Medical Research Archives

European Society of Medicine

OPEN ACCESS

Published: May 31, 2024

Citation: Tirtashi, R., H., et al., 2024. The real-life challenges in prebiopsy prostate mp-MRI: Experiences from a Middle Eastern Country. Medical Research Archives, [online] 12(5). https://doi.org/10.18103/mra.v12i5.5370

DOI: https://doi.org/10.18103/mra.v12i5.5370

ISSN: 2375-1924

RESEARCH ARTICLE

The real-life challenges in prebiopsy prostate mp-MRI: Experiences from a Middle Eastern Country

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ABSTRACT

Prostate Imaging Reporting and Data System (PI-RADS) has brought a standardized framework for the acquisition and interpretation of prostate multiparametric magnetic resonance imaging. To date, the most of studies implementing PI-RADS v2.1 in clinical practice have been conducted in developed Western countries. Our real-life experience from a developing country within the Middle East revealed that implementing PI-RADS v2.1 in prebiopsy multiparametric magnetic resonance imaging among 88 biopsy-naïve patients who underwent 12-core standard systematic biopsy, combined with magnetic resonance cognitive targeted biopsy, resulted in relatively lower cancer detection rates compared to developed countries. Therefore, we have discussed the limitations and challenges that might have influenced our results, including factors such as our equipment and technological capabilities, the experience and expertise of experts, and our biopsy methodology. Our lower cancer detection rates could be attributed to several factors, including the magnetic field strength of our scanner (1.5T), the shortage of expert and trained magnetic resonance imaging technologists in developing countries, the level of experience of our radiologist, the location and size of our index lesions, and inherent limitations of magnetic resonance cognitive targeted biopsy, particularly for lesions located at the apex and base of the prostate, as well as the number of biopsy cores obtained. Considering the challenges faced by radiologists in developing countries, incorporating artificial intelligence into the acquisition and interpretation of prostate multiparametric magnetic resonance imaging, and combining the PI-RADS scoring system with parameters with predictive value for prostate cancer diagnosis, like prostate-specific antigen density, prostate health index, and apparent diffusion coefficient value, could result in a significant improvement in prostate cancer detection and risk stratifications.

1. Introduction

Prostate Imaging Reporting and Data System (PI-RADS) provides an essential framework for standardizing the interpretation of prostate multiparametric magnetic resonance imaging (mp-MRI) scans to detect clinically significant prostate cancer (csPCa). An updated version, PI-RADS v2.1, was established to overcome the inconsistencies and limitations of the previous version.[1] A recent meta-analysis, comprising 17 studies from developed countries, revealed that the pooled cancer detection rates (CDR) were 16%, 59%, and 85% for PI-RADS scores of 3, 4, and 5, respectively. This analysis also identified a significant association between higher PI-RADS v2.1 scores and increased CDRs.[2]

2. Methods and the study design

In our practical experience, we conducted a survey at a center in Golestan Province, located in the north of Iran, with a low burden of prostate cancer (PCa).[3] Over the past three and a half years, men suspected of prostate cancer (PCa) underwent prebiopsy prostate mp-MRI before any surgical interventions. Regarding this, after administrating a bowel preparation (30 mg bisacodyl) and antispasmolytic (20 mg of Hyoscine-N-Butyl Bromide), a 1.5 T Philips Ingenia scanner was used for mp-MRI acquisition with the following specific sequences: Axial T2 weighted image (T2WI), coronal T2WI, axial diffusion-weighted imaging (DWI) with zoom protocol and maximum b-value of 1400-1600, axial T1 volumetric interpolated breath-hold examination (VIBE), axial dynamic contrast enhancement (DCE) T1VIBE with administration of gadolinium at 0.1 mmol/kg, and Axial post-contrast classic T1. Subsequently, the mp-MRI images were evaluated, and the findings were reported following the standardized format of the PI-RADS v2.1 guideline.[1] Additionally, sector map diagrams were provided based on PI-RADS v2.1 (consisting of 38 sectors/regions) to facilitate further interventions by our urologist, something looking like magnetic resonance (MR) cognitive targeted biopsy (cog-MRGB). Patients then underwent a transrectal ultrasonography (TRUS) 12-core biopsy, followed by cog-MRGB, which was guided by the sector map diagrams. Furthermore, the histopathological results were documented in accordance with the International Society of Urological Pathology recommendation, and the Gleason score (GS) ≥ 7 was identified as a csPCa.[4] Additional details regarding our study materials and methods are also available in a preprint that was previously published to investigate a subset of our dataset (76 patients with PI-RADS scores of 4 and 5).[5]

3. Results and Discussion

Our dataset includes 88 biopsy-naïve men (130 lesions) with varying PI-RADS scores: 3 (8 individuals, 9.1%), 4 (37 individuals, 42%), and 5 (43 individuals, 48.9%). Of these, PCa was diagnosed in 46 patients (52.3%), with 33 patients (37.5%) showing csPCa. Notably, while no PCa cases were detected among patients with a PI-RADS score of 3, the CDRs were 35.1 % for a PI-RADS score of 4 (6 patients with csPCa, 16.2%) and 76.7% for a PI-RADS score of 5 (27 patients with csPCa, 62.8%). Compared to developed countries, our results revealed relatively lower CDRs, particularly for a PI-RADS score of 4. Considering our limited sample size, we

explore the potential factors influencing this divergence, including the magnetic field and setting of our scanner, the experience and expertise of our technologists and radiologist, limitations in the performance of PI-RADS v2.1, as well as technical challenges and limitations associated with cog-MRGB. These aspects will be further discussed in the following paragraphs.

3.1. EXPLORING MRI TECHNOLOGY AND TECHNOLOGISTS

Not only is there extreme inequity in accessing MRI units in low- and middle-income countries, such as Iran, compared to high-income countries, but also most of the available units in countries like Iran are low-field.[6] While most studies included in the meta-analysis by Oerther et al.[2] utilized a 3T mp-MRI, our scanner operates at 1.5T. In line with the PI-RADS v2 guideline published in 2015, both 1.5T and 3T MRI can yield reliable diagnostic results, although the majority of the PI-RADS Steering Committee members prefer and recommend 3T for prostate MRI.[4] [Level of evidence of 3, Grade B [7]] The key benefit of 3T lies in an elevated signal-to-noise ratio (SNR), which is associated with enhanced spatial resolution and image quality.[4,7] Regarding this, a prospective study revealed that while both field strengths produced comparable SNR and contrast-to-noise ratio (CNR) for T2-weighted images (T2WI), 3T provided significantly higher SNR and CDR in diffusion-weighted images (DWI), crucial for diagnosing csPCa in the peripheral zone (PZ) of the prostate.[8] Nevertheless, this study's authors emphasized that 1.5T did not significantly compromise the PI-RADS scoring compared to 3T. Moreover, a meta-analysis of 4 studies utilizing both 1.5T and 3T in patients with PCa, demonstrated that while 3T showed slightly higher diagnostic accuracy than 1.5T, this difference was not statistically significant.[9]

Prostate mp-MRI is a demanding exam to perform and achieving high-quality mp-MRI images depends on the trained technologists' experience and expertise.[10] Along with the scarcity of modern MRI units in countries like Iran, there is also a lack of formal training for MRI technologists.[6] It is recommended that employing technologists trained in prostate MRI, with knowledge about the anatomy and pathology of the prostate, as well as specific artifacts and technical issues, can enhance image quality.[7] Additionally, technologists' ability to acquire various sequences of prostate mp-MRI accurately based on standardized protocols, plays an important role in ensuring accurate and high-quality images for radiologists to interpret, particularly in DWI sequence, which is an essential component of identifying focal csPCa within the periphery of prostate gland.[10] Throughout our study, we cannot exclude the potential effects of the knowledge and expertise of our technologists, as well as the scanner setting, on our results, particularly during the early stage of the study.

3.2. EXPLORING RADIOLOGIST EXPERIENCE AND EXPERTISE

A single radiologist with five years of experience in prostate MRI has been reporting prostate mp-MRI findings in our center. Regarding the interobserver reproducibility of the PI-RADS v2.1, several investigations have compared inter-reader agreement between PI-RADS v2 and 2.1,

showing higher and better inter-reader agreement for PI-RADS v2.1 regardless of the radiologists' experience levels in prostate MRI.[11-13] However, a significant difference was found only in the study conducted by Wei et al.[13] Respecting this, a 6-year assessment of fellowship-trained abdominal radiologists, who evaluated and reported over 200 prostate MRI examinations without previous PI-RADS experience, suggesting that radiologists' experience did not significantly affect the accuracy of mp-MRI interpretations for detecting PCa. However, after the initial 50 examinations, the precision of radiologists' positive predictive values was improved.[14] Moreover, a recent meta-analysis revealed that more experienced readers were not associated with a significant increase in PI-RADS v2.1 performances.[15] In light of these findings, the impact of our radiologist's experience on our results, particularly during the initial phases of the study, is undeniable. Nevertheless, we believe that active communication between radiologists and urologists along and receiving feedback from histopathological results may potentially enhance radiologists' ability to distinguish malignant lesions from benign lesions and improve PI-RADS scoring performance.

3.3. EXPLORING PI-RADS V2.1 PERFORMANCE IN PROSTATE TRANSITION ZONE

In our dataset, 55 lesions (42.3%) were located at the transition zone (TZ) of the prostate, of which 28 lesions (50.9%) belonged to the PI-RADS 4 category. Even with advancements in prostate mp-MRI and targeted biopsies to evaluate and detect PCa in the TZ, accurately identifying and diagnosing PCa in this zone remains an ongoing challenge in clinical practice. [12,16] Compared to the PZ, imaging the TZ is difficult due to its higher cellular density and the presence of dense muscle fiber bundles.[17] In addition, almost all patients assessed by mp-MRI for PCa showed numerous hyperplastic nodules and intervening tissue in the TZ due to glandular and stromal hyperplasia related to benign prostatic hyperplasia (BPH), creating a challenging background for evaluating the likelihood of PCa in suspicious findings and assigning a PI-RADS category.[1,17] Considering the significant revisions for evaluating TZ in PI-RADS v2.1 [1], an exploration of 6 studies with 1426 lesions located at the TZ in a meta-analysis revealed that PI-RADS v2.1 performed better in detecting csPCa in the TZ compared to PI-RADS v2, with a qualitatively slightly higher area under the curve of the receiver operating characteristic curve for PI-RADS v2.1 [15] However, PI-RADS v2.1 showed significantly lower pooled specificity than PI-RADS v2, while the pooled sensitivity was marginally significantly higher for V2.1. Moreover, no significant differences were found in positive and negative predictive values between these two versions.[15] Regarding this, in accordance with PI-RADS v 2.1 guidelines, T2WI serves as the primary sequence in prostate mp-MRI for assessing TZ lesions, complemented by DWI.[1] Considering the difficulty of scoring TZ lesions based on morphological features observed in the T2WI, notably for less experienced readers[18], recent research has underscored the impact of DWI information in influencing biases in T2WI scoring for TZ lesions, especially among inexperienced radiologists.[17] Consequently, the authors recommended establishing T2WI scores for TZ lesions before evaluating DWI images.

It is worth mentioning that classifying prostate mp-MRI findings into PI-RADS 4 or 5 is predominantly based on lesion size (size cutoff= 15 mm) instead of MRI findings. [4] Park et al.[19] demonstrated that CDRs were significantly higher in PI-RADS 4 index lesions ≥ 10 mm compared to lesions <10 mm. (59.3% vs. 39%, p value= 0.0008) Similarly, in the study conducted by Kilic et al.[20], the prevalence of csPCa increased with greater PI-RADS 4 lesion diameter. Furthermore, the size of PI-RADS 4 lesions was significantly associated with predicting PCa in multivariate analysis. However, this association was not significant for csPCa. The number of PI-RADS 4 lesions within our dataset was 54 (41.53%) with a median diameter of 13 mm [interquartile range (IQR) 10-13], of which 28 lesions (51.9%) were located at the TZ. Interestingly, only 8 lesions (14.8%) were <10 mm, of which 3 lesions (37.5%) were located at TZ. In light of these findings, although, we cannot solely attribute our lower CDRs in the PI-RADS 4 category to lesion diameter, our lower CDRs could be partially explained by the zonal distribution of our index lesions.

3.4. EXPLORING UROLOGIST EXPERIENCE AND EXPERTISE AND BIOPSY PROCEDURE

Throughout our study, a single expert urologist performed all biopsy procedures, and a single expert pathologist evaluated and reported histopathological findings. Considering the high cost of fusion equipment, applying cog-MRGB appears to be a practical and lower-cost option in countries like Iran to potentially improve prostate biopsy accuracy, especially for large lesions located at the PZ.[21-23] However, several factors may affect cog-MRGB results, including the smaller size of the anterior lesions, particularly those located at the base or apex of the prostate, the absence of imaging confirmation for accurate biopsy, and its high dependency on the operator.[21,23,24] In our opinion, the prostate topographic map and active communication between our radiologist and urologist, combined with the expertise of our urologist (with over 30 years of experience), could ensure the acceptable capability of our urologist to synchronously combine mp-MRI findings with transrectal ultrasonography. Concerning this, a recent study examining the impact of variability among radiologists and urologists on the diagnosis of PCa found that while variability among urologists in performing prostate biopsies had minimal influence on PCa detection, variability among radiologists in interpreting mp-MRI images and scoring PI-RADS significantly affected diagnosis.[25] However, we cannot overlook the limitations and challenges in cog-MRGB in the apex and base of the prostate due to the risk of damaging the anterior fibromuscular stroma and the bladder, respectively. Furthermore, in this study, most of the participants received 2 additional cognitive cores per index lesion. Although the standard two-core per index lesions can diagnose most cancers among biopsy-naïve men, it may miss csPCa detected in further biopsy or active surveillance.[26,27] Hence, it is anticipated the highest detection rate of csPCa can be achieved by obtaining 5 cores per target lesion. [26,28]

3.5. EXPLORING COMPLEMENTARY PARAMETERS AND PREDICTORS FOR DIAGNOSING CSPCA

An emerging body of evidence suggests several predictors for csPCa combined with

prebiopsy mp-MRI. Prostate-specific antigen density (PSAD), for example, has shown a complementary role in risk assessment and decision-making for prostate biopsy, especially among men with negative or equivocal mp-MRI findings.[29,30] In addition, prostate health index (PHI), a biomarker integrating various PSA forms [([-2]proPSA /free PSA) × √total PSA)], when combined with PI-RADS score, has demonstrated the potential to improve detection rates of PCa and csPCa while reducing unnecessary biopsies, notably in cases with PI-RADS 3 lesions.[31,32] Moreover, quantitative apparent diffusion coefficient (ADC) values can help distinguish high-risk PCa from low-risk cases with moderate accuracy, as well as differentiate csPCa from insignificant PCa.[33,34] In recent years, there has been increasing interest in the application of artificial intelligence (AI) in prostate mp-MRI acquisition, interpretation, and localization. AI has the potential to enhance the speed and quality of prostate mp-MRI by reducing scan time, cost, and motion artifacts, while also providing improved image features for PCa diagnosis and risk stratification.[35] A recent systematic review revealed that deep learning (DL)-based models in mp-MRI for the diagnosing of csPCa have demonstrated comparable diagnostic performance to expert radiologists. However, compared to expert radiologists, DL-based models have shown slightly lower sensitivity in both patient-level csPCa detection for PI-RADS ≥4 and lesion-level localization of csPCa.[36] Moreover, according to another systematic review, AI methods generally outperformed clinical assessment methods for the detection and prediction of PCa, particularly in diagnosing csPCa and predicting adverse pathology features.[37] Although further investigations are needed to establish the key role of AI in prostate mp-MRI and PCa detection, we believe that equipping MRI centers and radiologists in developing countries with AI could be a cost-effective approach to enhance radiologists' diagnostic capabilities for PCa and help to identify candidates for prostate biopsy. This can be complemented by incorporating various predictor variables, such as PSAD and ADC value.

4. Conclusion

Our real-world experience of implementing PI-RADS v2.1 among biopsy-naïve men in a developing country within the Middle East highlighted the impact of several factors on the detection rate of PCa. These factors include limitations and challenges such as low magnetic field strength of scans, a shortage of trained MRI technologists, radiologists' expertise, lesion characteristics including location and size, biopsy methodology, and the number of biopsy cores taken. In light of these findings, incorporating additional predictive factors such as ADC value and PSAD combined with the PI-RADS scoring system, as well as the integration of AI in prostate mp-MRI acquisition and interpretation, might lead to improving the performance of PI-RADS in diagnosing csPCa.

Declarations

COMPETING INTERESTS:

The authors have no relevant financial or non-financial interests to disclose.

FUNDING:

No funds, grants, or other support were received during the preparation of this manuscript.

ACKNOWLEDGMENTS:

This research did not receive any specific grant from any funding agency in the public, commercial, or not-for-profit sector.

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