PI-RADSv2.1: Current status

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ABSTRACT

Multiparametric magnetic resonance imaging (mpMRI) has played an increasing role in the detection and local staging of prostate cancer over the last 15 years. Prostate mpMRI, due to various factors, is prone to high inter-reader variability necessitating standardized reporting guidelines that provide accurate and actionable information to the ordering clinician. The Prostate Imaging-Reporting and Data System version 2.1 (PI-RADSv2.1) was released in March 2019 as an update to PI-RADSv2.0 with the hope of further standardizing the reporting process of prostate mpMRI, improving the detection of clinically significant cancer, reducing the biopsy rate of indolent tumors, and decreasing inter-reader variability. Early data show an improved performance of PI-RADSv2.1 over PI-RADSv2.0. Updates included in PI-RADSv2.1 and its current experience in clinic will be reviewed in this review.

Keywords: Early detection; mpMRI; PI-RADS; PI-RADSv2.1; prostate cancer; prostate MRI.

Introduction

Prostate cancer is a major health problem and the second most frequent malignancy (after lung cancer) in men worldwide, causing an estimated 358,989 deaths in 2018.[1,2] The incidence of prostate cancer is higher in developed countries, reflecting a greater use of screening and diagnostic testing. Multiparametric magnetic resonance imaging (mpMRI) has played an increasing role in the detection and local staging of prostate cancer over the past 15 years, with continuous technical advancements for better accuracy in cancer diagnosis. However, findings of mpMRI can be nonspecific and current evaluation of prostate mpMRI depends mostly on qualitative evaluation. Additionally, mpMRI involves several sequences, and a large volume of diagnostic information to be analyzed. With the advent of new imaging techniques, it can be challenging to organize reports in a way that is useful and actionable to the ordering clinician. This makes prostate mpMRI prone to inter-reader variability and has highlighted the need for standardized methods of prioritizing MRI lesions for biopsy.[3]

The very first standardized guideline for prostate MRI was released in 2012 by the European Society of Urogenital Radiology to increase consistency of prostate MRI reporting.[4] Three years later, the Prostate Imaging Reporting and Data System version 2.0 (PI-RADSv2.0) was released to address several practical problems identified with the first set of guidelines.[5] PI-RADS is intended to be a "living" document, with updates made by the PI-RADS steering committee as it becomes more widely implemented, and clinical information is made available and reviewed. PI-RADSv2.0 was simpler and assigned each lesion a single overall score from 1-5 as opposed to a summation score based on various assessments. PI-RADSv2.0 specified a dominant sequence used to evaluate lesions based on the anatomic location in the prostate, with T2W being the dominant sequence for evaluating transition zone (TZ) lesions and DWI the dominant sequence for the peripheral zone (PZ). PI-RADSv2.0 also recognized the dynamic contrast-enhanced (DCE) sequence as a less influential part of the study than T2W and DWI, now used only to promote peripheral zone lesions from PI-RADS 3 to PI-RADS 4.

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Once again, after several years of clinical use, PI-RADS was re-evaluated in attempts to further improve standardization and inter-reader agreement.[6-8] The current version, PI-RADSv2.1 was released in 2019.[9] This review serves to discuss the current status of PI-RADSv2.1 and what is known thus far about its clinical performance.

New Aspects of PI-RADSv2.1

While PI-RADSv2.1 did not introduce nearly as many changes as version 2.0, it does include minor updates to the guidelines for interpretation of T2W, DWI, and DCE sequences.[9] PI-RADSv2.1 still assigns a single overall category from 1-5 to each identified prostatic lesion and assigns a secondary role to the DCE sequence, but the definitions of categories 2 and 3 on DWI, categories 1 and 2 on T2W, and positive/negative on DCE have been altered in attempts to more accurately stratify the cancer risk of each lesion. Qualitative, descriptive detail was added to each of these classifications to clarify subtle differences between lesions in these subcategories with the expectation that this would translate to more standardized and reliable reporting of mpMRI.

DWI category 2 now includes "linear/wedge shaped" lesions on ADC and high-b value DWI. DWI category 3 now specifies that the pattern of hypointensity must be "discrete and different from background" and specifies that the hypointensity on ADC map/hyperintensity on high-b value DWI may be "marked" on one sequence or the other, but not both. The new definition for DWI subcategory of 3 got rid of the terms "mildly" and "moderately" in describing intensity on DWI since these may be more prone to subjective interpretation.

The changes to T2W subcategories 1 and 2 aim to clarify characteristics of benign nodules in the transition zone. T2W category 1 now includes "round, completely encapsulated" nodules, whereas PI-RADSv2.0 would have considered these T2W subcategory of 2. This change eliminates unnecessary clinical suspicion of adenomas secondary to benign prostatic hyperplasia (BPH). T2W subcategory 2 now includes the description of "atypical" BPH nodules.

Main Points:

- Prostate Imaging-Reporting and Data and System version 2.1 (PI-RADSv2.1) was published in 2019 and aims to standardize the reporting process of prostate multiparametric MRI (mpMRI).
- Early data on PI-RADSv2.1 suggest improvement over version 2.0.
- There is a direct correlation between cancer detection and PI-RADSv2.1 category, however specificity remains low.
- Inter-reader variability in prostate mpMRI remains an ongoing concern; potential solutions include educational workshops and computer-aided diagnosis with deep-learning methods.

Importantly, the overall PI-RADSv2.1 category of 3 now includes transition zone lesions that have a T2W score of 2, but a DWI score of 4 or 5. This emphasizes the importance of diffusion restriction on risk assessment, even in the transition zone where BPH nodules are highly prevalent. Formerly this would have been in the overall PI-RADS 2 category, but with this change, these lesions will be biopsied at a much higher rate. Finally, the definition of a negative DCE score was modified to include enhancing extruded BPH nodules in the PZ, as this finding is not cause for concern.

In addition to added qualitative details in these PI-RADS subclassifications, there are new technical specifications included in PI-RADSv2.1. These include acquiring T2W in an axial and an additional plane, specific b-values to be used in DWI sequence acquisition and ADC calculation, and the temporal resolution of DCE. The motivation for these technical specifications is that standardized reporting is more likely to occur if image quality is also more uniform.

Current Experience in Clinic

Available data on the performance of PI-RADSv2.1 since its release in 2019 is very limited but suggest an improved performance over PI-RADSv2.0 in clinical practice. One study incorporating 535 consecutive mpMRI studies retrospectively evaluated each scan with both PI-RADSv2.1 and v2.0. The most prominent change was observed in the TZ with the downgrading of typical BPH nodules from category 2 to category 1. Additionally, 16.1% of PI-RADS 3 lesions were downgraded to PI-RADS 2 using the updated PI-RADS classification system.[10] Another study compared v2.0 with v2.1 for detection of cancer in the transition zone in 58 patients with elevated PSA.[11] Two radiologists with 7 and 12 years of experience evaluated the images and inter-reader agreement was higher with v2.1, with a kappa value of 0.58 for v2.0 and 0.65 for v2.1. For both readers, the AUC was higher for v2.1 than for v2.0, but the findings only approached significance for one reader and were insignificant for the second. These findings were replicated in another study evaluating diagnostic accuracy and inter-observer agreement of PI-RADSv2.0 and v.2.1 for the evaluation of transition-zone lesions, and concluded that PI-RADSv2.1 is both more accurate and has a higher inter-observer agreement than version 2.0, and that reader experience continues to impact the performance of mpMRI interpretation with version 2.1.[12]

The new upgraded PI-RADS 3 category, introduced in PI-RADSv2.1 (T2W score of 2, with DWI score of 4 or 5), has been clinically evaluated and found to be of lower but comparable risk to conventional T2W score of 3 nodules, with 28% of up-

graded PI-RADS 3 lesions containing prostate cancer (PCa) and 8% having clinically significant prostate cancer (CS-PCa, ISUP grade group 2 or higher). This is in comparison to 44% and 20%, respectively, in conventional T2W score 3 lesions.[13]

PI-RADSv2.1 has been shown to be a useful tool in predicting postoperative biochemical failure, with 2-year biochemical failure-free survival being higher in patients with PI-RADS 4 lesions than PI-RADS 5. Additionally, they found that zonal location of an index lesion may be a useful biomarker for predicting postoperative recurrence, with transition zone lesions less likely to result in biochemical failure after surgery than peripheral zone lesions.[14] Similarly, PI-RADS has been demonstrated to predict likelihood and time to progression on active surveillance. PI-RADS 5 lesions have a 50% greater chance of progression to Gleason grade group 3 or higher than PI-RADS 4 lesions on active surveillance, and twice as fast.[15]

While PI-RADSv2.1 does not include any specific recommendations in support of the use of biparametric MRI (bpMRI), a study of 103 patients utilizing PI-RADSv2.1 demonstrated a significantly higher sensitivity with mpMRI and a significantly higher specificity with bpMRI.[16] The study, thus, concluded comparable performance and interobserver reliability between mpMRI and bpMRI, however the higher sensitivity of mpMRI would support the recommendation to use mpMRI in patients with higher clinical suspicion or cancer risk factors.

Potential Strengths and Weaknesses

Strengths of PI-RADSv2.1 are that it serves as a guideline for radiologists to create standardized reports of mpMRI and works as a functional risk assessment tool for prostate lesions. While inter-observer agreement in PI-RADSv2.0 was extensively studied and repeatedly reported to be suboptimal, new literature evaluating PI-RADSv2.1 seems to report inter-observer variability as less of an issue.[10,17-20]

A possible weakness of PI-RADSv2.1 is that the only quantitative assessment is the 1.5 cm size criteria used to upgrade lesions from overall category 4 to 5. Perhaps with the advent of artificial intelligence (AI) applications, a more standardized quantitative analysis of regions of interest could provide prognostic value.[21] ADC values have been shown to inversely correlate with tumor aggressiveness and can serve as a quantitative metric to assist with assigning PI-RADS DWI subcategories 4 and 5.[22] Additionally, AI has already shown great promise in increasing the sensitivity of prostate cancer detection and decreasing variability among readers, however these algorithms require the continued curation of extensive and high-quality training datasets that are time- and research-intensive.[23-25] Educational workshops are another potential solution to variability among readers as it has been shown that the inter-reader variability is highest among inexperienced radiologists. It is difficult to reach all practicing prostate radiologists, technologists, and urologists; however, educational efforts should remain ongoing.[26,27]

Some may consider a lack of management recommendations a weakness of PI-RADSv2.1. Other reporting guidelines like the Breast Imaging Reporting and Data System (BI-RADS) include patient management recommendations, while PI-RADS includes only a risk category. There is still much research to be done regarding management of equivocal PI-RADS 3 lesions as well as more aggressive PI-RADS 4 and 5 lesions. Questions remain to be answered regarding whether to biopsy and how urgently, how many cores are necessary, and whether proceeding to prostatectomy without biopsy is feasible in select patients.[28,29]

Conclusion

In summary, PI-RADSv2.1 can provide an improvement over PI-RADSv2.0 in both diagnostic accuracy and inter-observer agreement and is a good tool for prostate lesion risk stratification. PI-RADSv2.1 still seems to be more sensitive than specific, making it a good rule-out tool during cancer evaluation. While there are a small number of mpMRI-invisible clinically significant prostate tumors, this is not a reflection of the PI-RADS classification but rather an inherent limitation of mpMRI as a detection tool. In general, cancer detection rates increase with increasing PI-RADSv2.1 categories. Inter-reader agreement is expected to improve with reader experience. Educational workshops and assistance using artificial intelligence may decrease inter-reader variability.

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