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Araştırma Makalesi–Research Paper

IS UPGRADE IN GLEASON SCORE AFTER RADICAL PROSTATECTOMY PREDICTABLE WITH PREOPERATIVE MULTIPARAMETRIC PROSTATE MRI?: COMPARISON OF ADC, K-TRANS, TUMOR SIZE AND PI-RADS SCORE

RADİKAL PROSTATEKTOMİ SONRASI GLEASON SKOR ARTIŞI PREOPERATİF MULTİPARAMETRİK PROSTAT MRG ILE ÖNGÖRÜLEBİLİR Mİ?: ADC, K-TRANS, TÜMÖR BOYUTU, PI-RADS SKORUNUN KARŞILAŞTIRILMASI

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Özet

Bu çalışmada, MRG parametreleri ile radikal prostatektomi sonrası Gleason skor artışı arasındaki ilişki araştırılmıştır. Kasım 2017–Temmuz 2020 tarihleri arasında prostat kanseri şüphesi ile multiparametrik MRG yapılan olgulardan, TRUS eşliğinde sistematik ve kognitif füzyon biyopsi ve sonrasında radikal prostatektomi yapılan 112 çalışma kapsamına alındı. Hastalar, cerrahi sonrası Gleason skor artış olanlar ve olmayanlar şeklinde iki grupta incelendi. Bu iki grup; ADC, k-trans, tümör boyutu ve PI-RADS skoru açısından karşılaştırıldı. Radyolojik değerlendirme, klinik bilgiden yoksun iki radyolog tarafından PI-RADS versiyon 2.1 kullanılarak konsensüs ile yapıldı. ADC ve k-trans değerleri MR iş istasyonunda ölçülüp kaydedildi. Patolojik değerlendirmede ISUP skorlama sistemi kullanıldı. Çalışmayı oluşturan 112 olgunun 51'inde RP sonrası Gleason skor artışı saptandı. Bu olguların yalnızca 2'si PI-RADS1 idi. Gleason skor artış oranı PI-RADS skor < 4 için %15,6; skor ≥4 için ise %84,3 olarak bulundu. En sık skor artışı ISUP 1'den, ISUP 2'ye görüldü. Skor artışı görülen ve görülmeyen grubun karşılaştırılmasında, PSA, PSAd tümör boyutu, k-trans ve ADC değerleri açısından anlamlı fark görülmedi. PI-RADS skoru ≥4 olan olgularda veya mpMRG'de transizyonel zon tutulumunda Gleason skor artışı anlamlı derecede yüksekti ($p<0,05$). mpMRG, radikal prostatektomi sonrası Gleason skor artışını öngörmede etkin bir yöntemdir. Bu amaçla PI-RADS skoru ≥ 4 veya transizyonel zon tutulumu bağımsız bir öngörü değerine sahiptir.

Anahtar Kelimeler: Multiparametrik MRG, PI-RADS, Gleason, Prostat Kanseri, Prostat Biyopsi

Abstract

In this study, the relationship between MRI parameters and upgrade in Gleason score after radical prostatectomy was investigated. Between November 2017 and July 2020, 112 patients who underwent multiparametric MRI with suspected prostate cancer, TRUS systematic and cognitive fusion biopsy and subsequent radical prostatectomy were involved this study. The patients were evaluated in two groups as those with and without the Gleason score upgrade after surgery. These two groups was compared in terms of ADC, k-trans, tumor size and PI-RADS score. Radiological evaluation was consensus using PI-RADS version 2.1 by two radiologists who lacked clinical knowledge. ADC and k-trans were measured in the MR workstation. ISUP scoring system was used in pathological evaluation. Upgrade in Gleason score was found in 51/112 of the cases. Only 2/51 cases were PI-RADS score 1. Upgrade rate of Gleason score were 15,6% for PI-RADS score <4; and 84,3% for score ≥4. The most frequent upgrade was from ISUP 1 to ISUP 2. There was no significant difference in PSA, PSAd tumor size, k-trans and ADC in comparing between two groups. Upgrade was significantly higher in cases with PI-RADS score ≥4 and the transitional zone involvement on MRI ($p<0.05$). mpMRI is an effective method of predicting upgrade in Gleason score after radical prostatectomy. PI-RADS score ≥4 or transitional zone involvement has an independent predictive value.

Keywords: Multiparametric MRI, PI-RADS, Gleason, Prostate Cancer, Prostate Biopsy

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1. INTRODUCTION

The risk stratification of prostate cancer (Pca) includes the Gleason score (GS), serum prostate-specific antigen (PSA) and rectal examination (D'Amico et al.,1998, pp. 1-6). Patient management changes according to risk stratification and different treatment options are performed (Heidenreich et al.,2014, pp. 20).The GS is the most critical parameter in risk stratification, as it is determined by biopsy. However, random prostate biopsy results in deficiencies in the sampling. There may be a mismatch between the radical prostatectomy (RP) GS and the transrectal ultrasonography-guided (TRUS) biopsy GS. Studies reported that 50% of the patients have an upgrade in the GS after RP (Cohen et al.,2008, pp. 11-13). This mismatch causes high-risk patients with aggressive tumors to undertreatment, while low-risk patients are lacking in referring to active surveillance (Corcoran et al.,2012, pp. 5-8). Therefore, it is important to detect the mismatch between TRUS biopsy GS and post-RP GS preoperatively.

Multiparametric prostate MRI (mpMRI), on the other hand, has found a wide area of use in daily practice in Pca screening. Due to its many advantages such as its high sensitivity in detecting clinically significant cancer and the possibility of targeted biopsy with the fusion biopsy technique (Turkbey et al.,2016, pp. 8). MpMRI contributes to the selection of the right treatment by showing the presence of clinically significant cancer with PI-RADS scoring. There are few studies in the literature emphasizing that PI-RADS score is useful in predicting upgrade in GS.

In this study, the relationship between preoperative mpMRI parameters and an upgrade in GS after RP was investigated.

2. METHODS

2.1. Patient Selection

This retrospective study was approved by Izmir Katip Celebi University clinical research ethics committee (No:918, date: 17.09.2020). Between November 2017 and July 2020, patients who underwent mpMRI with the suspicion of Pca with elevated PSA and/or abnormal rectal examination were evaluated. After MRI, patients who underwent TRUS-guided systematic + cognitive fusion biopsy and subsequent RP were included in the study. Patients who underwent biparametric MRI due to contraindications, non-diagnostic MRI images, more than 6 months between mpMRI and RP, and received different treatments such as hormonotherapy/radiotherapy before mpMRI or RP were excluded. A total of 112 patients were included in the study (Figure 1).

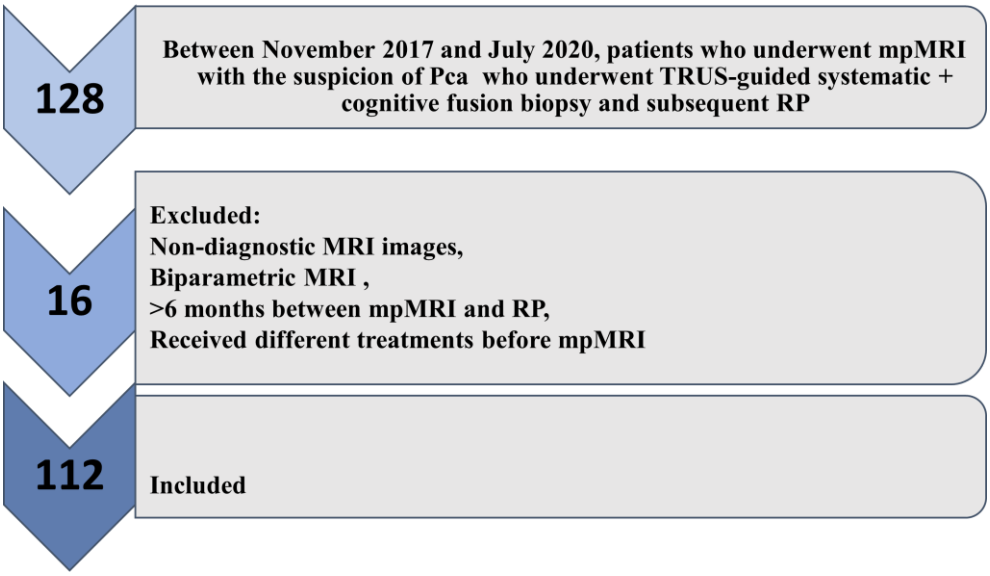

Figure 1: Flow chart of the study.

2.2. MpMRI protocols

MpMRI was performed with an 18-channel pelvic superficial coil and 1.5 T scanner (Magnetom Aera, Siemens Healthineers, Erlangen, Germany). Endorectal coil was not used. The protocol included the following sequences: Turbo spin-echo T2-weighted imaging (T2WI) with axial, sagittal, and coronal orientations (Axial T2WI parameters were as follows: repetition time, 5660 msec; echo time, 99 msec; the field of view, 200×180 mm; acquisition matrix, 320×288; slice thickness, 3 mm with no gap), a diffusion-weighted imaging (DWI) with an axial orientation (repetition time, 4000 msec; echo time, 76 msec; b-values, 0, 200, 600 and 1400 sec/mm2; the field of view, 200×180 mm; acquisition matrix, 100×90; slice thickness, 3 mm with no gap) with apparent diffusion coefficient (ADC) mapping, and dynamic contrast-enhanced (DCE) sequences with an axial orientation (repetition time, 2.48 msec; echo time, 1.52 msec; the field of view, 260×215 mm; acquisition matrix, 160×108; slice thickness 3 mm with 0.3 mm gap; temporal resolution, 7 sec). All parameters were complied with proposal of the PI-RADSv2.1 guideline. Gadobutrol (Gadovist®) was used at a dose of 0.1mL/kg (Table 1).

Table 1: Parameters of mpMRI

Parameters	Axial T2A	DWI*	DCE**
FOV (mm)	200 × 180	200 × 180	260 × 215
Matrix	320 × 288	100 × 90	160 × 108
Slice thickness (mm), gap (mm)	3, 0	3, 0	3, 0.3
TR (msec)	5660	4000	4.07
TE	99	76	1.52
Time (min:s)	6:15	6:40	2:48
NEX	6	18	1

* DWI, diffusion weighted images; b values 0, 200, 400, 800 ve 1400 sn/mm2

**DCE dynamic-conrast enhanced images, temporal resolution 7 sn

2.3. Histopathological Analysis

Systematic TRUS-guided twelve quadrant biopsy was performed as standard in all patients. In the presence of a lesion with a PI-RADS score of 3 or higher in mpMRI, cognitive fusion was performed, 2 cores for each lesion. The histopathological evaluation was based on the pathology reports. Tumors were graded by the genitourinary pathologists as proposed by the International Society of Urological Pathology (ISUP) in 2016(Epstein et al.,2016, pp. 21-25).

A uropathologist was blinded to mpMRI score reported the index lesion location and GS. Index lesion localizations described in RP specimen reports were matched with lesions on MRI.

2.4. MpMRI Analysis and Image Evaluation

mpMRIs were evaluated by two radiologists individually (reader 1 with 4 years of experience in prostate imaging; reader 2 with 3 years of experience in this field). The radiologists were blinded to any clinical or pathological information. The radiologists scored

the lesions two times using PI-RADSv2.1 guideline. After a one-month forgetting period, PI-RADSv2.1 scoring was performed with consensus by two radiologists. Consensus scores were used in statistical analysis. In the presence of multifocal lesions, PI-RADSv2.1 scores of the index lesion were used in statistical analysis.

RP-GS and TRUS-GS were compared. The patients were divided into two groups as those with and without GS upgrade after RP. These two groups were compared in terms of ADC, k-trans, PI-RADS score and tumor size. As recommended by the PI-RADSv2.1 guideline, the size of the transitional zone (TZ) lesions were measured on T2W images, and the sizes of peripheral zone (PZ) lesions were measured on the ADC map. Quantitative ADC measurements were made on the workstation using the Syngo.via (Siemens Healthineers, Erlangen, Germany) software.

Quantitative ADC measurements were made by free-handed ROI (Region Of Interest) in 3 different regions with the highest diffusion restriction, and the average values of these measurements were recorded. Similarly, ADC values were measured and recorded from the normal-appearing peripheral zone. The ratio of lesion ADC / normal ADC was calculated. K-trans measurements were performed at the workstation, from the same lesion and normal parenchyma area. Age, the lastest serum PSA level before mpMRI and PSA density (PSAd) were recorded.

2.5. Statistical Analysis

Statistical analysis was performed using SPSS version 20 (IBM incor., NY, USA). These two groups was compared by T test, in terms of PSA, PSAd, ADC value, lesion ADC/normal ADC ratio, k-trans and tumor size. PI-RADSv2.1 score was compared by chi-square test. $p<0,05$ was accepted as statistically significant.The correlation between the RP ISUP score and the PI-RADSv2.1 score was analyzed by Spearman's test. Those with PI-RADSv2.1 score > 4 and PI-RADSv2.1 score <3, were compared with the Fisher Exact test in terms of upgrade. Similarly, those with and without TZ involvement on mpMRI were compared with the Fisher Exact test in terms of upgrade.

Kappa statistic was used to determine inter-reader agreement. Accordingly, it was classified as follows: 0.01–0.20, slight; 0.21–0.40, fair; 0.41–0.60, moderate; 0.61–0.80, substantial, and 0.81–0.99, almost perfect (Feinstein et al., 1990, pp. 543-549; Lantz et al., 1996, pp.431-434; Shankar et al., 2014, pp. 100-10).

3. RESULTS

The median age of the 112 patients included in the study was 67 years (range: 47–80). The median serum PSA was 7.89 ng/ml (range:1.61–75.66 ng/ml), median PSAd was 0.166

ng/ml/cm3 (range:0.04–2.68 ng/ml/cm3), and median lesion size was 15 mm (range:0–51mm) (Table 2).

Table 2: Demographic, clinical and MRI features of cases and lesions.

Number of cases	112
Number of lesions	98
Age	67±7,1 (47-80)
Serum PSA, ng/ml	7,89±10,4 (1,61-75,66)
PSAd, ng/ml/cm3	0,166±0,03 (0,04-2,68)
Lesion dimension, mm	15±9,4 (0-51)
Lesion localisation on MRI	
Right	29 (%29,6)
Left	36 (%36,7)
Bilateral	33 (%33,7)
PZ	83 (%84,7)
TZ	7 (%7,1)
Both	8 (%8,2)
Whole zones	10 (%12)
Multifocal	37 (%37,8)

MpMRI indicated no lesion in 14 cases. According to mpMRI, the index lesion was located in the PZ in 83 patients, the TZ in 7 patients, and in both PZ and TZ in 8 patients. Multifocal tumor was observed in 37 patients, while tumoral infiltration was seen in the entire gland in 10 patients (Table 2).

The number of patients with PI-RADS v2.1 scores 1–5 was 14, 8, 7, 33, and 50, respectively. TRUS biopsy revealed no tumor in one case, while the number of cases with ISUP scores 1–5 was 60, 29, 14, 6, and 3, respectively. The number of patients with post-RP ISUP scores 1–5 was 29, 37, 30, 10, and 6, respectively. After RP, 51 (45.5%) patients had GS upgrade, while 61 (54.5%) did not. Spearman correlation analysis showed a strong correlation between PI-RADS v2.1 and ISUP scores after RP ($p < 0.001$) (Tables 3 and 4).

Table 3: Comparison of PI-RADSv2.1 and ISUP scores of RP and TRUS-biopsy

Score	PI-RADS	TRUS-biopsy ISUP	RP-ISUP
1	14	60	29
2	8	29	37
3	7	14	30
4	33	6	10
5	50	3	6
Total	112	112	112

Table 4: Comparison of PI-RADSv2.1 and RP ISUP scores

PI-RADS	ISUP 1	ISUP 2	ISUP 3	ISUP 4	ISUP 5	Total
Score 1	12	2	0	0	0	14
Score 2	4	3	1	0	0	8
Score 3	4	2	1	0	0	7
Score 4	6	16	7	3	1	33
Score 5	3	14	21	7	5	50
Total	29	37	30	10	6	112

The 51 patients with GS upgrade after RP had a median age of 68 years (range: 53–79), median serum PSA of 8.64 ng/ml (range: 3.45–75.66 ng/ml), and median PSAd of 0.211 ng/ml/cm3 (range: 0.06–1.06). In these cases, median tumor size was 16 mm (range: 0–51 mm), median ADC was 0.652 μm2/sec (range:0–1.19), and median lesion ADC to normal ADC ratio was 0.495 (range: 0–0.87) (Table 5).

Of the 51 patients with GS upgrade after RP, mpMRI indicated no lesions in only two patients (3.9%). According to mpMRI, the index lesion was located in the PZ in 38 patients, in the TZ in 5 patients, and in both the PZ and TZ in 6 patients. While multifocal tumor was observed in 18 patients on mpMRI, tumoral infiltration was seen in the entire gland in 10 patients (Table 5).

Table 5: Demographic, clinical and MRI characteristics of lesions with Gleason score upgrade

Features of Upgraded Lesions	
Number of cases	51
Number of lesions on MRI	49
Age	68± 6,7 (53-79)
Serum PSA, ng/ml	8,64± 11,3 (3,45-75,66)
PSAd, ng/ml/cm3	0,211±0,22 (0,06-1,06)
Lezyon dimension, mm	16±9,1 (0-51)
ADC, (µm2/sn)	0,652±0,21 (0-1,19)
Lesion ADC/normal ADC	0,495±0,15 (0-0,87)
Lesion localisation on MRI	
Right	18 (%36,7)
Left	16 (%32,6)
Bilateral	15 (%30,6)
PZ	38 (%77,5)
TZ	5 (%10,2)
Both	6 (%12,2)
Whole zones	10 (%20,4)
Multifocal	18 (%36,7)

The number of upgrade cases with PI-RADS v2.1 scores 1–5 was 2, 3, 3, 17, and 26, respectively. The number of cases with TRUS biopsy ISUP score 1–5 was 34, 12, 2, 2, and 0, respectively. The number of patients with post-RP ISUP score 1–5 was 1, 20, 20, 5, and 5, respectively (Table 5–7).

No significant difference was found between patients with GS upgrade after RP and those without in terms of PSA, PSAd, lesion size, ADC, and lesion ADC to normal ADC ratio (p values were 0.422, 0.908, 0.079, 0.057, and 0.077, respectively) (Table 11). There was a significant correlation between PI-RADS v2.1 score ≥4 and GS upgrade (p = 0.031) (Table 8). Score ≥4 had a sensitivity of 84.3%, specificity of 34.4%, positive predictive value of 51.8%, and negative predictive value of 72.4% in predicting the upgrade in GS. There was also a significant difference in GS upgrade with TZ involvement on mpMRI (p = 0.026) (Table 9).

Table 6: Comparison of TRUS Biopsy and RP ISUP results of cases with Gleason score upgrade

Cases	Biopsy ISUP	RP ISUP
1	0	1
20	1	2
12	1	3
2	1	4
8	2	3
1	2	4
3	2	5
2	3	4
2	4	5

Table 7: Comparison of PI-RADS scores of patients with Gleason score upgrade and ISUP results after RP.

ISUP	PI-RADS1	PI-RADS2	PI-RADS3	PI-RADS4	PI-RADS5	Total
Score 1	0	0	0	0	1	1
Score 2	2	2	2	9	5	20
Score 3	0	1	1	5	13	20
Score 4	0	0	0	2	3	5
Score 5	0	0	0	1	4	5
Total	2	3	3	17	26	51

Table 8: Comparison of PSA, PSAd, tumor size, and ADC results of subjects with and without Gleason Score upgrade

Variable	Upgrade + *(mean)*	Upgrade - *(mean)*	Upgrade + *(median)*	Upgrade - *(median)*	*p value*
PSA, ng/ml	11,6 ±11,3	10 ±9,6	8,64 ±11,3	7,89 ±10,4	0,422
PSAd, ng/ml/cm^3	0,27 ±0,22	0,26 ±0,38	0,211 ±0,22	0,166 ±0,03	0,908
Tumor size, mm	16 ±9,1	13 ±9,6	16 ±9,1	15 ±9,4	0,079
ADC, µm2/sn	0,66 ±0,21	0,55 ±0,30	0,652 ±0,21	0,62 ±0,27	0,057
Lesion/normal ADC	0,50 ±0,15	0,42 ±0,23	0,495±0,15	0,50±0,23	0,077

Table 9: Distribution of Cases with and without Gleason score increase according to PI-RADS score 4

PI-RADS	Upgrade +	Upgrade -	Total
Score<4	8	21	29
Score≥4	43	40	83
Total	51	61	112

Perfusion parameters were evaluated in only 78 patients due to technical reasons. In patients without GS upgrade after RP, median values of k-trans, measured from the lesions was 0.11 (range: 0.004–0.297), and from the normal PZ were 0.06 (range: 0.003–0.178), On the other hand, for patients with GS upgrade after RP, the median values of k-trans was 0.11 (range: 0.004–0.377), and from the normal PZ were 0.66 (range: 0.001–0.550) When patients with and without GS upgrade were compared, no statistically significant difference was found in terms of k-trans (p=0.765).

Inter-reader agreement was “good” and the Kappa value was 0.678 (Figure 2-3).

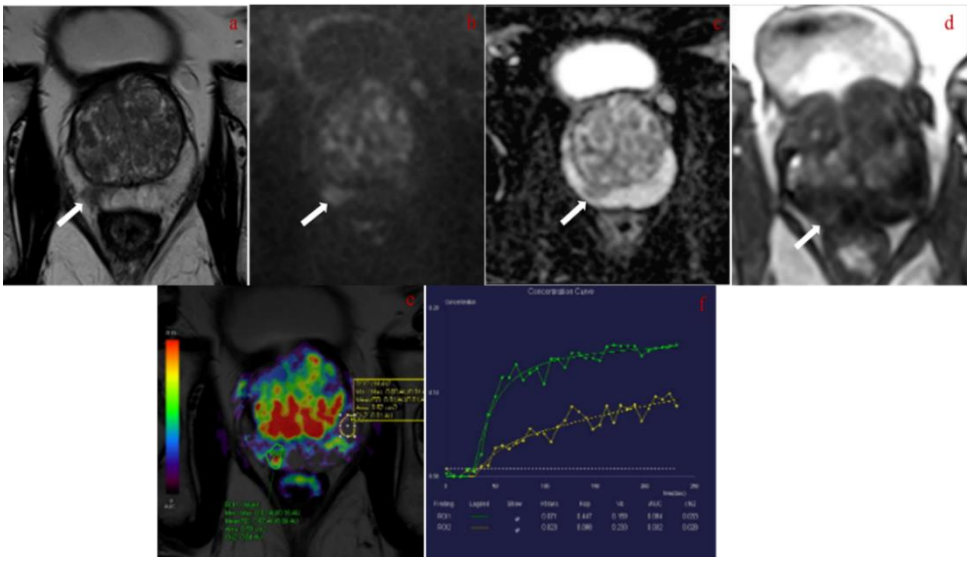

Figure 2: mpMRI images of a 72-year-old patient with PSA 8.55ng/ml and PSAd 0.09ng/ml/cm3; From a to d, axial T2W, DWI, ADC, DMI, and from e to f, perfusion maps measured from lesion and normal tissue. Reader 1, reader 2, and consensus PI-RADS scores were 4, 4, and 4, respectively (white arrows). TRUS cognitive biopsy result was ISUP 1 in the right mid PZ. RP result was ISUP 2, 5% involvement; ie upgraded.

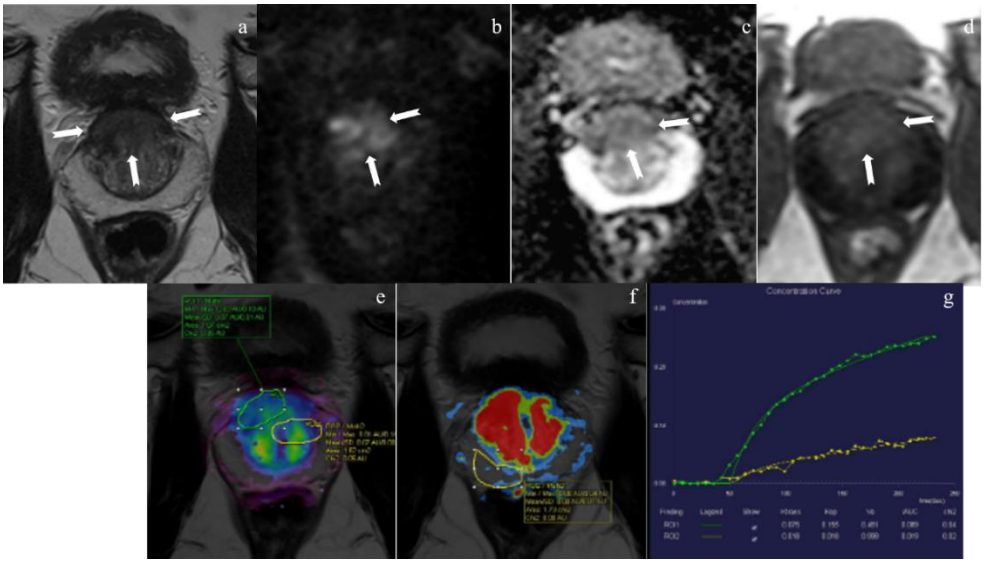

Figure 3: mpMRI images of a 71-year-old patient with PSA 29.81ng/ml and PSAd 0.64 ng/ml/cm3; From a to d, axial T2W, DWI, ADC, DMI, and perfusion maps measured from lesion and normal tissue from e to g, respectively. Reader 1, reader 2, and consensus PI-RADS scores were 5, 5, and 5, respectively (white arrows). TRUS cognitive biopsy result was ISUP 1 in mid anterior TZ. The result of RP was ISUP 3, 45% involvement; Upgrade followed.

4. DISCUSSION

In the present study, GS upgrade was significantly higher in patients with PI-RADS score ≥4 or TZ involvement on mpMRI ($p < 0.05$). GS is one of the most important parameters used to predict the behavior and prognosis of Pca (Epstein et al.,2010, pp. 22-25). Accurate preoperative prediction of GS is critical for safe treatment such as active surveillance(Heidenreich et al.,2014, pp.7-10). Approximately 20–60% of patients with a GS of 6 on TRUS biopsy have an increase in score after RP(Cohen et al.,2008, pp.10-13; Boorjian et al.,2009, pp. 499-501; Hong et al.,2009, pp.235-239). Patients with high-grade cancers are particularly at risk due to this discrepancy and are more likely to develop biochemical recurrence earlier (Pinthus et al.,2006, pp. 116-118; Gofrit et al.,2007, pp. 455-459). As a result, a high-grade cancer that is underdiagnosed on TRUS biopsy may be followed-up with an active surveillance by mistake. This increases the importance of accurate preoperative diagnosis.

There are many studies in the literature on tumor size, GS, and prognosis. In one study, large tumor diameter was shown to be a significant and independent predictor of biochemical recurrence(Eichelberger et al.,2005, pp.594-595). Nelson et al. (2006, pp. 252) reported that tumor volume in RP material was associated with pathological stage, extraprostatic extension, and biochemical recurrence. They also reported that tumor volume measured after RP had a potential predictive value for prognosis. Vargas et al. (2012, pp. 8-9) reported that lesions ≥1 cm3 are detectable on MRI regardless of GS. In the light of this information, mpMRI is very useful for accurate measurement of tumor volume and index lesion determination in the preoperative period. While the PI-RADS guideline primarily recommends single axis diameter measurement for size, volume assessment is offered as an alternative option(Weinreb et al.,2016, pp. 17-19). Additionally, in the PI-RADS guidelines, 15 mm is the only size criterion, which increases the score from 4 to 5. In our study, the median lesion size was 16 mm in patients with GS upgrade and 15 mm in patients without GS upgrade, and no significant difference was found between the groups in terms of predicting the GS upgrade. This suggests that preoperative tumor size alone is not successful in predicting upgrade.

Studies also revealed a negative correlation between the mean ADC values of the tumor and the GS. Furthermore, it has been reported that ADC values of low, intermediate, and high-risk tumors are different from each other. There is a significant decrease in ADC values as tumor grade increases(Tamada et al.,2008 pp.66-68; deSouza et al.,2008, pp. 13; Mazaheri et al.,2009, pp. 87-88).Van As et al.(2008, pp.97-99) reported that the ADC value of a tumor with a GS of 9 was much lower than the ADC value of tumors with GS of 6 or 7. Türkbey et al. (2011, pp.12-15) reported that the ADC value is an indicator of aggressive tumor behavior, hence also an indicator of the GS. The authors indicated that ADC value may be helpful in selecting patients for active surveillance in combination with other clinical parameters. There is no optimum cut-off for the ADC. In one study, ADC values were between 0.79 and 0.99

μm2/sec in tumors with high GS compared to 0.94 μm2/sec in low-grade tumors. In another study, the mean ADC value in high-grade tumors was found to be 0.81 μm2/sec (Van As et al.,2008, pp.5; Wang et al.,2009, pp. 8-9; Zelhof et al.,2008, pp. 7; Woodfield et al.,2010, pp.3-7). In the present study, the median ADC value in patients with GS upgrade was 0.65 μm2/sec. In addition, the median value of the lesion ADC to normal ADC ratio was calculated as 0.49 μm2/sec. These values were not statistically significant when compared with the patients without GS upgrade; therefore, it was considered not to be a significant parameter in predicting GS upgrade.

The revised PI-RADS guidelines aim to "efficiently and reproducibly detect clinically significant cancer with mpMRI". Pre-biopsy MRI has recently shown great promise in the detection and characterization of Pca (Ahmed et al.2008, pp. 22-24). A negative scan (no lesion seen on mpMRI) has a high-negative predictive value in ruling out the presence of clinically significant cancer (Itatani et al.,2008, pp.8-9). Park et al. (2016, pp.492-494) reported that PI-RADS v2 is a useful preoperative tool to predict clinically significant cancer. They reported that the GS upgrade rate was 81.1%–83.3% when PI-RADS v2 score was >4. In addition, Park et al. (2013, pp. 342-344) investigated the role of PI-RADS v2 in the PRIAS (The Prostate Cancer Research International Active Surveillance) protocol and showed that with the combination of PRIAS and PI-RADS v2, the specificity for Pca detection increased from 89.6% to 92.8%, suggesting that PI-RADS v2 helps to direct patients with clinically significant cancer to a treatment other than active surveillance. Song et al. (2018, pp. 292-296) reported the rate of upgrade in GS was reported to be 68.9% in patients with a PI-RADS v2 score of 4 and 85.6% in those with a score of 5. In another study, Seo et al. (2017, pp. 1163-1168) reported that experienced radiologists identified patients with low-grade Pca on biopsy but with clinically significant cancer and stated that PI-RADS-v2 was useful in predicting GS upgrade. For this distinction, the optimal cut-off value for PI-RADS score was ≥4. Zhai et al. (2018, pp. 334-339) reported that in patients with PI-RADS score >3 on pre-biopsy mpMRI, the rate of GS increase after RP was as high as 85.7%. The authors concluded that this may be a contraindication for active surveillance and further investigations such as targeted biopsy may be needed. On the other hand, in patients with PI-RADS score ≤3, this rate was only 38.1%, which the authors concluded to be relatively safe for active surveillance.

In our study, similar to many studies in the literature, GS upgrade was found to be significantly higher in patients with PI-RADS score ≥4 ($p < 0.05$). The rate of upgrade in GS was 15.6% for PI-RADS score <4 and 84.3% for PI-RADS score ≥4. GS upgrade most commonly occurred from ISUP 1 to ISUP 2 (20 cases), and the second most common group was ISUP 1 to ISUP 3 (12 cases), which is consistent with the literature (Alqahtani et al.,2020, pp.5-7). These results show the importance of targeted biopsy. The results obtained in the present study and evidence from existing literature encourages radiologists to perform targeted biopsy based on the PI-RADS score in biopsy planning. In addition, PI-RADS score also

indicates the presence of clinically significant cancer, further encouraging its use in treatment planning.

DCE imaging has been increasingly discussed in recent years and also included in the latest version, PI-RADS v2.1, where biparametric MRI was mentioned for the first time. The most important use of DCE is the detection of recurrence or residuals after treatment (Scialpi et al.,2017, pp.503-507). In a study of 87 patients in whom DCE was performed before and after radiation therapy, Low et al. (2011, pp.443-446) showed that k-trans values correlated with the GS. The authors reported that the highest k-trans values corresponded to the highest GS of 9 and these differences in k-trans persisted 2 months after treatment. In 75% of cases, there was a decrease in k-trans values after treatment. Moradi et al. (2012, pp. 1063-1065) found a significant correlation between GS and k-trans, Ve, and Vp. Türkbey et al. (2010, pp. 456-457) found that lesions were generally easier to detect as the GS increased and that DCE findings correlated with the GS. In the present study, perfusion parameters were similar in patient groups with and without GS upgrade after RP, and no significant difference was found between the two groups. Our data support the theory that "visual assessment is more useful than quantitative measurement" in interpreting DCE.

One of the major problems with the PI-RADS v2 guidelines is the low to moderate inter-reader reliability (Kappa value: 0.46–0.80). This is mainly due to the subjective and visual assessment in scoring. Discordance varies according to rater experience, lesion location, and PI-RADS score. For example, inter-reader reliability is higher for PZ lesions than in TZ lesions, and lesions with PI-RADS score ≥4 compared to lesions with PI-RADS score <4 (Girometti et al.,2019, pp. 809-810; Smith et al.,2019, pp. 543-548). The most recent version PI-RADS v2.1 also showed no significant improvement in inter-reader reliability (Kappa value: 0.51–0.64) (Hö Tker et al.,2020, pp. 859-860; Tamada et al.,2019, pp. 725-728). In the present study, the Kappa value was 0.67, which is higher compared to the literature. Higher inter-reader reliability was most likely due to more patients with high PI-RADS scores who underwent RP being included in the study group.

There are certain limitations of this study. First, it is a retrospective, single-center study with a relatively small patient group. This creates the risk of biased case selection. To mitigate this risk, assessments were made without clinical, laboratory, and pathological results. Second, targeted biopsies were performed with the cognitive fusion technique. Although it is a targeted biopsy technique, the tumor site may not be optimally sampled. Upgraded results may have been affected in cases where a high or low grade part of the tumor was sampled. In addition, anterior or midline tumors may have been missed in targeted biopsy. A more effective targeted biopsy can be performed using MR-fusion technique; however, this software is not available in our center. Third, the consensus PI-RADS score was used as the basis for statistical analysis.

The consensus was reached by two readers and there may be cases where both readers made mistakes.

5. CONCLUSION

PI-RADSv2.1 score of ≥4 or TZ infiltration may predict GS increase after RP with a sensitivity of 84.3%. Therefore, preoperative mpMRI should be performed to determine the risk stratification of patients, to choose the treatment method, and to predict the prognosis of the disease by detecting PI-RADS v2.1 score and TZ infiltration.

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