

Multiparametric MRI Assessment of Atypical Transitional Zone Nodules in PI-RADS v2.1

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ABSTRACT

Objective: In Prostate Imaging Reporting and Data System v2.1, atypical nodules that are mostly encapsulated or homogeneously circumscribed obtain a score of 2. If the diffusion score is marked at ≥ 4 , the nodule is upgraded to category 3. This study aims to determine the prevalence of clinically significant prostate cancer (csPCA), in diffusion-weighted imaging (DWI)-upgraded atypical nodules and compare it with T2-weighted score 3 transitional zone (TZ) nodules.

Methods: Patients who underwent multiparametric magnetic resonance imaging before targeted transrectal ultrasound-magnetic resonance imaging fusion biopsy between January 2021 and February 2022 were retrospectively evaluated. Patients with the TZ lesions category ≤ 3 were included in this study. Lesions were classified as category 2, 2 + 1, and 3. The prevalence of prostate cancer (PCa) in each group was presented as number and percentage using descriptive statistics. The Kruskal-Wallis test and the chi-squared test were used to compare the groups.

Results: Forty-four patients with 64 lesions were included in the study. Sixteen of 64 were classified as category 2, 36 of 64 as category 2 + 1, and 12 of 64 as category 3. Among 36 DWI-upgraded atypical nodules (category 2 + 1), two (5.5%) had csPCA. Of the twelve nodules with T2-weighted score 3, three (25%) had csPCA. There was no significant difference between the groups, regarding the rate of csPCA. Pca was not diagnosed in 16 category 2 TZ nodules.

Conclusion: We found a lower rate of csPCA in DWI-upgraded TZ nodules (5.5%) compared to nodules with T2-weighted score 3 (25%), although this difference was not statistically significant. Our study demonstrates the value of DWI in identifying PCa in atypical nodules.

Keywords: Atypical nodule, multiparametric prostate MRI, PI-RADS v2.1, transitional zone, TRUS-MRI fusion biopsy

INTRODUCTION

Multiparametric magnetic resonance imaging (mpMRI) of the prostate has been used for the detection and localization of clinically significant prostate cancer (csPCA). The Prostate Imaging Reporting and Data System (PI-RADS) was established in 2012 by the European Society of Urogenital Radiology for the evaluation and reporting of mpMRI data.¹ In 2015, PI-RADS was updated to version 2 (v2) and adopted much more widely.² PI-RADS v2 was updated in 2019 and

termed PI-RADS v2.1 to address system limitations and inconsistencies that had been identified since its release in 2015.³ Transitional zone (TZ) lesions are categorized based on T2-weighted image characteristics. According to PI-RADS v2, all TZ lesions are assigned a score of 3, except for normal TZ (score 1), typical benign prostatic hyperplasia (BPH) nodules (score 2), and clearly suspicious lesions (scores 4 or 5). However, this category includes atypical cases, ranging from stromal type BPH nodule to TZ prostate cancer (PCa).²



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Therefore, the clinical diagnosis of TZ cancers remains challenging since BPH is present in almost all elderly patients, and mpMRI findings overlap with csPCa.^{4,5} The updated PI-RADS v2.1 includes significant changes for TZ assessment, particularly concerning lesions with low T2 weighted imaging (T2WI) scores. A typical nodule with a complete hypointense capsule was downgraded to a score of 1. Atypical nodules that are mostly encapsulated or homogeneously circumscribed obtain a score of 2, and if there is marked diffusion restriction, they are upgraded to category 3 (diffusion score of 4 or higher). This modification has the potential to influence the decision to perform a biopsy on TZ lesions upgraded to category 3, thus guiding diagnostic strategies to reduce false positives and minimize unnecessary biopsies.⁶

Compared to category 2 TZ lesions, category 2 + 1 TZ lesions demonstrated a markedly higher likelihood of detecting International Society of Urological Pathology ≥ 2 cancer, suggesting that the use of the DWI upgrade rule increases the probability of identifying clinically significant disease.⁶

Although these revisions highlight the importance of diffusion-weighted imaging (DWI) and apparent diffusion coefficient (ADC) mapping in PCa detection, few studies have investigated the prevalence of csPCa in upgraded atypical TZ nodules that restrict diffusion in PI-RADS v2.1.³ The purpose of this study was to investigate the rates of csPCa detection in atypical TZ nodules that were upgraded to category 3 according to PI-RADS 2. One due to diffusion restriction.

MATERIAL AND METHODS

This retrospective observational study was approved by the Institutional Ethics Committee of Selçuk University (approval no.:2023-39, date:17.01.2023). The ethics committee approved the waiver of informed consent due to the retrospective nature of the study. In addition, permission was obtained from the institution for the use of medical records and databases in this retrospective study.

Patients

A total of 246 patients who had mpMRI before targeted transrectal ultrasound-magnetic resonance imaging (US-MRI) fusion biopsy between January 2021 and February 2022

were retrieved retrospectively from the picture archiving and communication system. The study included category 2 and 3 transition zone lesions on MRI with targeted transrectal US-MRI fusion biopsies. Patients with peripheral zone lesions, TZ lesions category 1, 4, and 5, low-quality mpMRI scans, or a history of previous surgery and treatment were excluded from the study (Figure 1).

The following data were collected from the patients' electronic medical records: indication, age, prostate-specific antigen (PSA), free PSA, prostate volume, PSA density, and biopsy results. Biopsy results were considered the reference standard.

Prostate MRI Technique and Interpretation

Multiparametric prostate MRI was performed using a 3T system (MAGNETOM Skyra; Siemens Healthineers AG, Erlangen, Germany) with a pelvic-phased array coil in line with PI-RADS v2.1. The MRI techniques comprised axial, coronal, and sagittal T2WI, DWI, and dynamic contrast-enhanced (DCE) imaging. On DCE, 0.1 mmol/kg gadobutrol (Gadovist; Bayer-Schering, Berlin, Germany) was administered intravenously at a rate of 3 mL/sec using an automated injector, followed by a 30 mL saline flush. Table 1 summarizes the MRI technique in detail. At our institution, a standardized reporting format compatible with PI-RADS v2. One is employed, and the report specifies the localization, size, and PI-RADS score (overall assessment and score for each pulse sequence) of each lesion.

One board-certified radiologist (A.K., with 3 years of experience in prostate mpMRI interpretation) established the patient population retrospectively based on study inclusion criteria and recorded their clinical information. In the initial sessions, two other board-certified radiologists (H.Ö. and M.K., with 4 and 6 years of mpMRI experience, respectively)—who were aware of the prior mpMRI report but blinded to biopsy results—independently scored TZ lesions on mpMRI according to the PI-RADS v2.1 at a dedicated workstation (Syngo.via, Siemens Healthineers, Forchheim, Germany). In the second session, the same two radiologists (H.Ö. and M.K.) reached an agreement on the final PI-RADS score, mean ADC value, and longest diameter of each TZ lesion.

Biopsy Technique

Since 2020, our institution has been performing mpMRI scanning in line with PI-RADS v2.1, and since 2021, we have been performing targeted transrectal US/MRI fusion biopsies. Transrectal US-MRI fusion biopsy was performed for the targeted lesions with the Vnav, Logic S8, GE Healthcare system. Transrectal US-MRI fusion biopsies of the prostate were performed by a radiologist, with three years of experience (more than 200 biopsy procedures), using an 18 -gauge side-cutting needle.

Prior to transrectal US-MRI fusion biopsy, suspected TZ lesions were targeted on multiparametric MRI. Each lesion was targeted and tagged separately in patients who had multiple TZ lesions, enabling direct imaging-histological correlation. At least two cores were obtained for the targeted lesions, and a transrectal US-guided 12-core systematic biopsy was performed immediately after the targeted cores were obtained. All biopsy cores were evaluated histopathologically.

MAIN POINTS

- Diffusion-weighted imaging (DWI) plays a crucial role in upgrading atypical transition zone nodules, improving the classification of Prostate Imaging Reporting and Data System (PI-RADS) category 3 lesions and potentially enhancing clinically significant prostate cancer (csPCa) detection.
- In our study, no prostate cancer was detected in category 2 patients without DWI restriction.
- Although PI-RADS v2.1 has improved the performance of category ≥ 3 lesions in diagnosing csPCa, our study found no significant difference in the detection rates of any prostate cancer and csPCa in DWI-upgraded lesions.

Statistical Analysis

The Shapiro-Wilk test was used to determine whether the distribution of continuous numerical variables was normal. Descriptive statistics were reported as mean ± SD or median (range) for continuous data (age, prostate volume, lesion size, free PSA, PSA, PSA density, mean ADC value) and count and percentage (%) for categorical data (biopsy result). The Kruskal-Wallis test and chi-square analysis were used to compare continuous and categorical data among category 2, 2 + 1, and 3 TZ lesions. All data were evaluated using version 21.0 of the Statistical Package for the Social Sciences (IBM Corporation,

Armonk, NY, USA). In this study, a p value of 0.05 was selected to represent statistical significance in all statistical tests.

RESULTS

The study enrolled a total of 44 patients with 64 category 2, 2+1 and 3 TZ lesions in accordance with PI-RADS v2.1. The mean age was 64.41 ± 7.65 years (range, 41-82 years). The mean prostate volume was found to be 85.06 + 44.37 mL. The mean PSA level was 11.63 ± 8.92 ng/mL and the mean lesion size was 10.84 ± 4.45 mm. Based on PI-RADS v.2.1, 16 out of 64 nodules in the TZ were classified as category 2, 36 as category 2 + 1, and 12 as category 3. Table 2 provides a detailed explanation of

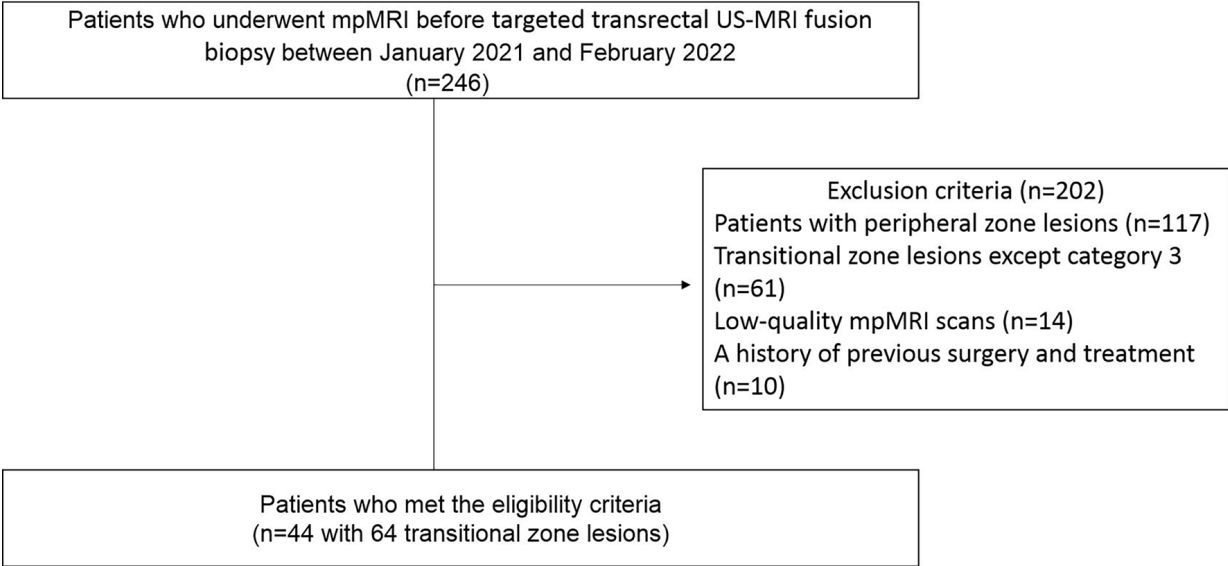


Figure 1. Study population flow chart.
US-MRI, ultrasound-magnetic resonance imaging; mpMRI, multiparametric magnetic resonance imaging.

Table 1. Multiparametric MRI Acquisition Parameters								
Type of imaging	Parameters							
	TR (msec)	TE (msec)	FOV (mm)	b value (s/mm²)	Flip angle (°)	Slice thickness (mm)	Turbo factor	NSA
T2W (axial)	5060	106	200 x 200	-	129	3	23	3
T2W (coronal)	5000	110	200 x 200	-	121	3.5	25	3
T2W (sagittal)	5500	100	200 x 200	-	123	3.5	23	2
DWI (axial)	4500	76	200 x 200	50.1000.1500	90	3	55	3
DCE (axial)	5.08	1.77	259 x 259	-	15	3.5	1	1

MRI, magnetic resonance imaging; TR, repetition time; TE, echo time; T2W, T2-weighted; T1W, T1 weighted; DWI, diffusion weighted imaging; FOV, field of view; DCE, dynamic contrast-enhanced; NSA, numbers of signals averaged.

patient data. There were no significant differences in mean age, prostate volume, PSA value, or lesion size between the groups ($P > 0.05$).

There was no evidence of PCa in 16 atypical nodules without DWI upgrade, classified as category 2. There were 36 atypical nodules with diffusion restriction (category 2 + 1), of which 1 (2.8%) had clinically insignificant PCa, and 2 (5.5%) had csPCa, respectively. Of the 12 nodules with a T2-weighted score of 3, 1 (8.3%) had clinically insignificant PCa and 3 (25%) had csPCa. The incidence of any PCa and csPCa was not significantly different between groups (Table 3). A representative patient was shown in Figure 2.

DISCUSSION

In PI-RADS v2, biopsies were mostly performed when the lesion score was 3 or higher.^{6,7} The success of detecting clinically significant cancer in category 3 lesions varied significantly between studies.⁸⁻¹⁰ The discrepancy in results is due to PI-RADS category 3 lesions demonstrating a lack of consensus among readers because of the ambiguous terminology employed in this classification, such as “obscured margins”.¹¹⁻¹³ Therefore, some studies have proposed that the optimal threshold for targeted biopsy in TZ tumors should be ≥ 4 .¹⁴⁻¹⁶ In the updated PI-RADS v2. One, the term for an atypical nodule in the transition zone has been added.³ Additionally, another important change in PI-RADS v2. One is the inclusion of DWI features in atypical nodules for upgrading to category 3 lesions.³ Previous studies

have shown that DWI plays an additional role to T2 scores of PI-RADS v2.^{8,17} With this new approach, the performance of category ≥ 3 lesions in diagnosing csPCa has increased.⁸

DWI has also been a part of PI-RADS v2, where the category is upgraded from 3 to 4 when the DWI score is 5. The results of a study by Rosenkrantz et al.¹⁸ even suggested that upgrading category 3 to 4 based on a DWI score of 4 may add value in detecting csPCa.

In our study, we compared the pathological results of DWI-upgraded atypical nodules (category 2 + 1), and conventional T2-weighted score 3 lesions. We found that the detection rates of any PCa and csPCa in DWI-upgraded lesions were 8.3% and 5.5%, respectively. In comparison, detection rates of any PCa and csPCa in conventional T2-weighted score 3 lesions were 33.3% and 25%, respectively. No statistically significant difference was found between the two groups. This could be due to the small number of patients in the study. Lim et al.¹⁹ evaluated 104 patients with 109 lesions and reported that 28% of patients were diagnosed with any PCa and 8% were diagnosed with csPCa in DWI-upgraded lesions. In line with our study, there was also no significant difference in the detection of either any PCa or csPCa between groups.¹⁹ In DWI-upgraded lesions, Byun et al.²⁰ found a significant improvement in the detection of csPCa and anyPCa. In their study, DWI-upgraded lesions were diagnosed with csPCa at a higher rate than the conventional T2-weighted-score-3 lesions.²⁰ In a prospective study with 1,238 eligible patients, Costa et al.²¹ found that 6%

Table 2. Demographics and Clinical Variables

	Atypical nodules without DWI restriction (n=16)	DWI-upgraded atypical nodules (n=36)	T2-weighted MRI score 3 nodules (n=12)	P
Age	63 ± 9.8	66.6 ± 6.3	60.3 ± 7.5	0.157
Prostate volume	80.6 ± 26.2	93.9 ± 51.1	67.1 ± 35.3	0.209
PSA (ng/mL)	10.4 ± 5.4	13.6 ± 7.6	7.5 ± 3.3	0.071
Lesion size (mm)	8.6 ± 2.2	12.1 ± 5.1	10.1 ± 3.2	0.260
Pathology				
Benign	75.0 (12/16)	41.7 (15/36)	50.0 (6/12)	
Prostatitis	25.0 (4/16)	50.0 (18/36)	16.7 (2/12)	
ISUP grade 1	-	2.8 (1/36)	8.3 (1/12)	
ISUP grade 2 and 3	-	5.5 (2/36)	25.0 (3/12)	

Values are expressed as mean ± SD or percentage with numbers in parentheses. DWI, diffusion weighted imaging; MRI, magnetic resonance imaging; PSA, prostate-specific antigen; ISUP, International Society of Urological Pathology.

Table 3. Rates of Any Prostate Cancer and Clinically Significant Prostate Cancer by Type of Nodules

	DWI-upgraded atypical nodules (n=36)	T2-weighted MRI score 3 nodules (n=12)	P
Pathology			
Any PCa	8.3 (3/36)	33.3 (4/12)	0.055
csPCa	5.5 (2/36)	25.0 (3/12)	0.092

Values are percentages with numbers in parentheses. DWI, diffusion weighted imaging; PCa, prostate cancer; csPCa, clinically significant PCa; MRI, magnetic resonance imaging.

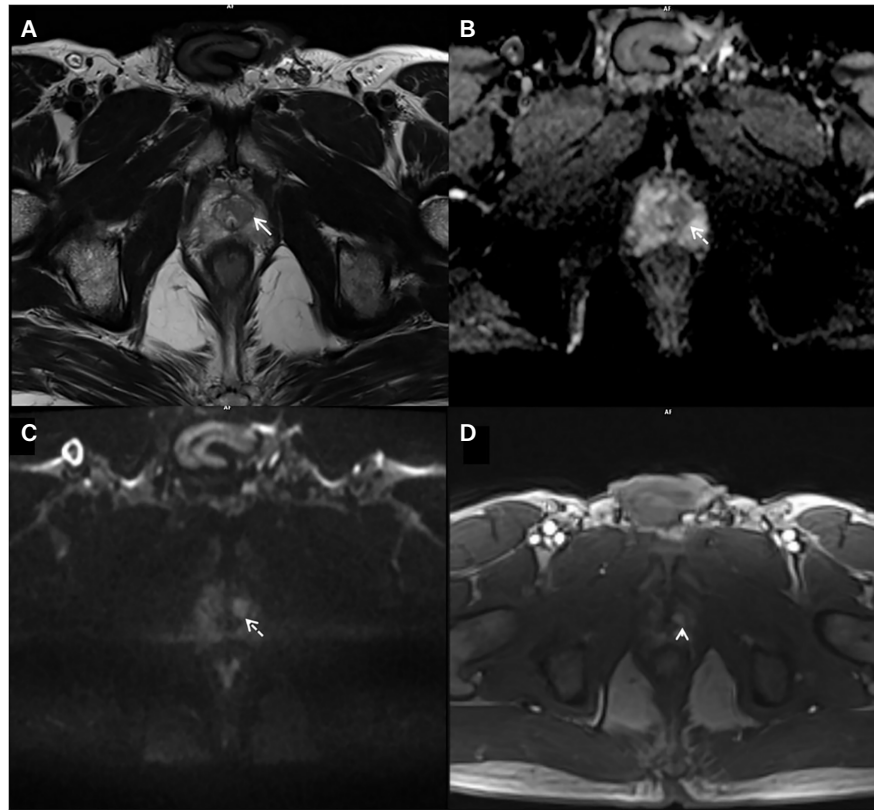


Figure 2. (A) Axial T2-weighted image shows a circumscribed hypointense atypical nodule in the anterior aspect of left apex transitional zone (arrow). (B) Apparent diffusion coefficient map shows marked hypointensity in the lesion compared to the background (dashed arrow) and (C) diffusion weighted images (DWI) ($b=1500 \text{ s/mm}^2$) show marked hyperintensity in the lesion compared to the background (dashed arrow), respectively. (D) Dynamic contrast-enhanced image shows early contrast enhancement in the nodule (arrowhead) (T2 score: 2, DWI score: 4, dynamic contrast-MRI: positive, Prostate Imaging Reporting and Data System category 2 + 1).

MRI, magnetic resonance imaging.

of patients had DWI-upgraded lesions and 7% had conventional T2-weighted category 3 lesions. Clinically significant cancer was detected in 6% of 49 patients with DWI-upgraded lesions and in 11% of 61 patients with conventional T2-weighted category 3 lesions.²¹ The rate of csPCa was not statistically different between groups.²¹

Consistent with the findings of Lim et al.¹⁹, we found no evidence of PCa in atypical nodules without DWI upgrade. This may be due to the small number of atypical nodules without DWI upgrade in both studies.¹⁹

A recent meta-analysis found that the PCa detection rates for TZ DWI-upgraded and conventional T2-weighted score 3 lesions were 12% and 19%, respectively. There was a non-significant difference in PCa detection rates between the two groups. It was thought that it might also originate from the small sample size in studies.²²

Study Limitations

There were some limitations of our present study. First, it was a retrospective study with a small number of patients and was carried out at a single institution. Moreover, only transrectal US/MRI fusion biopsies were included in the study. Accepted as a reference standard, transrectal US/MRI fusion biopsy may

lead to mis-sampling or inadequate sampling. In addition, some patients may not have undergone biopsy due to variations in the management of PI-RADS 3 lesions.

In conclusion, no PCa was not detected in category 2 patients without DWI restriction. csPCa was detected in 5.5% of patients with DWI-upgraded atypical nodules and in 25% of patients with conventional T2-weighted score 3. There was no statistically significant difference between the two groups. The updates to TZ assessment in PI-RADS v2.1 may improve the detection rate of csPCa. However, prospective studies with larger patient groups are needed.

Ethics

Ethics Committee Approval: Ethics committee approval was received for this study from the Ethics Committee of Selçuk University (approval no.: 2023/39, date: 17.01.2023)

Informed Consent: The ethics committee approved the waiver of informed consent due to the retrospective nature of the study. In addition, permission was obtained from the institution for the use of medical records and databases in this retrospective study.

Footnotes

Author Contributions

Concept Design – H.Ö., A.K., M.K., M.K.; Data Collection or Processing – H.Ö., B.B.A., U.A., E.A., M.K., M.K.; Analysis or Interpretation – H.Ö., B.B.A., U.A.; Literature Review – B.B.A., U.A., A.K.; Writing, Reviewing and Editing – H.Ö., B.B.A., U.A., E.A., M.K.

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