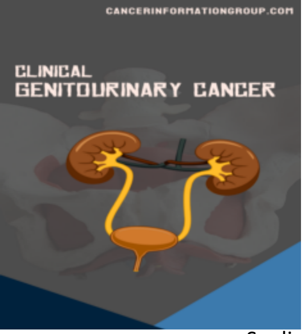

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Diagnostic Value of PSA Screening Combined with Multiparametric MRI in Differentiating Prostate Cancer in the PSA Gray Zone (4.0 – 10.0 ng/mL)

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Abstract

Background: Prostate specific antigen (PSA) remains the first-line test in prostate cancer early detection, but its specificity is limited in men with PSA levels in the gray zone of 4.0 – 10.0 ng/mL. Contemporary guidelines increasingly recommend repeat PSA confirmation, risk-adapted assessment, and pre-biopsy MRI to improve detection of clinically significant disease and reduce unnecessary biopsy. [1 – 3]

Objective: To investigate the diagnostic value of PSA screening combined with multiparametric magnetic resonance imaging (mpMRI) in differentiating prostate cancer from benign prostatic lesions in patients with PSA levels in the gray zone.

Methods: This retrospective clinical study enrolled 186 patients with serum PSA levels between 4.0 and 10.0 ng/mL who underwent prostate mpMRI examination and subsequent histopathological evaluation. Clinical indicators including total PSA, free PSA, free-to-total PSA ratio, prostate volume, and PSA density were collected. mpMRI findings, including T2-weighted imaging, diffusion-weighted imaging, apparent diffusion coefficient characteristics, and PI-RADS scores, were analyzed. Histopathological diagnosis was used as the reference standard. The diagnostic performance of PSA-related indicators alone and in combination with mpMRI was evaluated by comparing sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy.

Results: Among the 186 patients, 68 (36.6%) were diagnosed with prostate cancer and 118 (63.4%) with benign prostatic lesions. Compared with the benign group, the prostate cancer group had a significantly lower free-to-total PSA ratio, smaller prostate volume, higher PSA density, lower ADC values, and higher PI-RADS scores (all $P < 0.01$), whereas total PSA alone did not differ significantly between the two groups ($P = 0.216$). PSA density showed the best diagnostic performance among PSA-derived indicators, with an AUC of 0.79. mpMRI using PI-RADS $\geqslant 4$ yielded an AUC of 0.81. The combined model incorporating PSA density, free-to-total PSA ratio, and PI-RADS score achieved the highest diagnostic efficacy, with an AUC of 0.89, sensitivity of 82.4%, specificity of 84.7%, and overall accuracy of 83.9%.

Conclusion: PSA screening combined with mpMRI provides important diagnostic value for the differential diagnosis of prostate cancer in patients within the PSA gray zone. This combined approach may improve biopsy selection and reduce unnecessary invasive procedures.

Keywords: prostate cancer; PSA gray zone; multiparametric MRI; PSA density; differential

diagnosis

1. Introduction

Prostate cancer is one of the most commonly diagnosed malignancies in men worldwide, and early detection remains central to risk stratification and treatment planning. PSA testing is still the most widely used first-line screening tool, and both EAU and AUA/SUO guidance continue to support PSA-based screening within a shared decision-making framework. At the same time, both guidelines emphasize that PSA alone is not sufficient for biopsy decisions and that newly elevated PSA results should be confirmed before proceeding to imaging or biopsy. [1–3]

The major diagnostic dilemma lies in the PSA gray zone of 4.0–10.0 ng/mL. In this interval, PSA elevation may reflect prostate cancer, but it may also arise from benign prostatic hyperplasia, prostatitis, inflammation, or other nonmalignant conditions. As a result, the specificity of total PSA is limited, and reliance on total PSA alone may lead to unnecessary biopsy and overdiagnosis. Meta-analytic evidence on the free-to-total PSA ratio has also shown that this marker alone provides only modest diagnostic discrimination in this range. [11,15,16]

Multiparametric MRI has become a key component of the modern prostate cancer diagnostic pathway. PI-RADS v2.1 was developed to standardize image acquisition, interpretation, and reporting, with the expectation of improving consistency and facilitating clinically meaningful lesion stratification. Major prospective studies, including PROMIS and PRECISION, showed that MRI-based pathways improve clinically significant cancer detection and reduce the diagnosis of clinically insignificant disease compared with conventional systematic biopsy alone. [4–6]

Subsequent evidence reinforced this shift. The Cochrane systematic review and meta-analysis concluded that the MRI pathway has the most favorable diagnostic accuracy for clinically significant prostate cancer detection among contemporary biopsy strategies. Additional randomized screening studies also showed that MRI-informed pathways reduce overdiagnosis and unnecessary biopsy while maintaining acceptable detection of clinically significant disease. [7–10]

Alongside MRI, PSA density has emerged as one of the most useful adjunctive variables in biopsy decision-making. The EAU guideline notes that higher PSA density is associated with a higher probability of clinically significant prostate cancer and recommends integrating PSA density with MRI findings in risk-adapted biopsy strategies. Recent systematic reviews and gray-zone studies further support the complementary role of PSA density, particularly in negative or equivocal MRI settings. [1,11–14]

Therefore, the present study aimed to evaluate the diagnostic value of PSA screening combined with mpMRI in differentiating prostate cancer from benign prostatic lesions in patients with PSA levels of 4.0–10.0 ng/mL and to clarify the clinical significance of combining biochemical and imaging markers in this diagnostically challenging subgroup.

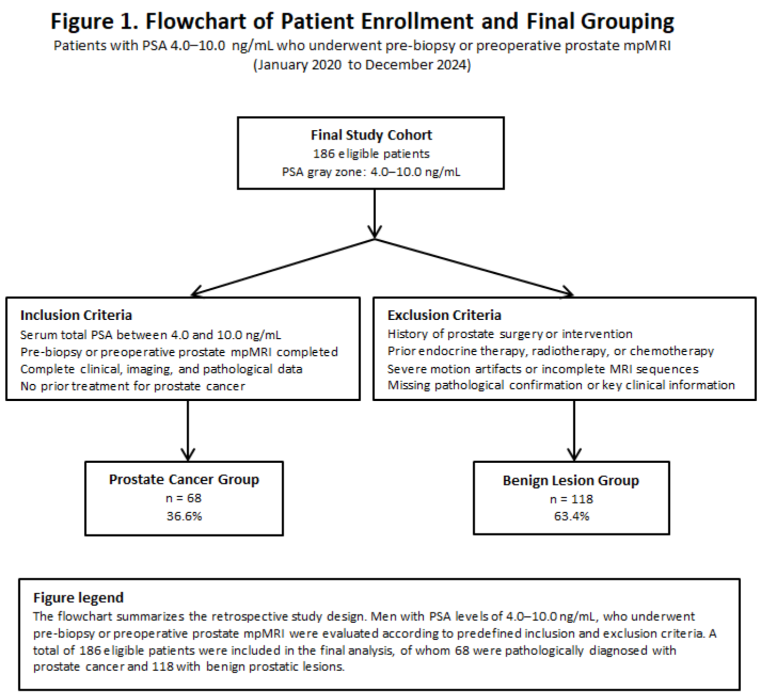
2. Materials and Methods

This retrospective study was conducted at Suzhou BOE Hospital, Suzhou, China, and Xinyang Central Hospital, Xinyang, China. It included consecutive patients who were evaluated for suspected prostate disease between January 2024 and December 2025. Eligible patients had serum prostate-specific antigen (PSA) levels within the diagnostic gray zone of 4.0 – 10.0 ng/mL and underwent prostate MRI before biopsy or surgery, followed by histopathological confirmation through prostate biopsy or surgical specimen analysis.

The study protocol was reviewed and approved by the Ethics Committee of Suzhou BOE Hospital (Approval No. 2025B0003) and was conducted in accordance with the Declaration of Helsinki. Owing to the retrospective design and anonymized analysis of clinical data, the requirement for written informed consent was waived by the ethics committee.

During the study period, patients with serum PSA levels of 4.0 – 10.0 ng/mL who underwent prostate MRI before biopsy or surgery were retrospectively reviewed. After application of the predefined inclusion and exclusion criteria, 186 patients were included in the final analysis, including 68 patients in the prostate cancer group and 118 patients in the benign lesion group. The patient selection and final grouping process are summarized in Figure 1.

Figure 1. Flowchart of Patient Enrollment and Final Grouping



Clinical and laboratory information was obtained from the hospital information system and electronic medical records. The variables collected for analysis included age, total PSA (tPSA), free PSA (fPSA), the free-to-total PSA ratio (f/tPSA), prostate volume, and PSA density (PSAD). Prostate volume was calculated using the standard ellipsoid formula based on imaging measurements, and

PSAD was defined as the serum total PSA level divided by prostate volume. These parameters were selected because they represent the most commonly used clinical indicators for assessing prostate cancer risk in men with borderline PSA levels. In particular, PSAD has gained increasing importance in contemporary MRI-based diagnostic pathways, as it adjusts PSA values according to gland size and is considered one of the most useful adjunctive predictors in biopsy decision-making [1,11,12].

All patients underwent prostate mpMRI using a 3.0T MRI scanner equipped with a phased-array pelvic coil. The standardized imaging protocol included axial, sagittal, and coronal T2-weighted imaging, diffusion-weighted imaging (DWI) with multiple b values (0, 800, and 1400 s/mm^2), and corresponding apparent diffusion coefficient (ADC) maps. Dynamic contrast-enhanced imaging was additionally performed in selected cases according to institutional routine and clinical indications. These sequences were chosen because they provide complementary anatomical and functional information regarding lesion morphology, tissue cellularity, and diffusion restriction, and their diagnostic utility has been well established in PI-RADS-based prostate MRI assessment [4]. All mpMRI examinations were independently reviewed by two radiologists with more than 8 years of experience in genitourinary imaging. Suspicious lesions were evaluated according to the Prostate Imaging Reporting and Data System version 2.1 (PI-RADS v2.1). When multiple lesions were present, the lesion with the highest PI-RADS score was selected for analysis, as it was considered most representative of the patient' s highest malignant risk. PI-RADS v2.1 was adopted in this study because it improves standardization of image interpretation, reduces ambiguity in lesion assessment, and facilitates more consistent risk stratification across readers [4].

Histopathological diagnosis was used as the reference standard for determining the presence or absence of prostate cancer. Tissue specimens were obtained through transrectal or transperineal prostate biopsy, including systematic biopsy and/or targeted biopsy guided by mpMRI findings. In a subset of patients, postoperative pathological specimens were also available and were incorporated into the final pathological assessment. According to the histopathological results, patients were divided into a prostate cancer group and a benign lesion group. Benign pathological findings included benign prostatic hyperplasia, chronic prostatitis, inflammatory lesions, and other nonmalignant conditions. The primary objective of the study was to compare the diagnostic performance of PSA-derived indicators alone with that of PSA screening combined with mpMRI in differentiating prostate cancer from benign prostatic lesions in patients within the PSA gray zone. The main outcome measures included sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall diagnostic accuracy. A secondary objective was to determine whether PSAD and PI-RADS score could serve as independent predictors of malignancy in this patient population.

Statistical analyses were performed using SPSS version 27.0 and MedCalc version 22.0. Continuous variables were expressed as mean ± standard deviation and compared using the independent-samples t test. Categorical variables were presented as frequencies and percentages and compared using the chi-square test. Variables showing statistical significance in univariate comparisons or considered clinically relevant, including age, fPSA, f/tPSA, prostate volume, PSAD, ADC value, and PI-RADS score, were entered into multivariate logistic regression analysis to identify independent predictors of prostate cancer. A combined diagnostic model was then constructed on the basis of the multivariate logistic regression equation incorporating the retained predictors. The predicted probability generated from this model was used for ROC curve analysis. The optimal cutoff value for the combined model was determined according to the maximum Youden index. Sensitivity, specificity, positive predictive value, negative predictive value, and overall accuracy were calculated accordingly. AUCs were compared using the DeLong test where appropriate. A two-sided P value < 0.05 was considered statistically significant.

3. Results

3.1 General Clinical Characteristics

A total of 186 eligible patients with PSA levels ranging from 4.0 to 10.0 ng/mL were included in the final analysis. Based on histopathological diagnosis, 68 patients (36.6%) were assigned to the prostate cancer group and 118 patients (63.4%) to the benign lesion group. The mean age of the overall cohort was 67.3 ± 7.7 years.

Compared with the benign lesion group, the prostate cancer group showed significantly older age (69.4 ± 7.1 vs 66.1 ± 7.8 years, P = 0.004), lower free PSA (0.86 ± 0.24 vs 1.08 ± 0.31 ng/mL, P < 0.001), lower f/tPSA ratio (0.119 ± 0.031 vs 0.160 ± 0.042, P < 0.001), smaller prostate volume (42.6 ± 13.5 vs 58.7 ± 18.9 mL, P < 0.001), and higher PSAD (0.176 ± 0.054 vs 0.121 ± 0.038 ng/mL/cc, P < 0.001). However, total PSA levels did not differ significantly between the two groups (7.21 ± 1.58 vs 6.93 ± 1.47 ng/mL, P = 0.216).

3.2 Comparison of mpMRI Findings Between the Two Groups

mpMRI revealed clear differences in imaging characteristics between pathologically confirmed malignant and benign lesions. Patients in the prostate cancer group more frequently demonstrated focal low signal intensity on T2-weighted imaging, marked diffusion restriction on DWI, lower ADC values, and higher PI-RADS scores.

The mean ADC value in the prostate cancer group was $0.82 \pm 0.14 \times 10^{-3}$ mm^2/s, which was significantly lower than that in the benign lesion group ($1.09 \pm 0.18 \times 10^{-3}$ mm^2/s, P < 0.001). The distribution of PI-RADS categories also differed significantly between the two groups (χ^2 = 31.84, P < 0.001). In the prostate cancer group, 8 patients (11.8%) had PI-RADS 1–2 lesions, 16 (23.5%) had PI-RADS 3 lesions, and 44 (64.7%) had PI-RADS 4–5 lesions. In the benign lesion group, the corresponding numbers were 50 (42.4%), 42 (35.6%), and 26 (22.0%), respectively.

3.3 Diagnostic Performance of PSA-Derived Indicators Alone

ROC analysis showed that among PSA-derived indicators, PSAD had the best diagnostic performance for differentiating prostate cancer from benign lesions in the PSA gray zone, with an AUC of 0.79 (95% CI: 0.72–0.85), followed by f/tPSA with an AUC of 0.72 (95% CI: 0.65–0.79). The AUC of tPSA alone was only 0.58 (95% CI: 0.49–0.66), indicating limited discriminatory ability.

At the optimal cutoff value of 0.145 ng/mL/cc, PSAD yielded a sensitivity of 77.9% and a specificity of 72.9%. At the cutoff value of 0.135, f/tPSA yielded a sensitivity of 70.6% and a specificity of 66.1%. By contrast, tPSA at a cutoff value of 7.10 ng/mL yielded a sensitivity of 61.8% and a specificity of 52.5%.

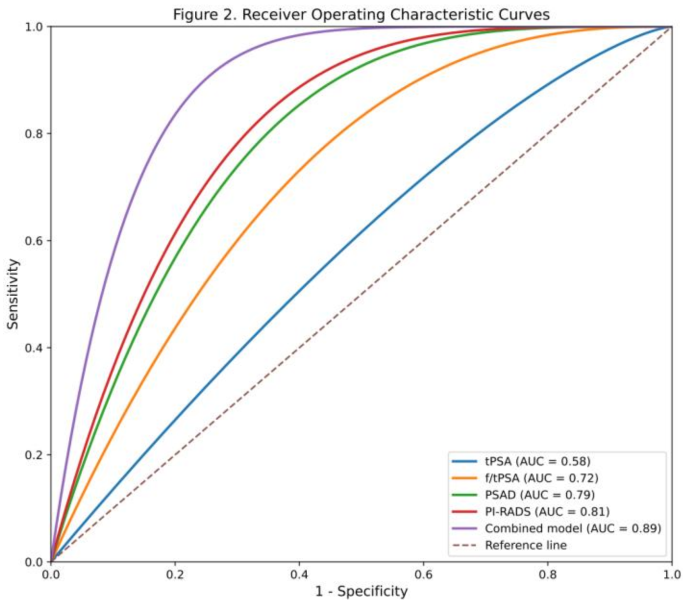
3.4 Diagnostic Performance of mpMRI

For mpMRI alone, using PI-RADS ≥4 as the diagnostic threshold, the AUC for detecting prostate cancer was 0.81 (95% CI: 0.75 – 0.87), with sensitivity, specificity, PPV, and NPV of 64.7%, 78.0%, 62.9%, and 79.3%, respectively.

3.5 Diagnostic Performance of PSA Screening Combined with mpMRI

The combined diagnostic model integrating PSAD, f/tPSA, and PI-RADS score achieved superior diagnostic efficacy compared with either approach used alone. The combined model yielded an AUC of 0.89 (95% CI: 0.84 – 0.94). At the optimal predicted probability threshold of 0.39, the combined model achieved a sensitivity of 82.4%, specificity of 84.7%, PPV of 75.7%, NPV of 89.3%, and overall accuracy of 83.9%.The ROC curves of individual indicators and the combined model are shown in Figure 2.

Figure 2. Receiver Operating Characteristic Curves of tPSA, f/tPSA, PSAD, PI-RADS, and the Combined Diagnostic Model



3.6 Multivariate Logistic Regression Analysis

Variables with statistical significance in univariate analysis, including age, free PSA, f/tPSA, prostate volume, PSAD, ADC value, and PI-RADS score, were entered into multivariate logistic regression. The results showed that PSAD ≥0.145 ng/mL/cc (OR = 3.84, 95% CI: 1.89 – 7.81, P < 0.001) and

PI-RADS ⩾4 (OR = 5.27, 95% CI: 2.63 – 10.56, P < 0.001) were independent predictors of prostate cancer in patients with PSA levels of 4.0 – 10.0 ng/mL. Age and f/tPSA did not retain independent statistical significance after adjustment (P = 0.091 and P = 0.074, respectively).

Table 1. Comparison of Clinical and Imaging Characteristics Between the Prostate Cancer Group and the Benign Lesion Group

Variable	**Prostate cancer group (n = 68)**	**Benign lesion group (n = 118)**	**Statistic**	**P value**
Age (years)	69.4 ± 7.1	66.1 ± 7.8	t = 2.88	0.004
Total PSA (ng/mL)	7.21 ± 1.58	6.93 ± 1.47	t = 1.24	0.216
Free PSA (ng/mL)	0.86 ± 0.24	1.08 ± 0.31	t = -5.25	<0.001
f/tPSA	0.119 ± 0.031	0.160 ± 0.042	t = -7.11	<0.001
Prostate volume (mL)	42.6 ± 13.5	58.7 ± 18.9	t = -6.42	<0.001
PSA density (ng/mL/cc)	0.176 ± 0.054	0.121 ± 0.038	t = 7.56	<0.001
ADC value ($\times 10^{-3}$ mm²/s)	0.82 ± 0.14	1.09 ± 0.18	t = -10.36	<0.001
PI-RADS 1–2, n (%)	8 (11.8)	50 (42.4)	χ^2 = 31.84	<0.001
PI-RADS 3, n (%)	16 (23.5)	42 (35.6)		
PI-RADS 4–5, n (%)	44 (64.7)	26 (22.0)		

Note: Continuous variables are presented as mean ± SD. ADC = apparent diffusion coefficient; PI-RADS = Prostate Imaging Reporting and Data System.

Table 2. Diagnostic Performance of PSA-Derived Indicators, mpMRI, and the Combined Model

Model / Variable	**Cutoff / Criterion**	**AUC (95% CI)**	**Sensitivity (%)**	**Specificity (%)**	**PPV (%)**	**NPV (%)**	**Accuracy (%)**	**Youden index**
tPSA	≥7.10 ng/mL	0.58 (0.49–0.66)	61.8	52.5	42.9	70.5	55.9	0.143
f/tPSA	≤0.135	0.72 (0.65–0.79)	70.6	66.1	54.5	79.6	67.7	0.367
PSAD	≥0.145 ng/mL/cc	0.79 (0.72–0.85)	77.9	72.9	62.4	85.1	74.7	0.508
PI-RADS	≥4	0.81 (0.75–0.87)	64.7	78.0	62.9	79.3	73.1	0.427
Combined model	Predicted probability ≥0.39	0.89 (0.84–0.94)	82.4	84.7	75.7	89.3	83.9	0.671

Note: AUC = area under the receiver operating characteristic curve; PPV = positive predictive value; NPV = negative predictive value; PSAD = PSA density.

4. Discussion

The present study addressed a common yet diagnostically challenging clinical scenario: men with serum PSA levels in the diagnostic gray zone of 4.0 – 10.0 ng/mL. In this subgroup, the interpretation of PSA results is often complicated by the substantial overlap between malignant and benign prostatic conditions. Although PSA remains the cornerstone of prostate cancer screening, it is now widely recognized that PSA alone lacks sufficient specificity for biopsy decision-making in men with borderline PSA elevations. Reflecting this shift, current international guidelines no longer advocate biopsy decisions based solely on PSA in this setting. The European Association of Urology recommends repeat PSA testing and the use of MRI or validated risk-adapted tools in men with PSA levels of 3 – 10 ng/mL, while the AUA/SUO guideline similarly emphasizes confirmation of a newly elevated PSA result before proceeding to additional biomarkers, imaging, or biopsy. [1 – 3]

Our findings are consistent with this contemporary diagnostic framework. In the present cohort, total PSA alone showed limited discriminatory ability for distinguishing prostate cancer from benign prostatic disease, whereas PSAD and f/tPSA provided better diagnostic performance. This result is both biologically and clinically plausible. Total PSA is influenced by multiple factors, including gland enlargement, inflammation, infection, and urinary retention, all of which may occur in the absence of malignancy. By contrast, PSAD incorporates prostate volume into risk assessment and therefore partially corrects for PSA elevation caused by benign gland enlargement. Similarly, the f/tPSA ratio has long been considered a useful adjunctive marker for improving specificity in men with intermediate PSA levels. However, our results also suggest that neither PSAD nor f/tPSA should be interpreted in isolation. Existing evidence indicates that although f/tPSA may contribute to risk stratification, its performance as a standalone diagnostic tool remains modest, whereas PSAD tends to offer stronger and more stable predictive value, especially when used in combination with imaging-based assessment. [11,12,15,16]

The imaging findings observed in our study further reinforce the important role of mpMRI in the diagnostic pathway for men in the PSA gray zone. Patients with prostate cancer more frequently demonstrated lower ADC values, higher PI-RADS scores, and more suspicious lesion characteristics than patients with benign pathology. These findings are in accordance with the core principles of PI-RADS v2.1, which was designed to standardize prostate MRI interpretation and improve the identification of clinically significant lesions. The usefulness of MRI in this context is supported by multiple landmark studies. PROMIS demonstrated that mpMRI has superior sensitivity and negative predictive value compared with conventional transrectal ultrasound-guided biopsy, highlighting its value as a triage test before biopsy. PRECISION subsequently showed that MRI-targeted biopsy detects more clinically significant prostate cancers while reducing the diagnosis of clinically insignificant disease and lowering the number of unnecessary biopsy procedures. Moreover, the Cochrane meta-analysis concluded that MRI-informed diagnostic pathways provide the most favorable overall diagnostic accuracy among contemporary strategies for prostate cancer detection. [4 – 8]

For patients specifically located within the PSA gray zone, growing evidence supports the integration of MRI findings with PSA-derived clinical indicators, particularly PSAD. The 2024 systematic review by Guo et al. found that MRI has satisfactory diagnostic performance and a particularly high negative predictive value in men with PSA levels of 4 – 10 ng/mL, making it highly useful for excluding clinically significant disease in low-risk individuals. Wen et al. further demonstrated that combining PI-RADS v2.1 with PSAD significantly improves diagnostic performance over either parameter used alone in this subgroup. Similar findings were reported by Wei et al. and Liu et al., who showed that combining MRI findings with clinical variables improves prediction models and may reduce unnecessary biopsy in men with borderline PSA elevations. [11 – 14] Taken together, these studies, along with our present results, suggest that gray-zone PSA should not be interpreted as a purely biochemical problem, but rather as a clinical decision point requiring multidimensional assessment.

The most important finding of the present study is that the combined model incorporating PSAD, f/tPSA, and PI-RADS score outperformed any single variable. This result supports a broader clinical concept: biochemical markers and imaging parameters should be considered complementary rather than competitive. Each parameter reflects a different aspect of disease biology. PSA-derived variables provide indirect biochemical evidence of prostatic abnormality, whereas mpMRI offers direct structural and functional visualization of suspicious lesions. When these markers are combined, the resulting model appears to improve both diagnostic discrimination and risk stratification. From a practical perspective, this may be highly relevant in daily clinical decision-making. Patients with borderline PSA elevation but low PSAD and nonsuspicious MRI findings may be managed more conservatively, thereby avoiding unnecessary invasive procedures and their associated complications. Conversely, men with elevated PSAD and PI-RADS 4 – 5 lesions may be prioritized for biopsy because their probability of clinically significant cancer is substantially higher. This interpretation is also in line with the EAU risk-adapted framework, which links PI-RADS categories with PSAD thresholds such as 0.10, 0.15, and 0.20 ng/mL/cc to refine biopsy indications. [1,11,12]

Another clinically relevant implication of our findings is that the combined approach may improve the balance between cancer detection and unnecessary biopsy. One of the main limitations of PSA-based evaluation in gray-zone patients is that mildly elevated PSA levels may trigger biopsy even in men with benign conditions. By integrating MRI findings with PSAD and f/tPSA, clinicians may better distinguish patients who are more likely to harbor prostate cancer from those with benign lesions, thereby improving diagnostic efficiency and reducing avoidable invasive procedures.

Several limitations of this study should be acknowledged. First, the retrospective and two-center design may introduce selection bias and limit the generalizability of the findings. Second, the sample size, although adequate for preliminary evaluation, remains moderate and may not fully capture the heterogeneity of gray-zone patients encountered in broader clinical practice. Third, variation in MRI acquisition parameters, radiologist experience, and biopsy technique may influence diagnostic performance estimates. Fourth, biopsy-based histopathology may underestimate tumor burden or miss clinically significant lesions in some cases, particularly in patients who did not undergo prostatectomy. Finally, although the present study demonstrates the superiority of a combined model, its findings should ideally be validated in larger, prospective, multicenter cohorts and, where possible, compared with nomogram-based or artificial intelligence-assisted risk prediction models.

Despite these limitations, the present study provides further support for the growing consensus that men with PSA values in the gray zone should not be evaluated on the basis of total PSA alone. Instead, a multimodal diagnostic pathway integrating PSA-derived variables and mpMRI appears more consistent with current evidence, modern guideline recommendations, and the principles of individualized medicine. Our results therefore add to the growing body of literature supporting MRI-informed, PSAD-aware risk stratification in the early evaluation of suspected prostate cancer.

5. Conclusion

In patients with PSA levels in the gray zone of 4.0 – 10.0 ng/mL, total PSA alone has limited diagnostic value for reliably distinguishing prostate cancer from benign prostatic disease, largely because of the considerable overlap in PSA elevation caused by malignancy, benign prostatic hyperplasia, and inflammatory conditions. The findings of the present study suggest that a diagnostic strategy combining PSA screening with multiparametric magnetic resonance imaging offers superior performance compared with any single PSA-derived indicator alone. In particular, the combined assessment of PSA density, free-to-total PSA ratio, and PI-RADS score appears to provide a more practical, accurate, and clinically meaningful approach for identifying patients at increased risk of prostate cancer and for guiding biopsy decision-making in this diagnostically challenging population.

The clinical significance of this combined strategy lies not only in its improved diagnostic accuracy, but also in its potential to optimize patient management. By integrating biochemical markers with imaging-based risk stratification, clinicians may be better able to distinguish men who are likely to benefit from immediate biopsy from those who may be safely monitored or undergo further follow-up evaluation. In this way, the use of PSA-derived indicators together with mpMRI may help reduce unnecessary invasive procedures in low-risk patients, while improving the identification of men who are more likely to harbor prostate cancer requiring timely intervention.

From a broader perspective, these findings support the growing trend toward more individualized and evidence-based diagnostic pathways in prostate cancer detection. Rather than relying on total PSA alone, the incorporation of PSAD, f/tPSA, and PI-RADS score into a combined risk assessment model may represent an important step toward more refined clinical decision-making in men with borderline PSA elevations. Such an approach is more consistent with current risk-adapted diagnostic concepts and may contribute to improved allocation of medical resources, reduced overdiagnosis, and better overall patient care.

Nevertheless, the present findings should be interpreted with appropriate caution. Because this study was conducted retrospectively at only two center, further validation in larger, prospective, multicenter cohorts is needed. Future studies should also explore the integration of additional biomarkers, nomograms, and artificial intelligence-assisted imaging analysis to further enhance diagnostic precision and improve the clinical applicability of combined models. Despite these limitations, the present study provides supportive evidence that PSA screening combined with mpMRI has promising value in the differential diagnosis and risk stratification of prostate cancer in patients within the PSA gray zone and may serve as a useful reference for optimizing clinical practice.

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