent risk for selection bias. Additionally, our study possesses a relatively small sample size in comparison to related literature. This small size, paired with the fact our sample stems from a demographic receiving treatment at a highly specialized cancer treatment center means our findings may not entirely represent those that could be expected in a more heterogenous patient population. In addition to the patient demographic, the specialized nature of our institution means the radiologists, pathologists, and urologists involved were highly experienced in prostate mpMRI and in-bore MR-guided prostate biopsies, although this is tempered by the mixture of PI-RADS scored by outside radiologists. Moreover, our study is also limited by its inclusion of patients with differing clinical history, with some patients being prostate biopsy naïve and others having undergone multiple prostate biopsies prior to in-bore MR-guided biopsy. This same issue could also be considered the strength of this study in order to validate the application of PI-RADS v2 to a broader practice setting where patients and treatments are more heterogeneous [11]. Finally, not all mpMRIs were assigned a PI-RADS

v2 score upon initial reading. Thus, some PI-RADSv2 scores were retrospectively scored in accordance with ESUR PI-RADSv2 criteria. Given that the radiologist retrospectively scoring these images was not blinded to the pathology, there is a risk of bias. Even with these limitations, we believe the effect size demonstrated by our data is large enough to indicate clinical significance and further contributes to the recent literature regarding the utility for PI-RADSv2 scoring in prostate cancer detection and management, even in a private practice setting.

Conclusion

PI-RADSv2 scoring can serve as a valuable tool in aiding decision making for prostate lesions that are amenable to biopsy. Our findings provide further evidence that PI-RADS v2 is sufficiently robust for application across academic and non-academic medical facility without significant deviation in prediction. Our results also provide further evidence that PI-RADS v2 will need further improvement in order to improve positive biopsy rate so as to avoid much of the un-necessary biopsy that occurs in PI-RADS 3 lesions. With the latest PI-RADS v2.1, there is already reduction in biopsy and increased concordance between radiologists. With further inclusion of laboratory data or improved management recommendation, it is expected that the efficacy of biopsy will continue to improve.

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