Original Article

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Correlation of Multiparametric Prostate MRI with Prostate Biopsy and Radical Prostatectomy Histopathology

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Abstract

Objective: Prostate cancer (PCa) is the most common cancer responsible for cancer deaths in men after lung cancer. In this study, we aimed to obtain information about the Gleason score of PCa by prostate image reporting and data system (PIRADS) scoring of multiparametric magnetic resonance imaging (mpMRI) by comparing mpMRI results with the histopathology of prostate biopsy and radical prostatectomy specimen.

Materials and Methods: A total of 214 patients who applied to the outpatient clinic of Hatay Mustafa Kemal University Faculty of Medicine, Department of Urology between January 2019 and April 2021 with elevated prostate-specific antigen (PSA) levels were included in the study. All patients underwent mpMRI before the biopsy procedure. PIRADS scoring was performed by the same radiologist. Prostate biopsy was systematically performed by experienced urologists as 12 quadrant biopsies.

Results: When the mpMRI results of the patients are evaluated; the most common patterns are seen as PIRADS 2 and PIRADS 4, followed by PIRADS 3 lesions, followed by PIRADS 5 lesions, and PIRADS 1 lesions, which were the least frequent. When the analysis was applied to predict PCa over the pyrans value, the receiver operating characteristics analysis result for the diagnosis of the disease showed statistically significant levels of area under the curve (0.860; p<0.001), with a sensitivity of 81% and a sensitivity of 3 and above PIRADS 3 and above. It can predict cancer with 75 specificity. In the correlation analysis, there was a low but significant correlation between PIRADS and PSA value (r=0.252; p<0.001).

Conclusion: We found that patients presenting with elevated PSA levels and mpMRI had a high power in detecting PCa. We also found a strong relationship between ISUP rating and PIRADS. As a result, it is thought that the pathology of the patients can be predicted using mpMRI.

Keywords: Gleason score, multiparametric magnetic resonance imaging, prostate cancer, radical prostatectomy

Introduction

Each year, approximately one million men worldwide are diagnosed with prostate cancer (PCa), resulting in approximately 300,000 deaths; PCa ranks as the second leading cause of cancer-related mortality among men, following lung cancer (1). The introduction of the prostate-specific antigen (PSA) test in the 1990s provided an easy and cost-effective means of detecting PCa at an earlier stage (2). Systematic biopsy guided by transrectal ultrasound (TRUS) is the next conventional step in the diagnostic process (3).

PSA has been used as a screening test for PCa because of its high sensitivity, yet it frequently faces criticism for its low specificity (4). The common use of PSA leads to the diagnosis of clinically insignificant PCas and subsequent overtreatment. Currently, PCa diagnosis relies on PSA measurement, and digital rectal examination (DRE) is employed as a screening method. PSA levels can also increase in cases of benign prostate hyperplasia and prostate infections. Screening based on serum PSA levels reduces disease-specific mortality. However, this benefit of PSA has led to a 70-80% rising in prostate biopsies performed (5). Multiparametric magnetic resonance imaging (mpMRI) of the prostate has been shown to be necessary for the diagnosis, treatment, and monitoring of localized PCa with strong evidence (6). MRI has been demonstrated to improve the detection of clinically significant cancer while reducing the identification of

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clinically insignificant cancer (7). Additionally, it is employed to illustrate extracapsular extension in patients diagnosed with PCa via biopsy. The use of mpMRI is beneficial in cases where the biopsy is negative but the PSA level remains consistently high, helping to identify the primary tumor and its exact location. Another indication is to investigate local recurrence in patients who have undergone radical prostatectomy with persistent elevation of PSA (8). The application of mpMRI for PCa has been revolutionary in the diagnosis and staging of PCa (8). MRI is the most efficient method for the detection, localization, and assessment of local invasion of PCa. mpMRI, which combines anatomical and functional sequences, is used for prostate MRI evaluation. Anatomical sequences include T1-weighted and T2-weighted (T1W and T2W) sequences, whereas functional sequences include diffusion-weighted imaging (DWI) and dynamic contrast-enhanced imaging (DCE). In the evaluation of mpMRI, the adoption of a shared language between clinicians and radiologists, the establishment of standardized reporting criteria, and the categorization of the likelihood of clinically significant cancer have contributed to the development of the prostate maging reporting and data system (PIRADS) framework (9).

PSA density (PSAD), while maintaining sensitivity, holds promise in augmenting the diagnostic utility of serum PSA alone by improving specificity. Nevertheless, its adoption in clinical practice remains limited. New multivariate risk prediction tools incorporating the mpMRI suspicion score and PSAD have been developed. The increased use of PSAD and mpMRI has resulted in enhanced localization, risk stratification, and diagnosis of PCa (4). In our study, we also examined the role and significance of PSAD along with mpMRI in the diagnosis and treatment of PCa. Clinically significant PCa defines PCa lesions that could threaten a patient's life or significantly impact their quality of life, indicating the identification of aggressive cancers requiring treatment. It is determined by factors such as tumor size and grade, PSA levels, imaging findings, and clinical characteristics.

Materials and Methods

Our article was retrospectively planned and certified by the Clinical Research Ethics Committee of Hatay Mustafa Kemal University with decision number 01 dated November 1, 2021. As the patients included in the study were retrospectively evaluated, no financial support was received. A total of 214 patients with elevated PSA levels in a University hospital Urology clinic between January 2019 and April 2021 were included in the study. mpMRI was performed on all patients before the biopsy procedure. PIRADS scoring was conducted by the same radiologist. Prostate biopsy was systematically performed by experienced urologists in 12 core biopsy quadrants. Before the biopsy, all patients received antibiotic prophylaxis with ciprofloxacin 500 mg 2x1 (1 day) and gentamicin 160 mg 1x1 (1 day). In addition, all patients were administered a rectal lavage the night before the procedure and in the morning, and the biopsy was performed with the TRUS-guided probe after prostate examination. Prostatic nerve block with lidocaine was administered for local anesthesia. Subsequently, 12-core prostate biopsy was performed, including both lateral and far lateral base and middle, and medial and lateral at the apex. All procedures were completed using standard grayscale ultrasonography and a 7.5-MHz frequency rectal probe, with an 18 Gauge 30 cm biopsy needle and an automatic biopsy gun. Patients were labeled with different numbers and sent for pathological examination. After explaining all possible complications to the patients, they were discharged after a 2-h observation period. Patients were instructed to return for the evaluation of possible biopsy complications in the 1st and 4th weeks following the biopsy.

All patients were T2-weighted with 3-Tesla MRI, dynamic contrast- and diffusion-weighted

The combined three sequences including images were examined.

The mpMRI results of the patients were evaluated by experienced radiologists in accordance with the literature using the PIRADS scoring system (PIRADS 1: Very low-clinically significant cancer is unlikely; PIRADS 2: Low-low likelihood of clinically significant cancer; PIRADS 3: Moderate-uncertain presence of clinically significant cancer; PIRADS 4: High-likely presence of clinically significant cancer; PIRADS 5: Very high-high likelihood of clinically significant cancer).

Before the biopsy procedure, DRE, serum PSA values, mpMRI results, hematological parameters including serum urea, creatinine, neutrophil, lymphocyte, white blood cell, and platelet values, racial distribution of patients (local population and immigrant population), histopathological examination results of biopsy materials, and ISUP grading results were recorded to obtain data.

Statistical Analysis

Data were analyzed using SPSS version 25.0 for Mac (SPSS Inc., Chicago, IL, USA). The Shapiro-Wilk test was used to determine the normal distribution. When values were not normally distributed, continuous values were presented as the median. Categorical variables are expressed as numbers and percentages. The Mann-Whitney U test was employed to compare values between the two groups, while the chi-square test was used for comparing categorical variables. Receiver operating characteristics (ROC) analysis was performed for effective factors in PCa. P-values less than 0.05 were deemed statistically significant.

Results

The patients had a median age of 66.00 years (61.00-71.00%). Comorbidities were present in 33% patients. The median prostate volume measured by TRUS of the patients was 55 milliliters (44.00-83.00). The median serum PSA and free PSA values of the patients were 7.37 nanograms (5.17-13.70) and 1.64 (1.10-2.98), respectively. When evaluating the mpMRI results of the patients, the most common patterns observed were PIRADS scores 2 and PIRADS scores 4. On histopathological examination, benign pathology constituted 64.5% of our biopsies. Adenocarcinoma Gleason 6 and Gleason 7 patterns followed this pattern.

When the analysis was carried out to predict PCa based on the PIRADS score, it was examined through ROC analysis for disease

diagnosis. The area under the curve (AUC) value for the PIRADS score parameters was found to be significant (AUC 0.860; p<0.001) (Figure 1) (Table 1). In addition, at PIRADS score 3 and above, mpMRI can predict cancer with a sensitivity of 81% and specificity of 75% (Table 2).

When the analysis was applied for the prediction of PCa through the PIRADS value, it was examined by ROC analysis for disease diagnosis (AUC 0.860: p<0.001) of the PIRADS parameters for disease diagnosis was significant (AUC 0.860; p<0.001) (Table 3).

When the correlation between PIRADS and PSA, free PSA, body mass index (BMI), neutrophil-lymphocyte ratio, platelet-to-lymphocyte ratio, and SII values was examined, the correlation analysis results indicated a significant but low correlation between PIRADS and PSA value (r=0.252; p<0.001). Additionally, a significant correlation was observed between free PSA and BMI (r=0.2; p<0.001) as well as free PSA and BMI (r=0.265; p<0.001) (Table 4).

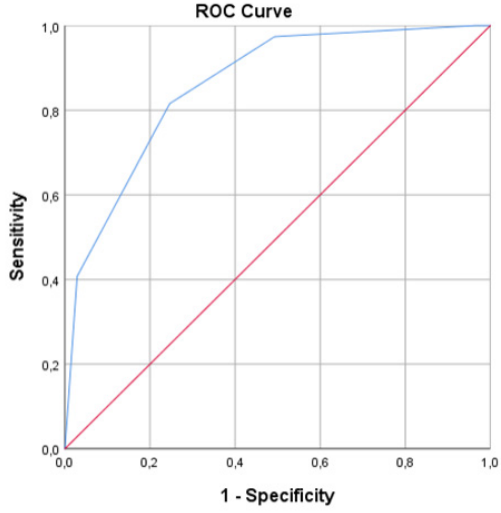

Figure 1. ROC curve for predicting disease with the PIRADS value

ROC: Receiver operating characteristics, PIRADS: Prostate image reporting and data system

Table 1. General demographic data and pathological results of patients		
		Value (Percentage)
Age (Median) (min-max)		66.00 (61-71)
BMI (Median) (min-max)		25.00 (24-26)
Rectal examination findings	**Grade 1**	140 (65%)
	Grade-2	74 (35%)
	Grade-3	0 (0.0)
Komorbid disease	**No**	143 (67%)
	Yes	71 (33%)
Prostate volume		55.00 (44-83%)
Multiparametric MRI	**PIRADS 1**	5 (2%)
	PIRADS 2	67 (31%)
	PIRADS 3	46 (21%)
	PIRADS 4	61 (28%)
	PIRADS 5	35 (16%)
PSA		7.37 (5-13%)
Free PSA		1.64 (1-3%)
Pathology result	**Benign**	138 (64%)
	G6 (3+3)	22 (10%)
	G7 (3+4)	18 (8%)
	G7 (4+3)	15 (7%)
	G8 (4+4)	4 (2%)
	G9 (4+5)	6 (3%)
	G9 (5+4)	3 (1%)
	G10 (5+5)	8 (4%)
ISUP grade	**1.00**	22 (29%)
	2.00	18 (24%)
	3.00	15 (20%)
	4.00	4 (5%)
	5.00	17 (22%)

PIRADS: Prostate image reporting and data system, BMI: Body mass index, MRI: Magnetic resonance imaging, PSA: Prostate-specific antigen, ISUP: International Society of Urological Pathology, min-max: Minimum-maximum

Table 2. ROC analyses' result for predicting prostate cancer with PIRADS classification						
Test result variable(s)	**AUC**	**Std. error[a]**		**Asymptotic sig.[b]**	**Asymptotic 95% CI (lower bound)**	**Asymptotic 95% CI (upper bound)**
PIRADS	0.860	0.025		0.001	0.811	0.910

The test result variable(s): PIRADS has at least one tie between the positive and negative actual state groups. Statistics may be biased. ROC: Receiver operating characteristics, PIRADS: Prostate image reporting and data system, [a]Under the non-parametric assumption, [b]Null hypothesis: true area =0.5
AUC: Area under the curve, CI: Confidence interval

Table 3. PIRADS ROC analyses results						
Test result variable(s)	**Cut-off**	**AUC (%95 CI)**	**Std. error**	**Sensitivity**	**Specificity**	**p-value**
PIRADS	>3.50	0.860 (0.811- 0.910)	0.025	0.816	0.754	<0.001

AUC: Area under the curve, CI: Confidence interval, PIRADS: Prostate image reporting and data system

Table 4. Correlaton analysis results of factors influencing prostate cancer

		PIRADS	WBC	Neutrophil	Lymphocyte	Platelet	Urea	Creatinine	PSA	Free PSA	BMI	NLR	PLR	f/tPSA
Prostate volum	r	-0.198	0.119	0.168	-0.014	0.165	0.115	0.025	0.169	0.274	-0.031	0.179	0.161	0.184
	p	0.004	0.086	0.015	0.840	0.016	0.098	0.721	0.014	0.000	0.656	0.009	0.020	0.014
PIRADS	r	1.000	0.051	0.034	-0.010	0.042	0.107	0.121	0.252	0.281	0.265	-0.008	0.033	-0.170
	p		0.465	0.620	0.883	0.540	0.125	0.079	**<0.001**	**<0.001**	**<0.001**	0.914	0.632	0.023
WBC	r		1.000	0.888	0.418	0.384	0.093	0.062	0.108	0.111	0.005	0.405	-0.077	0.005
	p			0.000	0.000	0.000	0.182	0.376	0.124	0.141	0.944	0.000	0.267	0.942
Neutrophil	r			1.000	0.069	0.328	0.090	0.082	0.143	0.198	0.020	0.724	0.176	0.068
	p				0.322	0.000	0.195	0.237	0.041	0.008	0.773	0.000	0.010	0.367
Lenfosit	r				1.000	0.184	-0.051	-0.063	0.006	-0.091	0.029	-0.569	-0.712	0.007
	p					0.008	0.463	0.368	0.930	0.230	0.678	0.000	0.000	0.928
Platelet	r					1.000	-0.060	-0.055	0.207	0.079	0.099	0.166	0.478	-0.240
	p						0.393	0.432	0.003	0.295	0.152	0.016	0.000	0.001
Urea	r						1.000	0.423	0.123	0.263	-0.014	0.097	0.021	0.061
	p							0.000	0.080	0.000	0.837	0.164	0.760	0.419
Creatinine	r							1.000	0.163	0.256	0.044	0.131	0.035	0.076
	p								0.019	0.001	0.524	0.059	0.611	0.319
PSA	r								1.000	0.792	0.207	0.106	0.151	-0.376
	p									0.000	0.003	0.130	0.031	0.000
Free PSA	r									1.000	0.128	0.195	0.163	0.159
	p										0.088	0.010	0.031	0.034
BMI	r										1.000	-0.009	0.013	-0.088
	p											0.893	0.847	0.242
NLR	r											1.000	0.624	0.053
	p												0.000	0.487
PLR	r												1.000	-0.153
	p													0.043
	p													0.407
f/tPSA	r													1.000
	p													

PIRADS: Prostate image reporting and data system, WBC: White blood cell, PSA: Prostate-specific antigen, BMI: Body mass index, NLR: Neutrophil-lymphocyte ratio, PLR: Platelet-to-lymphocyte ratio, free/total prostate-specific antigen, f/tPSA: Free/total prostate-specific antigen

Discussion

According to the 2024 cancer statistics, PCa remains the most prevalent type of cancer among men (10). Until now, the diagnostic pathway for detecting PCa has been initiated using PSA levels and DRE. In our study, we examined the role of mpMRI, which is a recent diagnostic method, in the diagnosis of PCa. mpMRI, along with PSAD, has a high diagnostic yield in the diagnosis of PCa.

Because of the low specificity of PSA in tissue, many unnecessary biopsies are conducted on patients. The current European Association of Urology guidelines recommend prostate biopsy for patients with a PIRADS score ≥3. An illustrative example is the PROMIS prostate MRI study, which demonstrated a sensitivity of approximately 93% in detecting clinically significant PCa (csPCa) (11). However, recent multicenter studies have demonstrated a notable degree of variation: the positive predictive value (PPV) of a PIRADS score of ≥3 for detecting clinically csPCa ranged from 27% to 48% across 26 centers (12).

According to Panebianco et al. (13), PCa was found in 38% of patients who underwent TRUS-guided biopsy. Of the 355 patients who had a negative TRUS-guided biopsy, post-biopsy mpMRI revealed a suspect focus in 208 patients, with 186 of them testing positive in the biopsy (equivalent to 52% of patients following the initial negative biopsy). In the imaging arm, 440 of 570 patients exhibited a positive MRI result, with 417 of them testing positive in the biopsy. In another investigation, the cancer detection rate was reported as 54% in the systematic biopsy group and 63% in the MRI group (14). Additionally, a meta-analysis including 14 studies and 698 patients found an average cancer detection rate of 37.5% after a negative biopsy (range 19.2-68.3). The combined sensitivity and specificity

were calculated as 57% and 90%, respectively. The PPV of mpMRI varied between 17 and 92 in these studies. However, in the majority of these studies, biopsies were conducted after cognitive evaluation following mp-MRI. The lack of standardization is a significant limitation of these studies (15). Likewise, Hoeks et al. (16) documented a 25% cancer invention rate (108 out of 438) among patients with a history of at least one negative biopsy for high PSA who underwent biopsy with mpMRI and MR guidance, with 87% of these cancers deemed clinically significant.

Recently, Le et al. (17) examined 122 men who underwent pre-radical prostatectomy mpMRI and found that mpMRI detected 80% of index tumors, demonstrating its high accuracy in identifying high-grade (Gleason score >6) and large-volume (diameter >1 cm) tumors. Likewise, Petrillo et al. (18) illustrated that the combined score derived from morphological T2-MRI, DWI, and MRSI achieved the highest sensitivity (0.84) and negative predictive value (0.93) in the detection of PCa. It also demonstrated a significant correlation with the Gleason score and exhibited a statistically distinct median value between significant and insignificant Gleason scores (18). Baco et al. (19) demonstrated that 95% of the index lesions identified on mpMRI were concordant with histopathology from 135 radical prostatectomy specimens. Rud et al. (20) assessed 199 men who underwent prostatectomy and found that mpMRI detected the index tumor in 92% of patients.

Weinreb et al. (21) demonstrated that mpMRI tends to underestimate both tumor volume and tumor size in comparison with histology. The ideal imaging plane and wave sequences for accurately measuring lesion size in MR-guided assessments have not been definitively established, necessitating further research to comprehend the significance of variations in lesion size across different wave sequences (21).

One of the biggest criticisms of mpMRI in the literature is its high negative predictive value for clinically significant cancer (22). Given that biopsies are avoided in men with a negative mpMRI result, it fails to capture the accurate cancer detection rate of clinically significant cancers (23). Therefore, the percentage of patients with undetectable cancers with MRG remains uncertain.

Similarly, in our study, cancer was identified in 36.5% of patients with a PIRADS 3 lesion and above. Our study also demonstrated that the PIRADS parameters are statistically significantly associated with the detection of cancer (AUC 0.860; $p<0.001$), and mpMRI can identify cancer with 81% sensitivity and 75% specificity.

Study Limitations

One of the major limitations of this study is its retrospective design. The relatively lower number of patients compared with other studies is also a limitation. Although the MRG interpretation was performed by a single radiology expert, the MRG device has changed over the years, which is a disadvantage. However, biopsies were performed by different doctors because they were in a training clinic, and the records were reviewed.

Conclusion

Our study showed that the combination of PSA elevation and mpMRI demonstrated high diagnostic efficacy in detecting PCa, and when combined with PSAD, its predictive value increased. In addition, we found a strong relationship between ISUP grading and PIRADS and a significant correlation between PSAD and PIRADS. In conclusion, we believe that mpMRI, along with PSAD, can predict clinically significant cancer in patients, and this correlation will be.

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Ethics

Ethics Committee Approval: Our article certified by the Clinical Research Ethics Committee of Hatay Mustafa Kemal University with decision number 01 dated November 1, 2021.

Informed Consent: Retrospective study.

Authorship Contributions

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