Cerrahpaşa Med J 2022; 46(3): 189-193

ORIGINAL ARTICLE

# Correlation Between Prostate-Specific Antigen Density and Findings from Multiparametric Magnetic Resonance Imaging of Prostate

Cansu Öztürk[1], Özlem Güngör[1], Hanife Ersay[2], Selma Uysal Ramadan[1]

[1]Department of Radiology, Ankara Atatürk Sanatoryum Training and Research Hospital, Ankara, Turkey
[2]Department of Radiology, Karabük Training and Research Hospital, Karabük, Turkey

***Cite this article as:*** Öztürk C, Güngör Ö, Ersay H, Uysal Ramadan S. Correlation between prostate-specific antigen density and findings from multiparametric magnetic resonance imaging of prostate. *Cerrahpaşa Med J.* 2022;46(3):189-193.

## *Abstract*

**Objective:** The present study is intended to investigate the relationship between multiparametric prostate magnetic resonance findings and prostate-specific antigen density in the diagnosis of prostate cancer.

**Methods:** The present study included 38 cases that underwent multiparametric prostate magnetic resonance between January 1, 2019, and February 28, 2022. Age, prostate-specific antigen, transrectal ultrasound biopsy, prostate-specific antigen density, and prostate imaging-reporting and data system results of all cases were recorded. Together with the prostate-specific antigen density threshold value, the sensitivity and specificity of prostate-specific antigen density and prostate imaging-reporting and data system scores in predicting histopathological outcomes were calculated.

**Results:** Of the patients undergoing transrectal ultrasound biopsy, 11 patients (28.9%) were diagnosed with prostate cancer. The median prostate-specific antigen density was higher in the group of malignant cases [0.2 (0.1-1.9) ng/mL$^2$] than in the group of non-malignant cases [0.1 (0.03-0.57) ng/mL$^2$] ($P < .0001$). With the prostate-specific antigen density threshold value set at 0.16 ng/mL$^2$, the sensitivity was 73% and the specificity was 89% in predicting prostate cancer, while positive predictive value was 73% and negative predictive value was 89% (area under the curve: 0.864, $P < .001$). Multiparametric prostate magnetic resonance findings had a sensitivity of 91% and a specificity of 85%, as well as positive predictive value of 71% and negative predictive value of 96% in predicting prostate cancer ($P < .001$). There was a strong correlation with the biopsy result in the prostate imaging-reporting and data system/prostate-specific antigen density positive group (Rho: 0.79, $P < .0001$) where the sensitivity, specificity, and negative predictive value were found to be 100%, 78%, and 100%, respectively.

**Conclusion:** The results of the present study demonstrated that the combined use of prostate-specific antigen density and multiparametric prostate magnetic resonance imaging helps obtain more robust results in diagnosing prostate cancer, compared to using either of them individually.

**Keywords:** Prostate-specific antigen, prostate cancer, magnetic resonance imaging

## Introduction

The gold standard in the diagnosis of prostate cancer (pCa) is tissue diagnosis. However, in addition to the invasive nature of biopsy and the complications developing in biopsy, it is also associated with lower rates of diagnostic success when performed blindly and difficulty in ensuring patient compliance. All these factors consequently require resorting to less-invasive diagnostic methods. For this purpose, prostate-specific antigen (PSA) has been used for many years in screening for prostate cancer (pCa) and evaluating treatment response or tumor progression in patients.[1] However, the reference ranges of PSA value reported for detecting pCa are quite wide (the rates of pCa detection for the PSA reference ranges 4-10 ng/mL, 10-20 ng/mL and 20<ng/mL of PSA are 11.8-20.5%, 20.5-25.0%, and 47.1-53.0%, respectively).[2-4] In addition, even when within these reference ranges, PSA is known to generate false positive results and lead to unnecessary biopsies due to its low specificity. For these reasons, other methods such as free-to-total PSA ratio, PSA velocity, PSA density (PSAd), and so on, are on trial to enhance the specificity of PSA, and thus have been targeted to increase the rate of pCa detection and reduce unnecessary prostate biopsy. Of these PSA-based parameters, PSAd is the ratio of PSA level to prostate volume and has gained more widespread use in recent years. Prostate-specific antigen density is known to be a useful predictor for the post-treatment period in localized pCa[5] and the best of all the PSA-based parameters in showing extra-prostatic extension.[6] In the light of these data, although PSAd has already become routine, issues such as the threshold value of PSAd to be applied remain controversial.[6] Therefore, along with laboratory data, diagnostic imaging is also needed for the diagnosis of pCa. Upon technical advances, multiparametric prostate magnetic resonance (mpMR) has been used in the evaluation of patients with indefinite diagnoses, and it is known that mpMR has achieved high success in the diagnosis of pCa if reported in line with the guidelines.[7] Therefore, to eliminate the specified disadvantages of PSA and systematic biopsy (transrectal ultrasound biopsy, TRUSb) in the diagnosis of pCa, mpMR has been integrated into the diagnostic algorithm.[8] Multiparametric prostate MR is superior to other methods since it helps detect pCa and evaluate for extra-prostatic extension. We thought that the use of PSAd in combination with mpMR may contribute to the differentiation of cases with pCa.

Therefore, our study intended to investigate the correlation between mpMR findings and PSAd in the diagnosis of PCa.

**Received:** June 25, 2022 **Accepted:** August 29, 2022 **Publication Date:** October 4, 2022
**Corresponding author:** Cansu Öztürk, Department of Radiology, Ankara Atatürk Sanatoryum Training and Research Hospital, Ankara, Turkey
**e-mail:** cnsozt@yahoo.com
**DOI:** 10.5152/cjm.2022.22048

## Methods

This retrospective study started after obtaining the approval of the ethics committee of our hospital (Ankara Atatürk Sanatoryum Training and Research Hospital ethics committee, date: April 26, 2022, number: 2499). There were a total of 70 cases identified to have undergone mpMRI between January 1, 2019, and February 28, 2022. After excluding patients with a history of local treatment before previous prostatic surgery or MRI, whose systematic biopsy (TRUSb) results were not obtained or who did not have a detailed pathology report, 38 patients with optimal images obtained during imaging procedures performed in accordance with the guidelines were included in the study. The reason for mpMR in all patients was PSA elevation and suspicion of pCa. In all patients, TRUS was performed after MRI; there were at least 4 days and no more than 3 weeks between them. The ages, PSA values, TRUSb results (malignant and non-malignant) of the cases included in the study were investigated from the hospital information system (HIS) and recorded. Prostate-specific antigen density was calculated as the ratio of PSA level to prostate volume.

All prostate MRI examinations were performed on an MRI machine with a magnetic strength of 1.5 T (Avanto, Siemens Healthineers, Erlangen, Germany). The MRI 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 (TR): 6400 ms; echo time (TE): 108 ms; field of view (FOV): 180 mm; acquisition matrix: 256 × 256; slice thickness: 3 mm with no gap), a diffusion-weighted imaging (DAG) with an axial orientation (TR: 4100 ms; TE: 96 ms; b-values: 50, 500, 1000, and calculated 1400 sec/mm$^2$; FOV: 200 mm; acquisition matrix: 102 × 102; slice thickness: 3 mm with no gap) with apparent diffusion coefficient mapping, and dynamic contrast-enhanced sequences with an axial orientation (TR: 4.97 ms; TE: 1.83 ms; FOV: 180 mm; acquisition matrix: 138 × 192; slice thickness: 3.5 mm with a 0.7-mm gap, temporal resolution: 13 s).

Prostate and lesion volumes on MRI were calculated using ellipsoid formula on the axial and sagittal images. Magnetic resonance images were evaluated in accordance with PI-RADS v2.1, by 2 radiologists (SUR: 15 years experience in abdominal radiology, CÖ: 12 years experience in general radiology) with consensus. When a consensus could not be reached, the prostate imaging-reporting and data system (PI-RADS) score determined by a radiologist experienced in abdominal radiology (SUR) was determined as the final decision. In PI-RADS scoring, a scale of 1: highly unlikely, 2: unlikely, 3: intermediate lesion, 4: likely, 5: extremely likely was employed to measure the PIRADS score of each case. The score with the highest PI-RADS score of all the lesions in 1 patient was accepted as the prostate score of the patient. In the mpMR results, patients with PI-RADS 1, 2, and 3 were grouped as the "non-malignant group" and those with PI-RADS 4 and 5 were grouped as the "malignant group." In cases with more than 1 lesion, the lesion with the highest volume and/or the highest PI-RADS score was used in the analysis.

To perform the histopathological evaluation, pathology reports were screened retrospectively from the HIS and recorded.

### Statistical Analysis

After testing the numerical values for distribution normality, the data without normal distribution were indicated as median (minimum-maximum), and the categorical variables were presented as frequency and percentage. The categorical variables were assessed by chi-square test and, where necessary, by Fisher's exact test. Mann–Whitney *U* test was used for comparing the numerical variables. The correlation between PSA, PSAd, mpMR results, and biopsy results was evaluated by Spearman's correlation analysis.

All analyses were performed using Statistical Package for the Social Sciences version 20 (IBM, Armonk, NY, USA) statistical program. $P < .05$ was considered statistically significant.

## Results

A total of 38 male patients [median age 66 years, (47-74 years)] with biopsy results were included in the study. The patients had a median PSA of 7.9 ng/mL (2.3-77 ng/mL) and a median PSAd of 0.11 ng/mL$^2$ (0.03-0.57 ng/mL$^2$). Of the patients undergoing TRUSb, 11 patients (28.9%) were diagnosed with pCa. The median PSAd value was higher in the group of malignant cases [0.2 (0.1-1.9) ng/mL$^2$] than in the group of non-malignant cases [0.1 (0.03-0.57) ng/mL$^2$] ($P < .0001$). With the PSAd threshold value set at 0.16 ng/mL$^2$, the sensitivity was 73% and the specificity was 89% in predicting pCa, while positive predictive value (PPV) was 73% and negative predictive value (NPV) was 89% (area under the curve (AUC): 0.864, $P < .001$). The distribution of PSAd according to the biopsy results is shown in Table 1.

The median prostate volume on MRI images was 60 cm$^3$ (20-230 cm$^3$) and the median volume of the dominant lesion was 3 cm$^3$ (0-22 cm$^3$). The prostate volume was greater in the non-malignant group. The median prostate volume was 67 cm$^3$ (20-230 cm$^3$) in the non-malignant group and 43 cm$^3$ (min-max: 30-102 cm$^3$) in the malignant group ($P = .035$). The lesion volume was higher in the group of malignant cases. The median lesion volume was 3.0 (1-22) cm$^3$ in the non-malignant group and 8.0 (1-12) cm$^3$) in the malignant group ($P = .049$).

In the mpMRI images of the patients, 8 patients (21%) were reported as PI-RADS 1-2, 16 (42%) as PI-RADS 3, and 14 (37%) as PI-RADS 4-5 (Figures 1 and 2), (Table 2). When we divided the PI-RADS scores into 2 groups as the malignant group with a high probability of malignancy (PI-RADS 4 and 5) and the non-malignant group (PI-RADS 1, 2, and 3) (Tables 2 and 3), mpMR had a sensitivity of 91% and a specificity of 85% in predicting pCa, as well as PPV of 71% and NPV of 96% ($P < .001$).

We considered patients with either of the PI-RADS and PSAd values being detected in the malignant group to have "malignant result" (PI-RADS/PSAd positive) and those with neither of the PI-RADS and PSAd values being detected in the malignant group to have "benign result" (PI-RADS 1-2-3 or PSAd ≤ 0.16). Accordingly, there was a strong correlation between this combined use of PI-RADS and PSAd and the biopsy result (Rho: 0.79, $P < .0001$). In this case, the sensitivity was 100%, the specificity was 78%, and the NPV was 100% (Table 3). If PSAd and PIRADS were positive together (PSAd > 0.16 and PIRADS 4-5), the sensitivity was 63%, specificity 96%, PPV 87%, NPV 86%.

## Discussion

In the management of prostate cancer, mpMR is becoming increasingly popular to better investigate on indications such as

**Table 1.** Distribution of PSAd According to Biopsy Results

| PSAd* | Benign (n) (%) | Malign (n) (%) | Total (n) (%) |
|---|---|---|---|
| ≤0.16 | 24 (89) | 3 (27) | 27 (71) |
| >0.16 | 3 (11) | 8 (73) | 11 (29) |
| Total | 27 (100) | 11(100) | 38 (100) |

PSAd, prostate-specific antigen density.

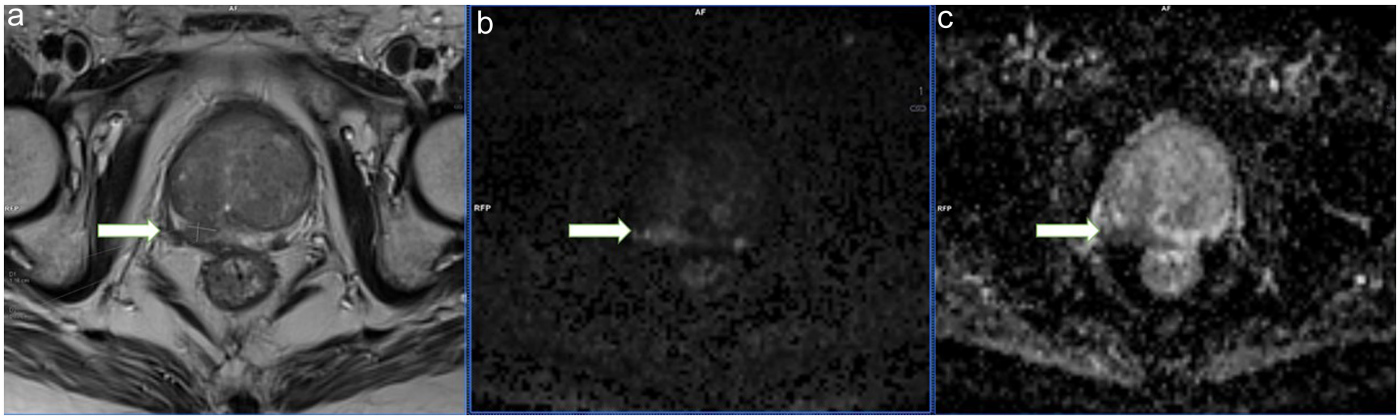


**Figure 1.** PIRADS 4 cases diagnosed with prostate adenocarcinoma. a) Axial T2W image shows hypointense nodular lesion in the right peripheral zone (white arrow). b) Calc. 1400 DWI, c) ADC map shows diffusion restriction of the lesion (white arrow).

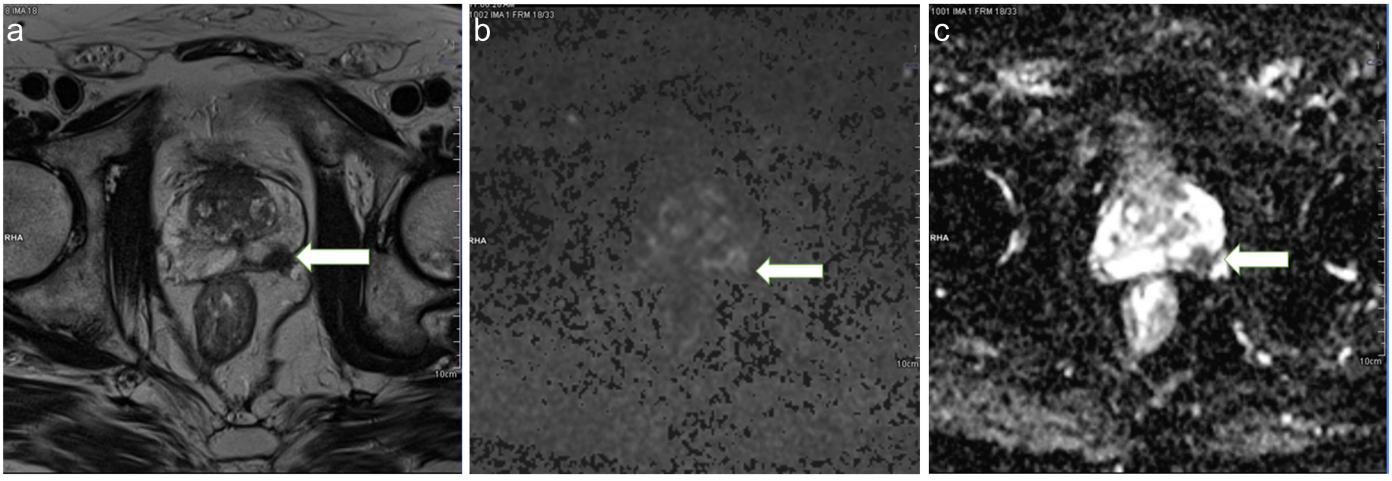


**Figure 2.** PIRADS 5 cases diagnosed with prostate adenocarcinoma. a) Axial T2W image shows hypointense nodular lesion and extraprostatic extension in the left peripheral zone (white arrow). b) Calc. 1400 DWI, c) ADC map shows diffusion restriction of the lesion (white arrow).

tumor detection, anatomical localization, lesion characterization, local staging, active surveillance, and recurrence detection, and so on.[7] In recent years, studies have been published stating that the use of PSA-based methods such as PSA and PSAd in combination with mpMR will help avoid unnecessary biopsies and increase the sensitivity and specificity of mpMR in detecting pCa. In our study, compared to when used individually, the combined use of PSAd and mpMR achieved higher sensitivity and NPV values in the prediction of malignancy.

In line with the literature, our study showed that PSAd value was significantly higher in cases with malignancy ($P < .0001$).[9-11] In studies where Hansen et al[12] set PSAd < 0.20 and Rico et al[10] set PSAd ≤ 0.15 as the threshold value for cases with a negative or indeterminate MRI result, mpMR was reported to increase sensitivity and NPV. In another study where PSAd 0.15 was accepted as the threshold value, the sensitivity and the specificity were found to be 99% and 34%, respectively.[9] However, the threshold value that should be used to achieve higher predictive value in

**Table 2.** Distribution of PI-RADS Findings According to Biopsy Result

| PI-RADS | Benign (n) | Malign (n) | Total (n) |
|---|---|---|---|
| PI-RADS 1-2-3 | 23 (85%) | 1 (9%) | 24 (63%) |
| PI-RADS 4-5 | 4 (15%) | 10 (91%) | 14 (37%) |
| Total | 27 (100%) | 11 (100%) | 38 (100%) |

PI-RADS, prostate imaging-reporting and data system.

**Table 3.** Sensitivity, Specificity, NPV, and PPV values of PSAd, PI-RADS, and PSAd/PI-RADS positive, PIRADS, and PSAd positive

| | Sensitivity (%) | Specificity (%) | PPV (%) | NPV (%) |
|---|---|---|---|---|
| PSAd > 0.16* | 73 | 89 | 73 | 89 |
| PI-RADS** | 91 | 85 | 71 | 96 |
| PI-RADS/ PSAd positive | 100 | 78 | 65 | 100 |
| PIRADS and PSAd positive | 63 | 96 | 87 | 86 |

PSAd, prostate-specific antigen density; PI-RADS, prostate imaging-reporting and data system; NPV, negative predictive value; PPV, positive predictive value.

predicting the malignancy remains controversial. According to our data, when the PSAd threshold value was taken as 0.16 ng/mL,[2] the sensitivity in predicting pCa was 73% and the specificity was 89% (AUC: 0.864, $P < .001$). In addition, when PSAd and mpMR were evaluated together, it was observed that the sensitivity and success in NPV were elevated to a higher level.

In the literature, the sensitivity and specificity values of mpMR in predicting malignancy are quite high and reported to be 74%-80% and 80%-93%, respectively.[13] In a meta-analysis investigating the reliability of mpMRI, the sensitivity was found to be 77% and the specificity was 88%.[8] In our study, in compliance with the literature, the sensitivity and specificity of mpMR in predicting malignancy were found to be quite high (91% and 85%, respectively) ($P < .001$). In our PIRADS 4-5 group, biopsy results of 4 cases were found to be benign, 1 of these cases had PSAd >0.16. In cases reported as PIRADS 4 and 5 in a recent meta-analysis, the probability of detecting malignancy is reported as 59% and 85%, respectively, like our results.[14] However, we think there may be several other reasons to explain this situation. First, the possibility of not sampling the lesion identified in MRI may be a probable reason due to the inability to perform fusion biopsy. Secondly, we do not know whether malignancy was detected in the short term, as we do not have follow-up data of the cases.

In a study by Porcaro et al.[15] it was found that the total prostate volume was smaller in pCa cases and that the possibility of detecting pCa in the biopsy decreased as the prostate volume increased. A study by Ankerst et al[16] also confirmed this inverse correlation between increased prostate volume and pCa detection, suggesting that pCa be incorporated into the risk calculation methods in use to achieve better predictive success. In the study of Raventós et al.[17] it was found that patients with prostate volumes of 45 $cm^3$ and above were more likely to have clinically insignificant cancer and recommended that such patients are classified as patients meeting the d'Amico's criteria. In the study of Omri et al.[6] it was shown that the sensitivity of PSAd value in detecting malignancy was higher in cases with small prostate volumes, suggesting that PSAd value is found to be higher in cases with malignancy.[6] In our study, the median prostate volume was smaller in the malignant group ($P = .035$), and we think that prostate volume led to higher PSAd values in the malignant cases even in the presence of equal PSA values. Therefore, in our study, we used PSAd and PI-RADS together, not PSA.

In our study, lesion volume was higher in the group of malignant cases ($P$: .049). It was also accepted in the PI-RADS classification that the increase in lesion size could increase the probability of malignancy detection, and the upper limit of 1.5 cm as the biggest size was used to differentiate between PI-RADS 4 and 5.[18] In fact, the contribution of 3-dimensional volume information for prostate lesion characterization in solid tumors such as pCa has also been investigated in the literature.[19] In the study of Martorana et al.[19] it was shown that the rate of cancer detection increases as the lesion volume increases. Although there is still insufficient evidence that lesion volume offers additional contributions to predicting malignancy or aggressiveness compared to the widest diameter, we think that it may be a better criterion than 1-dimensional measurement. Of course, volume measurement will be more time-consuming than 1-dimensional measurement. However, it can provide more objective follow-up, especially in cases planned to be followed up as PI-RADS 3 cases.

Similarly in the literature, the results vary in studies evaluating PSAd and PIRADS together.[10,20] In a study investigating the diagnostic safety of PSAd and PI-RADS, it was reported that the use of PIRADS alone had high reliability and that the combined use of PSAd and PI-RADS was not associated with significant changes in malignancy prediction.[11] Similarly, a study by Cuocolo et al[21] stated that the combined use of biparametric MR and PSAd does not increase the diagnostic performance of biparametric MR alone.[21] However, there are studies showing that the combined use of PSAd and PI-RADS increases the reliability in pCa detection.[9,10,20] Our results showed that the sensitivity decreased with the combined use of PSAd and mpMR, however, the specificity and PPV were slightly increased. In our study where we considered the cases with PIRADS 4-5 or PSAd > 0.16 had "malignancy," there was a strong correlation between the *malignancy* and the actual biopsy result ($P < .0001$, Rho: 0.79).

Our study has some limitations. Although the percentage of malignant cases in our study group is in compliance with the literature, a higher number of cases could have helped obtain better results. A second limitation was that fusion biopsy could not be used in histopathological sampling, and we think that if fusion biopsy were performed, the correlation between pathology and PI-RADS score would increase even more. Another limitation of ours was that although PI-RADS V2.1 recommended 3T magnetic field strength, the magnetic field strength of the MR device we used was 1.5 T.

To conclude, if a patient has a PI-RADS score of 4-5 or PSAd > 0.16, we are more likely to define malignant lesions as malignancies histopathologically. Our study suggests that compared to individual use of PSAd and mpMR their combination could be utilized to obtain more successful results in the diagnosis of pCa. If this information can be verified with larger series, the cost and time spent for the diagnosis can be successfully reduced and, instead of undergoing TRUSb, this group of patients can be directly scheduled for operation, thereby reducing morbidity.

**Ethics Committee Approval:** Ethical committee approval was received from the Ethics Committee of Ankara Atatürk Sanatoryum Training and Research Hospital (Date: April 26, 2022, Approval No: 2499).

**Informed Consent:** Due to the retrospective design of the study, informed consent was not taken.

**Peer-review:** Externally peer-reviewed.

**Author Contributions:** Concept – S.U.R., C.Ö.; Design – S.U.R., C.Ö.; Supervision – S.U.R.; Materials – ÖG., HE.; Data Collection and/or Processing – C.Ö., H.E.; Analysis and/or Interpretation – S.U.R., C.Ö., Ö.G.; Literature Review – S.U.R., Ö.G., C.Ö.; Writing – C.Ö., Ö.G., H.E.; Critical Review – S.U.R., C.Ö.;.

**Declaration of Interests:** The authors declare that they have no competing interest.

**Funding:** The authors declared that this study has received no financial support.

## References

1. Wang ZB, Wei CG, Zhang YY, et al. The role of PSA density among PI-RADS v2.1 categories to avoid an unnecessary transition zone biopsy in patients with PSA 4-20 ng/mL. *BioMed Res Int*. 2021;2021:3995789. [CrossRef]
2. Narayanaswamy A, Abul F, Mathew TC. Detection rate and clinical pattern of prostate cancer in Kuwait: a single-center experience. *Med Princ Pract*. 2011;20(1):34-38. [CrossRef]
3. Tang P, Du W, Xie K, et al. Transition zone PSA density improves the prostate cancer detection rate both in PSA 4.0-10.0 and 10.1-20.0 ng/ml in Chinese men. *Urol Oncol*. 2013;31(6):744-748. [CrossRef]
4. Kandıralı E, Temiz MZ, Çolakerol A, Yürük E, Semercioöz A, Müslümanoğlu AY. Does the prostate volume always effect cancer

detection rate in prostate biopsy? Additional role of prostate-specific antigen levels: A retrospective analysis of 2079 patients. *Turk J Urol*. 2019;45(2):103-107. [CrossRef]
5. Sfoungaristos S, Perimenis P. Evaluating PSA density as a predictor of biochemical failure after radical prostatectomy: results of a prospective study after a median follow-up of 36 months. *ISRN Urol*. 2013;2013:984951. [CrossRef]
6. Omri N, Kamil M, Alexander K, et al. Association between PSA density and pathologically significant prostate cancer: the impact of prostate volume. *Prostate*. 2020;80(16):1444-1449. [CrossRef]
7. O'Connor LP, Lebastchi AH, Horuz R, et al. Role of multiparametric prostate MRI in the management of prostate cancer. *World J Urol*. 2021;39(3):651-659. [CrossRef]
8. de Rooij M, Hamoen EH, Fütterer JJ, Barentsz JO, Rovers MM. Accuracy of multiparametric MRI for prostate cancer detection: a meta-analysis. *AJR Am J Roentgenol*. 2014;202(2):343-351. [CrossRef]
9. Washino S, Okochi T, Saito K, et al. Combination of prostate imaging reporting and data system (PI-RADS) score and prostate-specific antigen (PSA) density predicts biopsy outcome in prostate biopsy naïve patients. *BJU Int*. 2017;119(2):225-233. [CrossRef]
10. Rico L, Contreras P, Vitagliano G, Rios Pita H, Ameri C, Blas L. Value of prostate-specific antigen density in negative or equivocal lesions on multiparametric magnetic resonance imaging. *Turk J Urol*. 2020;46(5):367-372. [CrossRef]
11. Tosun M, Uslu H. Prebiopsy multiparametric MRI and PI-RADS version 2.0 for differentiating histologically benign prostate disease from prostate cancer in biopsies: a retrospective single-center comparison. *Clin Imaging*. 2021;78:98-103. [CrossRef]
12. Hansen NL, Barrett T, Koo B, et al. The influence of prostate-specific antigen density on positive and negative predictive values of multiparametric magnetic resonance imaging to detect Gleason score 7-10 prostate cancer in a repeat biopsy setting. *BJU Int*. 2017;119(5):724-730. [CrossRef]
13. Stempel CV, Dickinson L, Pendsé D. MRI in the management of prostate cancer. *Semin Ultrasound CT MR*. 2020;41(4):366-372. [CrossRef]
14. Oerther B, Engel H, Bamberg F, Sigle A, Gratzke C, Benndorf M. Cancer detection rates of the PI-RADSv2.1 assessment categories: systematic review and meta-analysis on lesion level and patient level. *Prostate Cancer Prostatic Dis*. 2022;25(2):256-263. [CrossRef]
15. Porcaro AB, Tafuri A, Sebben M, et al. Prostate volume index is able to differentiate between prostatic chronic inflammation and prostate cancer in patients with normal digital rectal examination and prostate-specific antigen values <10 ng/mL: results of 564 biopsy naïve cases. *Urol Int*. 2019;103(4):415-422. [CrossRef]
16. Ankerst DP, Till C, Boeck A, et al. The impact of prostate volume, number of biopsy cores and American Urological Association symptom score on the sensitivity of cancer detection using the Prostate Cancer Prevention Trial risk calculator. *J Urol*. 2013;190(1):70-76. [CrossRef]
17. Raventós CX, Orsola A, de Torres I, et al. Preoperative prediction of pathologically insignificant prostate cancer in radical prostatectomy specimens: the role of prostate volume and the number of positive cores. *Urol Int*. 2010;84(2):153-158. [CrossRef]
18. Barrett T, Rajesh A, Rosenkrantz AB, Choyke PL, Turkbey B. PI-RADS version 2.1: one small step for prostate MRI. *Clin Radiol*. 2019;74(11):841-852. [CrossRef]
19. Martorana E, Pirola GM, Scialpi M, et al. Lesion volume predicts prostate cancer risk and aggressiveness: validation of its value alone and matched with prostate imaging reporting and data system score. *BJU Int*. 2017;120(1):92-103. [CrossRef]
20. Yadav K, Sureka B, Elhence P, et al. Can combined multiparametric magnetic resonance imaging of the prostate and prostate-specific antigen density improve the detection of clinically significant prostate cancer: A prospective single-center cross-sectional study. *J Cancer Res Ther*. 2021;17(2):372-378. [CrossRef]
21. Cuocolo R, Stanzione A, Rusconi G, et al. PSA-density does not improve bi-parametric prostate MR detection of prostate cancer in a biopsy naïve patient population. *Eur J Radiol*. 2018;104:64-70. [CrossRef]