ORIGINAL ARTICLE

The Diagnostic Value of Multiparametric-MRI in Locating Prostate Cancer in Comparison with Transrectal Ultrasound-Guided Biopsy

Sayed Mohammad Sakhaei [1], Sedighe Rahmani Firouzi [1*], Mohamad Ghazanfari Hashemi [2], Seyedeh Nooshin Miratashi Yazdi [3], Mohammad Ali Kaviani [4], Maryam Alaei [5], Helia Helali [5], Maedeh Ghazanfari Hashemi [6], Marjan Gholami [7], Vahid Talebi [2]

[1] *Department of Radiology, School of Medicine, Mazandaran University of Medical Sciences, Sari, Iran*

[2] *Cancer Institute, Tehran University of Medical Sciences, Tehran, Iran*

[3] *Advanced Diagnostic and Interventional Radiology Research Center, Tehran University of Medical Sciences, Tehran, Iran*

[4] *Department of Radiology, School of Medicine, Kerman University of Medical Sciences, Kerman, Iran*

[5] *School of Medicine, Shahid Beheshti Medical University, Tehran, Iran*

[6] *School of Medicine, Qazvin University of Medical Sciences, Qazvin, Iran*

[7] *School of Pharmacy, Islamic Azad University Pharmaceutical Sciences Branch, Tehran, Iran*

*Corresponding Author: Sedighe Rahmani Firouzi
Email: sedigherahmani1989@gmail.com

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Abstract

Purpose: The present study was designed to evaluate the potential efficacy of Multiparametric-Magnetic Resonance Imaging (MP-MRI) in the detection of prostate cancer locations compared to Transrectal Ultrasound (TRUS) guided biopsy, as the gold standard method.

Materials and Methods: A total of 66 subjects participated in this cross-sectional study. All individuals underwent MP-MRI imaging before the prostate TRUS. The findings of either method have been investigated and the comparison had been made using the Chi-squared test.

Results: The sensitivity and specificity of the MP-MRI in the diagnosis of prostate cancer were 81.8% and 93.9%, respectively. The positive and negative predictive values were 93.1% and 83.8%, respectively.

Conclusion: The current study indicates that the MP-MRI imaging method has sufficient sensitivity and specificity for detecting the location of prostate cancer and can potentially be employed as a clue-providing method prior to the TRUS-guided biopsy.

Keywords: Prostate Cancer; Magnetic Resonance Imaging; Ultrasound; Biopsy.

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1. Introduction

Prostate cancer is the second leading cause of cancer death in men [1]. Early detection of prostate cancer can potentially contribute to the chance for a more sufficient treatment plan and a reduction in its complications [2].

Patients with elevated Prostate-Specific Antigen (PSA) levels, abnormal Direct Rectal Exam (DRE), and also those with complaints about prostate problems such as the frequent urge to urinate, dribbling of urine, and need for urination during the night are recruited for prostate evaluation and prevalently undergo standard Transrectal Ultrasound (TRUS) guided biopsy of the prostate gland [3]. According to previous studies, in 10% of cases, prostate cancer is not diagnosed despite previous TRUS-guided biopsies, and the PSA levels continue to increase [4]. The re-use of TRUS in this group of patients who had a previous negative biopsy but had a high level of PSA is a point of controversy [5].

Recent advances in Multiparametric MRI (MP-MRI) have prompted the more frequent application of this modality, albeit challenges to its diagnostic accuracy exist [6]. It has been revealed that MP-MRI has high sensitivity and specificity concerning the diagnostic gold standard, which is TURS-guided biopsy. Moreover, the role of MP-MRI in localizing the lesion before the biopsy, especially in clinically-suspicious cases with negative results from the initial biopsies, has been discussed [7]. Also, it has been claimed that MP-MRI can be utilized as a triage method that can prevent unnecessary biopsies [8]. Other superiorities attributed to MP-MRI include its non-invasive nature and its potential ability to discriminate clinically significant from that of non-significant [9].

The current research was designed to investigate the diagnostic value of MP-MRI in localizing prostate cancer compared to TRUS-guided prostate biopsy. The standardized reporting scheme applied for the categorization of prostate lesion characteristics is the Prostate Imaging-Reporting and Data System (PI-RADS) that has been revised in 2019 and its second version (v2.1) was presented [10]. To compare the findings of the primary version (v.1) with the latest version (v2.1), both versions have been considered in this study.

2. Materials and Methods

In this cross-sectional study implemented in Imam Ali Hospital (Sari, Iran), a total of 66 subjects referred to the urology clinic with complaints about prostate problems were selected to undergo both MP-MRI and standard TRUS-guided prostate biopsy. A comparison of TRUS-biopsy (as the gold standard method) and MP-MRI in terms of sensitivity, specificity, positive predictive value, and negative predictive value or clinically significant prostate cancer was performed. The conduct and reporting of each examination were performed blind to the other examination findings. The objectives of the study were explained to the research participants, and the patients were included in the study after obtaining written informed consent about the outlined sampling method. Also, all ethical considerations of Helsinki were observed. This study was approved by the ethics committee of the Mazandaran University of Medical Sciences and registered with the reference code of IR.MAZUMS.IMAMHOSPITAL.REC.1397.094.

2.1. Patients Population and Inclusion/Exclusion Criteria

The enrolled subjects were male, older than 45 years who had PSA>4 ng/dl, and/or free PSA to total PSA ratio of less than 20%, and/or abnormal DRE findings and/or symptoms of prostate problems. The symptoms included frequent urge to urinate, dribbling of urine, weak urine stream, incomplete bladder emptying, bladder pain, and erectile malfunction. All patients were eligible for all stages of the procedures, including anesthesia and transrectal ultrasound study. Those with previous prostate biopsy or prostatectomy as well as a history of 5-alpha-reductase inhibitors use within 4 months before the procedure, a recent history of prostatitis, and evidence of urinary tract infection were excluded.

2.2. Procedures

2.2.1. MP-MRI

All selected subjects underwent MP-MRI using 1.5 Tesla (Siemens Medical System Inc., Erlangen, Germany). The imaging protocol was adapted from European Society of Uro-Radiology guidelines that

include T1-weighted, T2-weighted, Diffusion-Weighted (DWI), Dynamic Contrast-Enhanced (DCE) perfusion, and Magnetic Resonance Spectroscopic (MRS) images [11]. All MRI studies were reported by an expert uro-radiologist. Both PI-RADS v.1 and v2.1 reporting scales were applied to evaluate radiologic characteristics of the lesion by dividing lesions into PI-RADS 1 (very low suspicion for malignancy), PI-RADS 2 (low suspicion for malignancy), PI-RADS 3 (intermediate suspicion for malignancy), PI-RADS 4 (high suspicion for malignancy), and PI-RADS 5 (very high suspicion for malignancy) [10,12]. Also in MP-MRI reports, the prostate gland was divided into four quadrants, imaging findings of which had been reported separately (Figure 1).

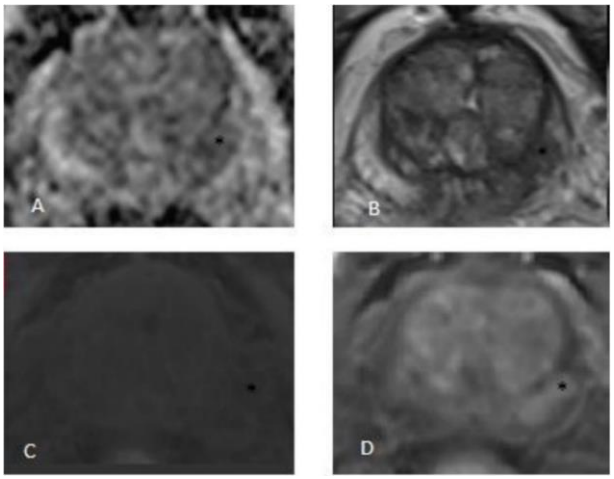

Figure 1. PI-RADS 4 lesion. Prostate MRI of a 66-year-old patient with Gleason score 7 (4+3). A) ADC, B) axial T2W, C) axial T1W with fat suppression, D) DCE (Dynamic Contrast Enhanced) sequences. Peripheral zone 8*13mm lesion (asterisk) with low T2 signal intensity showing contrast enhancement and restricted diffusion with low ADC signal

2.2.2. TRUS-Guide Biopsy

The patients were blinded to the findings of the MRI. All included subjects underwent TRUS-guided biopsy. Anticoagulants and antiplatelet agents were obligated to be ceased at least 5 days before the procedure. A single dose of Ciprofloxacin 750 mg 1 hour before the procedure was received by the subjects as the prophylaxis [13]. In addition, the patients were advised to use laxatives so as not to accumulate faeces in the rectum [14]. Glycerin cleansing enemas as well as opioid analogues were prescribed for some of the participants if had been indicated. A transrectal probe equipped with an 18G calibre needle was utilized for obtaining tissue samples from the peripheral zone of the prostates. During TRUS-guided biopsy, the prostate was divided into four hypothetical parts, the tissue samples of which were placed in a separate container and it was determined which part of the prostate each sample belonged to; 10–12 core biopsies in a sampling frame of approximately 5mm, as well as a biopsy from the reported lesions in the MP-MRI were obtained as per international standards approved by the Korean Society of Urogenital Radiology (KSUR) [15,16].

2.2.3. Histopathologic Assessment

Histopathologic assessments were performed by an expert uropathologist applying the Gleason scoring system [17]; Gleason score (GS)≤6 occurred in grade 1, GS=7 (3+4) occurred in grade 2, GS=7(4+3) occurred in grade 3, GS=8 occurred in grade 4, and GS=9 or GS=10 occurred in grade 5. The control group was defined as participants, the histopathologic assessments of whom show no evidence supporting the diagnosis of malignancy (grade 1), and the control group was defined as patients with GS≥7 (grade 2 and more).

2.3. Statistical Analysis

The data was analyzed employing SPSS v. 26 with a significance level considered less than 0.05. Quantitative data was recorded as numbers and percentages. A general estimating equation logistic regression model was utilized to assess the positive and negative predictive value of MP-MRI against the gold standard (TRUS-guided biopsy). The histopathologic findings were compared with the MP-MRI findings using the Chi-squared test.

3. Results

A total of 66 patients underwent all procedures during the research period. The mean age of the participants was 64.83 ± 10.01 (48-85 years). The mean interval between the MRI examination and the biopsy was 21.3 days. The mean prostate volume, PSA level, and PSA density were 54.57±16.75, 7.29±1.34, and 0.14±0.05, respectively.

Gleason scores of the participants (the case and control groups) are depicted in Figure 2. As shown in

this figure, grade 1 had the highest contribution (55%, 33 patients).

As depicted in Table 1, based on PI-RADS v.1&2.1, 42 patients (63.6%) were grouped as PI-RADS 2 (low suspicious and higher). Findings of the aforementioned subjects, about the involved quadrant, are depicted in Table 2. A significant correlation (p-value<0.001) was revealed between the involved locations detected in MP-MRI and TRUS-guided biopsy (histopathologic).

Histopathologic assessment of these 42 subjects showed that in 34 patients (81%), the lesion locates in the peripheral zone and in 8 patients (19%) in the transitional zone. Investigation and comparison of MP-MRI and TRUS-guided biopsy findings in the case and control group determined that the sensitivity, specificity, and positive and negative predictive value of MP-MRI were 81.8%, 93.9%, 93.1%, and 83.8%, respectively. Mean prostate volume in the case and control group were 66.5±14.6 and 42.5±75, respectively. In addition, the mean PSA levels in these groups were 7.8±1.2 and 6.8±1.1, respectively, and the mean PSA densities were 0.19±0.4 and 0.10±0.02. A significant difference was noticed in mean prostate volume, PSA level, and PSA density between the case and control groups; however, no significant difference was noted in the age range between the groups.

MP-MRI findings of the case and the control group classified using both PI-RADS v.1&2 are illustrated in Figures 3 and 4, respectively.

A significant correlation (p<0.001) was detected between Gleason scores and PI-RADS classification of the participants in the case group which is depicted in Tables 3 and 4. Moreover, significant compatibility was shown between the findings of PI-RADS v.1 and PI-RADS v2 classification (Table 5).

Table 1. MP-MRI assessment of subjects regarding the PI-RADS scoring system

PIRADS/lesion category	Very Low	Low	Intermediate	High	Very high
PI-RADS v.1	24 (36.4%)	8 (12.1%)	7 (10.6%)	20 (30.3%)	7 (10.6%)
PI-RADS v2.1	24 (36.4%)	8 (12.1%)	5 (7.6%)	22 (33.3%)	7 (10.6%)

Table 2. Involved quadrant in MP-MRI and histopathology

		Location reported in MP-MRI				Total
		Right Upper	Right Lower	Left Upper	Left Lower	
Location reported in the histopathologic study	Right Upper	10	0	0	0	10
	Right Lower	0	9	1	0	10
	Left Upper	0	0	11	1	12
	Left Lower	0	0	0	10	10
Total		10	9	12	11	42

Table 3. Subjects' characteristics regarding Gleason score and PI-RADS v.1 classification

		PI-RADS v.1					Total
		Very Low	Low	Intermediate	High	Very High	
Gleason score	Benign	23	7	1	2	0	33
	Grade 2	0	0	2	4	2	8
	Grade 3	1	1	4	3	2	11
	Grade 4	0	0	0	6	1	7
	Grade 5	0	0	0	5	2	7
Total		24	8	7	20	7	66

Table 4. Subjects' characteristics regarding Gleason score and PI-RADS v2.1 classification

		PI-RADS v2.1					Total
		Very Low	Low	Intermediate	High	Very High	
Gleason score	Benign	23	7	1	2	0	33
	Grade 2	0	0	2	4	2	8
	Grade 3	1	1	2	5	2	11
	Grade 4	0	0	0	6	1	7
	Grade 5	0	0	0	5	2	7
Total		24	8	5	22	7	66

Table 5. Subjects' characteristics regarding Gleason score and PI-RADS v2.1 classification

		PI-RADS v.1					Total
		Very Low	Low	Intermediate	High	Very High	
PI-RADS v2.1	Very Low	24	0	0	0	0	24
	Low	0	8	0	0	0	8
	Intermediate	0	0	5	0	0	5
	High	0	0	2	20	0	22
	Very High	0	0	0	0	7	7
Total		24	8	7	20	7	66

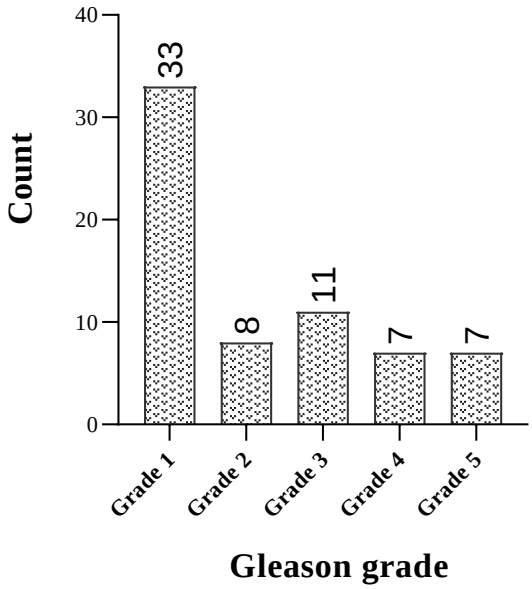

Figure 2. Gleason scores of the participants. Thirty-three patients showed Gleason score ≥7 and the rest were grade 1 which were very low suspicious for malignancy

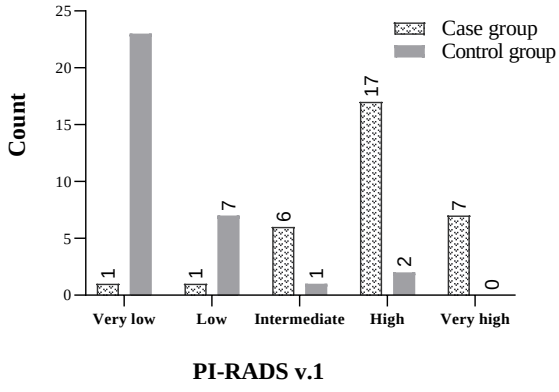

Figure 3. PI-RADS v.1 categorization in the case and the control group

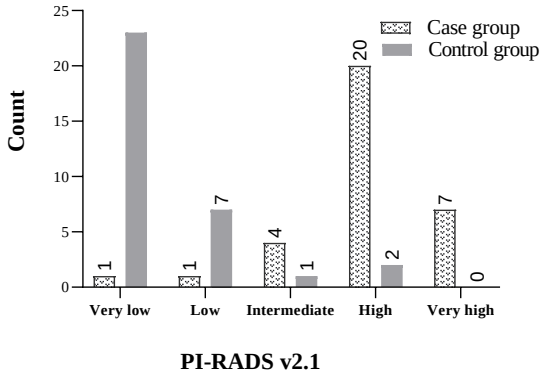

Figure 4. PI-RADS v2.1 categorization in the case and the control group

4. Discussion

An abundance of studies about this title had been conducted with a retrospective design which can be counted as a prevalent limitation in these sorts of studies [18,19]. Our study, prospectively examined the value of the MP-MRI to detect involved areas in prostate cancer and we have tried to investigate the sensitivity and specificity of MP-MRI imaging in comparison with TRUS-guided biopsy of the prostate gland. The participants initially underwent MP-MRI and then underwent TRUS-guided biopsy and were divided into two groups based on the histopathologic findings (prostate cancer or not). Imaging findings were interpreted based on PI-RADS v.1 and PI-RADS v2 classifications.

In a study conducted by Klotz *et al.*, 1040 subjects who underwent MP-MRI participated and those with PI-RADS greater than 3 underwent ultrasound-guided transrectal biopsy [7]. About 39.5% of the participants were diagnosed with prostate cancer; the sensitivity and specificity of MP-MRI were 90% and 22%,

respectively, and the negative and positive predictive values of MP-MRI were 77% and 43%. In our study, the sensitivity of the MP-MRI was lower than in the study of Klotz *et al.*, and the specificity and positive and negative predictive values were higher. This discrepancy might be because they performed a histopathologic study on patients with PI-RADS 3 or more; however, we evaluated all subjects. Another potential assumption is the dissimilarity in applied equipment. We utilized a 1.5 Tesla MRI scanner, but unfortunately, the details of MR imaging were not mentioned in their method which is of great importance with regard to sensitivity and predictive values. In Johnson *et al.*'s study, 588 proven prostate cancer were assessed; 75% moderate-grade and 12% high-grade. MP-MRI detected 45% of lesions, in 65% of which Gleason score was ≥ 7 (clinically valuable) and almost 80% of them were high-grade tumors. Overall, the MP-MRI has detected less than 50% of all tumors; nevertheless, 75% of solitary tumors, as well as 31% of multifocal tumors were not detected [20]; on the other hand, in our study, only 6% of the cases (n=2) with Gleason score ≥ 7 were not diagnosed by MP-MRI and almost 80% of all tumors were diagnosed. This noticeable difference can be related to the sample characteristics difference where in our study mean PSA values were 7.29 (vs. 6.0 in Johnson *et al.*'s study). Additionally, mean prostate volume differed (54.57 vs. 37.00). This revealed the potential effect of other factors such as prostate size and PSA level in the sensitivity of MP-MRI in diagnosing cancer, confirmation of which needs further focused studies. A study by Wysock *et al.* included 75 subjects, MP-MRI studies of whom were negative before the prostate biopsy [21]. In their research, the negative predictive value of MP-MRI for all prostate cancers was 82%; and for prostate cancers with a Gleason score greater than or equal to 7, it was 98%. Even though our MR studies were obtained by a 1.5 T MRI, the negative predictive value was 83.8%, which is almost the same as the study by Wysock *et al.* in which a 3 T MRI was utilized. In the meta-analysis conducted by Rooij *et al.* on 7 studies, the sensitivity and specificity of MP-MRI in the diagnosis of prostate cancer were 88% and 74%, respectively [22]. Furthermore, the negative predictive value varied from 65% to 94%, as our results were along the same line.

There were several limitations in our study; this study was a single-center study and selection bias was inevitable. We were supposed to take 10 to 12 biopsies and this might have led to missing potential foci of prostate cancer out of the sampling frame, especially in cases with a prostate volume of greater than 80cc. Despite following the approved protocols, the aforementioned limitation was inexorable. Also to ensure the exact pathological location of prostate cancer, multiple articles in the literature recommend Template Prostate Mapping (TPM) biopsy as a more valuable method than TRUS-guided biopsy, and it can accurately correlate the location of the lesion reported in MP-MRI [23,24]. Hence, it is recommended that for a more precise examination of the value of MP-MRI in the diagnosis of prostate cancer, patients who are candidates for TPM-biopsy should be enrolled and the correlation of the findings with the locations reported in the MP-MRI should be investigated. The cost-effectiveness of performing an MP-MRI study prior to TRUS-guided biopsy is still challenging and needs consideration of multiple factors, albeit studies such as ours, revealed high diagnostic accuracy of this modality in detecting probable foci of prostate cancer.

5. Conclusion

In the current study, we assessed the efficacy of MP-MRI in the detection of prostate cancer locations based on TRUS-guided biopsy findings. According to the MP-MRI results (significant sensitivity and specificity), this method can potentially be employed as a clue-providing method before the TRUS-guided prostate biopsy.

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