

Free-to-total PSA Ratio Predicts PSMA PET Uptake in Treatment-naïve Prostate Cancer

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Abstract

Objective

Prostate cancer (PCa) is a common malignancy worldwide, and PSMA PET/CT is increasingly used for initial staging and treatment guidance. However, its high cost, radiation exposure, and variable PSMA expression necessitate better patient selection. This study aimed to identify clinical and imaging factors associated with PSMA PET uptake in primary PCa lesions and to evaluate the diagnostic performance of the free-to-total PSA ratio (FTpsa) for predicting PSMA PET positivity.

Methods

A retrospective analysis was conducted on 130 treatment-naïve PCa patients (median age 68 years) from two Chinese centers who underwent ^{68}Ga -PSMA-11 PET/CT and mpMRI. PSMA PET uptake was quantified by SUVmax and PRIMARY score (1–2: negative; 3–5: positive). Spearman correlation, Mann-Whitney U test, multivariate logistic regression, and ROC curve analysis were performed.

Results

PRIMARY score was positive (> 2) in 115 patients (88.5%) and negative in 15 (11.5%). FTpsa ($P = 0.033$) and Gleason score ($P = 0.002$) were independent predictors of PRIMARY positivity. The optimal FTpsa cut-off was 0.09 (AUC = 0.713). At this cut-off, for predicting PSMA PET positivity (FTpsa > 0.09), sensitivity was 100%, specificity 41.7%, positive predictive value (PPV) 92.9%, and negative predictive value (NPV) 100%. For predicting negativity (FTpsa ≤ 0.09), NPV was equally 100%, but PPV dropped to 18.3%. In PI-RADS 3 patients ($n = 75$), 12% had PRIMARY-negative lesions. FTpsa ≤ 0.09 reliably excluded PSMA-avid tumors (NPV = 100%), while FTpsa > 0.09 indicated a 92.9% probability of positivity.

Conclusion

FTpsa is an independent non-invasive predictor of PSMA PET status in primary PCa. A cut-off of 0.09 provides 100% NPV, enabling safe deferral of PSMA PET in PI-RADS 3 patients with low FTpsa. This simple serum marker can help optimize PSMA PET referral and reduce unnecessary biopsies.

Introduction

Prostate cancer ranks among the most prevalent malignancies in males globally, with a continuously rising incidence in China. Early diagnosis and risk stratification are critical for formulating personalized therapeutic strategies^[1, 2]. Traditional clinical workup relies on serum prostate-specific antigen (PSA), multiparametric magnetic resonance imaging (mpMRI), and prostate biopsy.^[3] Nevertheless, PSA has

limited specificity and inevitably leads to overdiagnosis. PI-RADS 3 indeterminate lesions on mpMRI often bring clinical dilemma regarding biopsy indication, while PI-RADS 4–5 lesions still have false-positive results, resulting in unnecessary biopsies^[4]. Therefore, reliable noninvasive predictive tools are urgently needed to optimize biopsy decision-making.

In recent years, ⁶⁸Ga-PSMA-11 PET/CT has emerged as a pivotal imaging modality for tumor staging, recurrence surveillance, and treatment guidance, owing to its high sensitivity for primary and metastatic prostate cancer lesions^[5, 6]. Its diagnostic efficacy is superior to conventional imaging, especially in intermediate- and high-risk PCa patients. However, PSMA PET/CT is expensive, accompanied by ionizing radiation exposure, and some low-grade tumors present PSMA-negative expression^[7, 8]. How to precisely screen candidates who can benefit most from PSMA PET/CT remains an unmet clinical need.

At present, clinicopathological determinants of PSMA PET uptake intensity in primary PCa lesions have not been fully clarified. Several studies have reported that Gleason score, serum PSA level, and MRI apparent diffusion coefficient (ADC) value are correlated with PSMA expression^[9, 10]. However, evidence-based noninvasive biomarkers for predicting PSMA PET positivity to guide PSMA PET referral or immediate biopsy are still lacking.

Accordingly, this study retrospectively analyzed ⁶⁸Ga-PSMA-11 PET/CT and clinical data of newly diagnosed PCa patients. We aimed to explore clinicopathological factors associated with PSMA uptake (SUVmax and PRIMARY score) in primary lesions, identify optimal cutoff values of noninvasive indicators for predicting PSMA PET positivity, and provide evidence for optimizing PSMA PET indications and precise clinical risk stratification.

Materials and Methods

Study Population

From January 2024 to December 2025, a total of 130 patients pathologically confirmed with prostate cancer via prostate biopsy or radical prostatectomy were retrospectively enrolled from the First Affiliated Hospital of Bengbu Medical University and Ruijin Hospital Affiliated to Shanghai Jiao Tong University School of Medicine. Gleason grading was performed according to the International Society of Urological Pathology (ISUP) criteria. Tumor location was classified as peripheral zone or transition zone. Inclusion criteria: (1) Patients with complete clinical, pathological, multiparametric magnetic resonance imaging (mpMRI), and ⁶⁸Ga-PSMA-11 PET/CT data; (2) No prior anti-tumor treatment for prostate cancer before imaging examination, including surgery, radiotherapy, androgen deprivation therapy, or chemotherapy; (3) Available data on age, serum total PSA (tPSA) and free PSA (fPSA), with the free-to-total PSA ratio calculable.

⁶⁸Ga-PSMA-11 PET/CT Imaging

All patients underwent whole-body ^{68}Ga -PSMA-11 PET/CT examination. The radiotracer was intravenously injected at a dose of 1.8–2.2 MBq/kg. Whole-body scanning was performed after a 60-min uptake period. Image reconstruction was completed on a dedicated workstation. All images were independently interpreted by two associate chief physicians of nuclear medicine; discrepancies were resolved by consensus discussion. A region of interest (ROI) was delineated on the maximal cross-section of the primary lesion, and SUVmax was recorded. Primary prostate lesions were graded according to the PRIMARY scoring system: scores of 1–2 were defined as PSMA PET-negative (low uptake), and scores of 3–5 as PSMA PET-positive (high uptake).

mpMRI Examination and Quantitative Analysis

Prostate mpMRI was performed using a unified 3.0 T MRI scanner across the two centers, including T2-weighted imaging (T2WI), diffusion-weighted imaging (DWI, $b = 0, 800, 1400 \text{ s/mm}^2$), and dynamic contrast-enhanced (DCE) sequence. All mpMRI images were evaluated by an experienced abdominal radiologist blinded to pathological and PET results. Lesion classification followed PI-RADS v2.1 criteria: PI-RADS 3 was defined as indeterminate lesion, and PI-RADS 4–5 as highly suspicious for clinically significant prostate cancer (csPCa). The ROI was manually drawn on the maximal lesion slice of the ADC map, and the mean ADC (ADCmean, $\times 10^{-3} \text{ mm}^2/\text{s}$) was calculated.

Statistical Analysis

SPSS 26.0 software was used for statistical analysis. Continuous variables were presented as median (range) or mean $\pm$ standard deviation; categorical variables were described as case number (percentage). Spearman rank correlation was used for correlation analysis of continuous variables. The Mann-Whitney U test was adopted for intergroup comparison of non-normally distributed continuous variables, and the Chi-square test for categorical variables. Binary logistic regression was performed to screen independent predictive factors for PSMA PET positivity (PRIMARY score > 2), and the odds ratio (OR) with 95% confidence interval (CI) was calculated. ROC curve analysis was used to evaluate the diagnostic performance of F/T PSA ratio. A two-tailed $P < 0.05$ was considered statistically significant.

Results

Baseline Clinical Characteristics

A total of 130 patients with pathologically confirmed PCa were included in the study. Table 1 summarizes the baseline clinicopathological characteristics of the cohort. The median age was 68 years (range, 55–85 years). The median total PSA (tPSA) was 12.85 ng/mL (range, 1.39–346.00 ng/mL), and the median free PSA (fPSA) was 1.49 ng/mL (range, 0.29–35.40 ng/mL). The median fPSA/tPSA ratio was 0.10 (range, 0.04–0.35). The median tumor size was 15 mm (range, 5–60 mm). The median apparent diffusion coefficient (ADCmean) was $0.93 \times 10^{-3} \text{ mm}^2/\text{s}$ (range, $0.61\text{--}1.49 \times 10^{-3} \text{ mm}^2/\text{s}$), and the median maximum standardized uptake value (SUVmax) was 12.35 (range, 2.2–62.0). For

pathological and imaging classifications, Gleason score 7 was the most common (72 patients, 55.4%), followed by GS 6 (24, 18.5%), GS 8 (23, 17.7%), and GS 9 (11, 8.5%). PI-RADS scores were ≤ 3 in 75 patients (57.7%) and > 4 in 55 patients (42.3%). Most tumors were located in the peripheral zone (94, 72.3%), and the majority of patients had > 3 primary lesions (115, 88.5%).

Table.1. Characteristics of patients with prostate cancer

Variables	Median (minimum–maximum)	Variables	Number of cases
Age(years)	68(55–85)	Gleason Score	
PSA(ng/ml)	12.85(1.39–346.00)	6	24
fPSA(ng/ml)	1.49(0.29–35.40)	7	72
fPSA/PSA ratio	0.10(0.04–0.35)	8	23
Size(mm)	15(5–60)	9	11
ADCmean	0.93(0.61–1.49)	PI-RADS score	
SUVmax	12.35(2.2–62.0)	≤ 3	75
Variables	Number of cases	> 4	55
Tumor location		Primary lesion count	
Peripheral zone	94	≤ 2	15
Transition zone	36	> 3	115

Correlation Between Clinicopathological Features and SUVmax

Spearman correlation analysis showed that age, tPSA and fPSA were significantly positively correlated with SUVmax ($r = 0.176$, $r = 0.242$, $r = 0.184$, all $P < 0.05$). The F/T PSA ratio and ADCmean were significantly negatively correlated with SUVmax ($r = - 0.231$, $P = 0.009$; $r = - 0.229$, $P = 0.009$). Gleason score was positively correlated with SUVmax Prostate volume, PI-RADS category and tumor location showed no significant correlation with SUVmax (all $P > 0.05$). (Table 2). Subgroup analysis showed that SUVmax in GS 6 group was significantly lower than those in GS 7, GS 8 and GS 9 groups (all $P < 0.05$). No significant differences were found among GS 7, GS 8 and GS 9 subgroups (Fig. 1)

Table 2
Correlation between clinicopathological features and SUVmax of primary PCa lesions

Variables	Correlation	Pvalue	Variables	Correlation	Pvalue
Age	0.176	0.046	ADCmean	-0.229	0.009
PSA	0.242	0.006	GS	0.219	0.013
gfPSA	0.184	0.037	PI-RADS	-0.057	0.517
fPSA/PSA	-0.231	0.009	Location	-0.115	0.194
Size	0.066	0.454			

Comparison of Clinicopathological Features Between PRIMARY Positive and Negative Groups

A PRIMARY score ≤ 2 was defined as PSMA PET-negative, and a score > 2 was defined as PSMA PET-positive. Firstly, the proportion of PRIMARY-negative cases in different PI-RADS score groups was analyzed. Among 55 patients with PI-RADS 4–5, 6 cases had a PRIMARY score ≤ 2 , accounting for 10.9%. No significant difference was found in the PRIMARY negative rate between the two groups ($P = 0.847$) (Fig. 2, stacked column chart).

Further analyses are presented in Table 3. There were 15 patients (11.5%) in the PRIMARY-negative group and 115 patients (88.5%) in the PRIMARY-positive group. Comparison of clinicopathological parameters between the two groups showed that the free-to-total PSA ratio was significantly higher in the negative group than in the positive group (0.14 ± 0.05 vs. 0.11 ± 0.05 , $P = 0.007$). The distribution of Gleason score (GS) differed significantly between the two groups ($P = 0.003$): patients with $GS \leq 6$ accounted for 46.7% (7/15) in the negative group, whereas only 14.8% (17/115) in the positive group. No statistically significant differences were observed in other parameters, including age, total PSA, free PSA, prostate volume, ADCmean, PI-RADS score, and tumor location (peripheral zone vs. transition zone) between the two groups (all $P > 0.05$).

Table.2 Primary lesion score distribution by PI-RADS category, expressed as n (%).

Primary ≤ 2	PI-RADS 3	PI-RADS 4–5
	9(12%)	6(10.9%)
Primary > 2	66(88%)	49(89.1%)

Table 3
Patient characteristics stratified by primary lesion score.
Continuous data are shown as mean $\pm$ SD; categorical data as counts. P-values indicate between-group differences.

Variables	Primary(≤ 2)15	Primary(> 2)115	P value
Age	66.93 $\pm$ 5.23	68.92 $\pm$ 5.90	0.182
PSA	18.25 $\pm$ 26.48	33.79 $\pm$ 52.64	0.150
fPSA	2.31 $\pm$ 2.59	3.26 $\pm$ 5.45	0.548
fPSA/PSA	0.14 $\pm$ 0.05	0.11 $\pm$ 0.05	0.007
size	14.87 $\pm$ 6.45	17.79 $\pm$ 9.84	0.361
ADCmean	1.03 $\pm$ 0.14	0.93 $\pm$ 0.14	0.196
PI-RADS			0.847
≤ 3	9	66	
> 3	6	49	
GS			0.003
≤ 6	7	17	
> 7	8	98	
Location			0.257
peripheral zone	9	85	
transition zone	6	30	

Multivariate Logistic Regression Analysis

Multivariate logistic regression confirmed that F/T PSA ratio ($P = 0.033$) and Gleason score ($P = 0.002$) were independent predictors of PRIMARY positivity. A higher F/T PSA ratio correlated with lower probability of PSMA PET positivity, while a higher Gleason score correlated with higher PSMA PET positivity.(table.4)

Table 4
Multivariate logistic regression analysis for predicting PSMA PET positivity

	B	Significance	Exp(B)	95% confidence interval for EXP(B)	
				Lower limit	Upper limit
FTpsa	-10.764	0.033	2.1×10^{-5}	0.000	0.
GS	1.492	0.002	4.445	1.754	11.267

Diagnostic Efficacy of F/T PSA Ratio

ROC curve analysis (Fig. 3) showed that the AUC of the free/total PSA (F/T PSA) ratio for predicting PSMA PET positivity was 0.713, with an optimal cut-off value of 0.09 determined by the Youden index. Using F/T PSA ratio > 0.09 to predict PSMA PET positivity yielded a sensitivity of 100%, specificity of 41.7%, positive predictive value of 92.9%, and negative predictive value of 100%. The corresponding diagnostic parameters for F/T PSA ratio ≤ 0.09 in predicting PSMA PET negativity were 100%, 41.7%, 18.3%, and 100%(table.5), respectively. For the prediction of primary lesion PSMA uptake on PET imaging, an F/T PSA ratio < 0.09 presented a high negative predictive value.

Table 5
Diagnostic efficacy of F/T PSA ratio (cutoff = 0.09) in predicting PSMA PET status

PSMA PET	Sensitivity	Specificity	PPV	NPV
Predicting PSMA PET negativity	100%	41.7%	18.3%	100%
Predicting PSMA PET positivity	100%	41.7%	92.9%	100%

Discussion

This study retrospectively analyzed clinical, pathological, mpMRI and ⁶⁸Ga-PSMA-11 PET/CT data of 130 newly diagnosed PCa patients. We explored influencing factors of primary lesion PSMA uptake and evaluated the diagnostic value of F/T PSA ratio. The main findings were as follows: (1) Age, tPSA, fPSA, F/T PSA ratio, ADCmean and Gleason score were significantly correlated with SUVmax; (2) F/T PSA ratio and Gleason score were independent predictors of PRIMARY score stratification (≤ 2 vs > 2). At the cutoff of 0.09, F/T PSA ratio achieved 100% NPV for predicting PSMA PET positivity, providing important guidance for clinical decision-making especially in PI-RADS 3 patients.

In the present study, age, tPSA and fPSA were positively correlated with SUVmax, while F/T PSA ratio and ADCmean were negatively correlated with SUVmax. Gleason score was positively correlated with SUVmax, reflecting the complex regulation of PSMA expression by tumor biological behaviors including proliferation activity, hypoxia and androgen signaling pathway.

Nevertheless, SUVmax has obvious limitations in clinical application. The SUVmax ranged widely from 2.2 to 62.0 in this cohort. Although SUVmax differed across Gleason subgroups, obvious value overlap existed. SUVmax in GS 6 was significantly lower than GS 7–9, while no statistical difference was found among GS 7, 8 and 9. Previous studies have confirmed that benign prostate tissue and inflammatory lesions can also show moderate PSMA uptake (SUVmax 5–15), making it difficult to establish a unified benign-malignant cutoff^[11]. Therefore, it is unreliable to depend solely on SUVmax for diagnosis, and more stable evaluation tools are required.

Consistent with the correlation trend in our study, a retrospective study focusing on biochemically recurrent prostate cancer confirmed a significant positive correlation between lymph node lesion size

and PSMA tracer uptake, indicating that larger metastatic lesions tended to present higher SUVmax^[12].

It has been confirmed that neoadjuvant ADT can significantly reduce serum PSA level and PSMA uptake of primary and lymph node lesions. Gleason score and ISUP grade were closely related to the metabolic response and disease progression after treatment, further verifying that pathological grading is an important influencing factor of PSMA expression and tracer uptake^[13].

Another clinical study compared the diagnostic efficacy of PSMA PET/CT, mpMRI, PSA and SUVmax in evaluating seminal vesicle invasion, extraprostatic extension and lymph node metastasis. Although SUVmax was positively correlated with PSA, neither indicator could effectively distinguish patients with local invasion or lymph node metastasis. Only a marginal trend was observed between SUVmax and pathological invasion status, further confirming that SUVmax alone has limited reliability in clinical diagnosis and risk stratification^[14].

The PRIMARY score, established by Emmett et al. in the 2021 prospective PRIMARY trial, is a standardized semi-quantitative scoring system for primary prostate lesions on PSMA PET/CT^[15, 16]. It integrates PSMA uptake pattern and anatomical localization into five grades. PRIMARY 1–2 indicates high possibility of benign lesions, serving as a safe threshold to avoid unnecessary biopsy; PRIMARY 3–5 corresponds to gradually increased risk of csPCa, and PRIMARY 5 reaches nearly 100% PPV. Real-world studies have verified its good reproducibility and diagnostic accuracy. Currently, PRIMARY score has been incorporated into PROMISE v2 criteria and recommended for intraprostatic lesion interpretation.^[17]

In this study, PRIMARY 1–2 was defined as PSMA PET-negative, and 3–5 as positive. The positive rate was 88.5% (115/130), and the negative rate was 11.5% (15/130). Multivariate regression confirmed that F/T PSA ratio ($P = 0.033$) and Gleason score ($P = 0.002$) were independent influencing factors. Low F/T PSA ratio combined with high Gleason score constituted the phenotypic basis of high PSMA uptake. With the increase of F/T PSA ratio, the positive rate of primary lesion PSMA PET gradually decreased, suggesting good clinical application potential of this noninvasive serum marker.

Further ROC analysis showed AUC = 0.713 and optimal cutoff = 0.09. Notably, F/T PSA ratio achieved 100% NPV for predicting PRIMARY positivity. Although the specificity was moderate, this cutoff minimized false-negative results and helped rationalize PSMA PET referral. Clinically, PI-RADS 3 patients face a typical dilemma: immediate biopsy brings unnecessary trauma and overdiagnosis, whereas simple follow-up may delay csPCa diagnosis. The F/T PSA cutoff of 0.09 provides a quantifiable stratification indicator for this population. When F/T PSA ratio < 0.09, the probability of high PSMA uptake reaches 92.9%, and active PSMA PET/CT is recommended. If PSMA PET is still negative, the probability of csPCa is relatively low. When F/T PSA ratio ≥ 0.09 , the risk of PRIMARY negativity increases, and the proportion of low PSMA uptake tumors rises obviously. For such patients, close surveillance combined with digital rectal examination (DRE) and prostate health index (PHI) is still necessary even if PSMA PET is negative, to avoid missed diagnosis of csPCa.

The dynamic stratification strategy combining serological indicators, clinical signs and PI-RADS imaging can reduce overdiagnosis and overtreatment, and accurately screen high-risk patients requiring active intervention^[18].

Although Gleason score is a strong independent predictor (OR = 4.445), it relies on invasive biopsy and cannot be used for preoperative screening. For confirmed PCa patients, GS ≥ 7 had significantly higher PSMA uptake than GS 6, which still has clinical value^[19]. Patients with high Gleason score are more suitable for PSMA PET staging to guide surgical or radiotherapy planning. For newly diagnosed GS 6 patients with F/T PSA ratio ≥ 0.09 , PSMA PET false-negative risk is elevated, which requires cautious clinical interpretation^[20].

The present study has several limitations. All patients were pathologically confirmed, and the screening value of the cutoff in undiagnosed populations could not be evaluated. Second, the overall sample size was relatively small (n = 130), and the PRIMARY-negative subgroup only included 15 cases, which may affect the stability of multivariate regression results^[21].

Conclusion

The F/T PSA ratio is an independent noninvasive predictor of PSMA PET uptake status in primary prostate cancer. The optimal cutoff of 0.09 yields 100% NPV for predicting PRIMARY positivity. For PI-RADS 3 patients, this cutoff enables quantitative clinical stratification: patients with F/T PSA ratio < 0.09 are highly suggestive of high PSMA uptake and should receive prompt PSMA PET/CT; those with F/T PSA ratio ≥ 0.09 have elevated false-negative risk of PSMA PET and need comprehensive evaluation combining DRE, PHI and other indicators to avoid delayed csPCa diagnosis. The combined stratification model integrating serum markers, clinical signs and mpMRI PI-RADS can reduce unnecessary biopsy and overtreatment, and precisely identify high-risk populations needing clinical intervention.

Declarations

Ethics approval

This study was approved by the Ethics Committee (Approval Nr. LY2023-214-C).

Consent for publication

Informed consent was waived for all participants due to the retrospective nature of this study.

Data availability

The datasets generated and analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors have no relevant financial or non-financial interests to disclose.

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Author contributions

All authors contributed to the conception and design of this study. SH was responsible for patient recruitment. ZX and HYQ performed data collection and analysis. ZZ and YL drafted the original manuscript. WXY, XJY, and ZYF revised and polished the manuscript. All authors provided comments on the revised versions, and read and approved the final manuscript

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References

1. Raychaudhuri R, Lin DW, Montgomery RB. Prostate Cancer Jama, 2025. 333(16).
2. Litwin MS, Tan H-J. The Diagnosis and Treatment of Prostate Cancer. JAMA, 2017. 317(24).
3. Nguyen-Nielsen M, Borre M. Diagnostic and Therapeutic Strategies for Prostate Cancer. Semin Nucl Med. 2016;46(6):484–90.
4. Goh V, PI-RADS, Multiparametric MRI. The Shape of Things to Come for Prostate Cancer. Radiology, 2023. 307(4).
5. Algin E, et al. Impact of 68Ga-PSMA PET/CT on Survival and Management in Prostate Cancer. Current Medical Imaging Formerly Current Medical Imaging Reviews; 2024. p. 20.
6. Barakat A et al. Role of Early PET/CT Imaging with 68Ga-PSMA in Staging and Restaging of Prostate Cancer. Sci Rep, 2020. 10(1).
7. Houshmand S, Lawhn-Heath C, Behr S. PSMA PET imaging in the diagnosis and management of prostate cancer. Abdom Radiol. 2023;48(12):3610–23.
8. Farolfi A, et al. Current and Emerging Clinical Applications of PSMA PET Diagnostic Imaging for Prostate Cancer. J Nucl Med. 2021;62(5):596–604.
9. Cao R, et al. Joint Prostate Cancer Detection and Gleason Score Prediction in mp-MRI via FocalNet. IEEE Trans Med Imaging. 2019;38(11):2496–506.

10. Goldstein MR, Mascitelli L, Screening PSA. and Prostate Cancer Mortal Jama, 2024. 332(10).
11. Guo S, et al. Avoiding unnecessary biopsy: the combination of PRIMARY score with prostate-specific antigen density for prostate biopsy decision. Prostate Cancer Prostatic Dis. 2023;27(2):288–93.
12. Pepe P, et al. PSMA PET/CT Accuracy in Diagnosing Prostate Cancer Nodes Metastases. Vivo. 2024;38(6):2880–5.
13. Deniz ME, et al. PSMA PET/CT and Multiparametric MRI in Assessing Local Extension and Lymph Node Metastasis in Prostate Cancer. Int J Urol. 2025;32(12):1866–72.
14. Onal C, et al. The effect of androgen deprivation therapy on 68Ga-PSMA tracer uptake in non-metastatic prostate cancer patients. Eur J Nucl Med Mol Imaging. 2019;47(3):632–41.
15. Guo S, et al. The PRIMARY Score. Clin Nucl Med. 2024;49(1):37–44.
16. Kabasakal L, Turkay R, Onal B. Incorporating the [68Ga]Ga-PSMA PET/CT PRIMARY score into the selection criteria for prostate cancer patients eligible for active surveillance. Eur J Nucl Med Mol Imaging. 2024;51(5):1464–6.
17. Emmett LM et al. The PRIMARY Score: Using intra-prostatic PSMA PET/CT patterns to optimise prostate cancer diagnosis. J Nucl Med, 2022.
18. Anyango R, et al. Diagnostic accuracy of [-2]proPSA versus Gleason score and Prostate Health Index versus Gleason score for the determination of aggressive prostate cancer: a systematic review. JBI Evid Synthesis. 2021;19(6):1263–91.
19. Swanson GP, et al. Gleason Score Evolution and the Effect on Prostate Cancer Outcomes. Am J Clin Pathol. 2021;155(5):711–7.
20. Epstein JI, et al. A Contemporary Prostate Cancer Grading System: A Validated Alternative to the Gleason Score. Eur Urol. 2016;69(3):428–35.
21. Sandhu S, et al. Prostate cancer. Lancet. 2021;398(10305):1075–90.

Figures

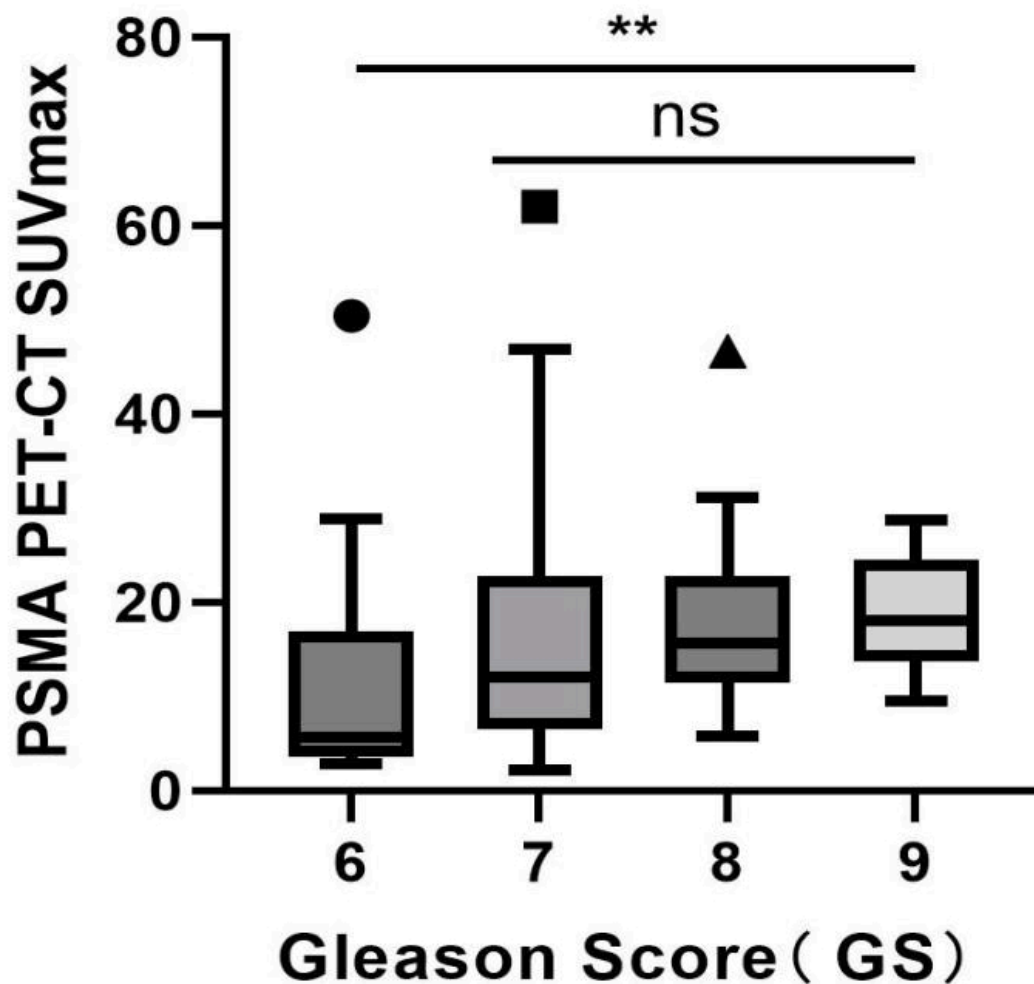


Figure 1

Distribution of PSMA PET-CT primary lesion SUVmax across different Gleason score groups in patients with prostate cancer.Box-and-whisker plot showing the distribution of maximum standardized uptake value (SUVmax) of primary prostate cancer lesions on PSMA PET-CT according to Gleason score (GS). The horizontal line inside each box represents the median value, the box indicates the interquartile range (IQR, 25th–75th percentiles), and the whiskers extend to the minimum and maximum values within $1.5 \times$ IQR. Outliers are plotted as individual points. ** $P < 0.01$; ns, not significant ($P \geq 0.05$), as determined by the Kruskal–Wallis test followed by Dunn’s post hoc multiple comparisons test.

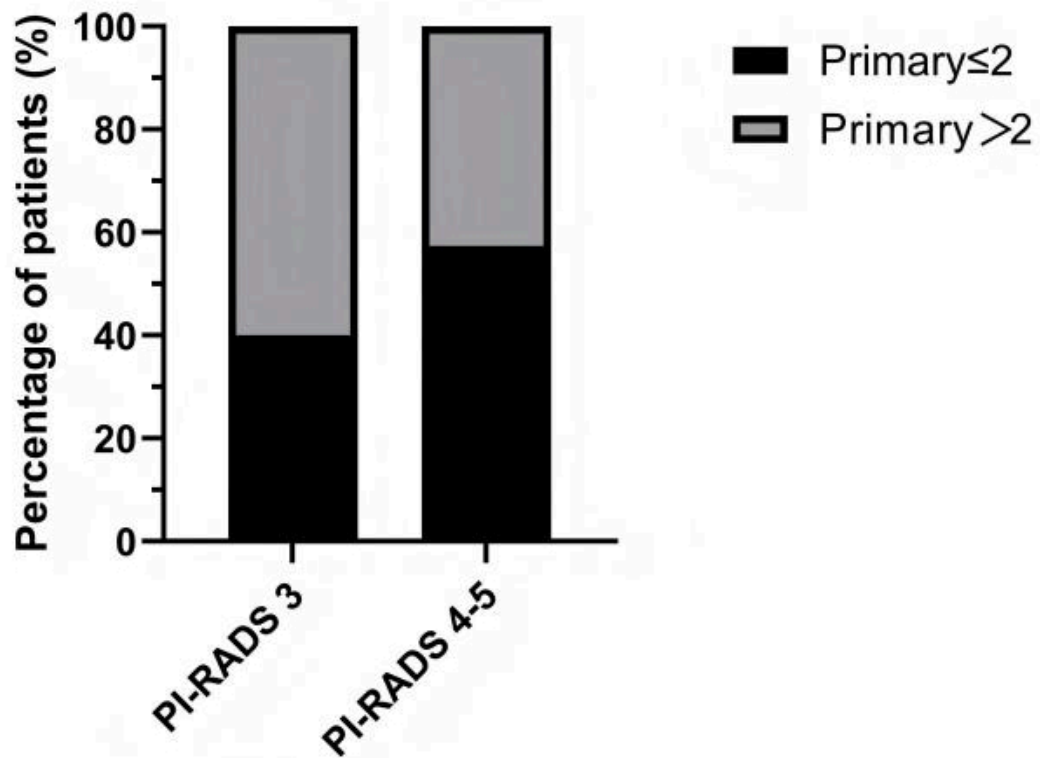


Figure 2

Stacked bar chart showing the distribution of primary lesion scores (Primary ≤ 2 vs. Primary > 2) across different PI-RADS categories (PI-RADS 3 vs. PI-RADS 4-5). The y-axis represents the percentage of patients within each PI-RADS group.

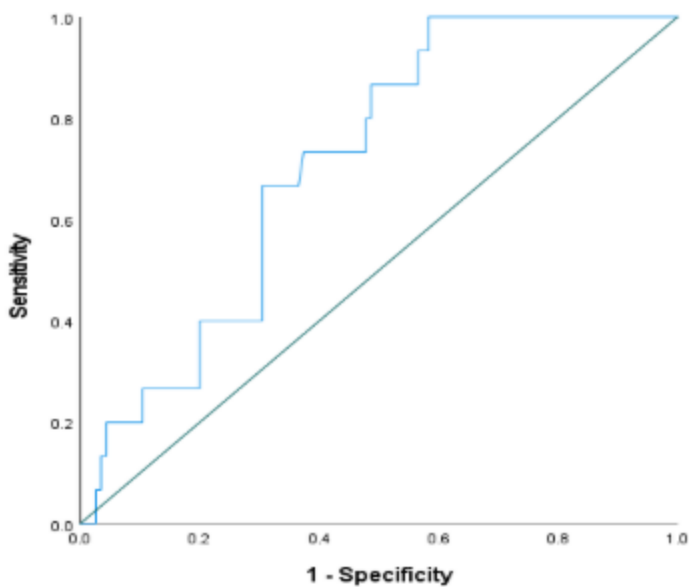


Figure 3

Receiver-operating characteristic (ROC) curve for the free-to-total PSA (F/T-PSA) ratio to predict primary-lesion PSMA-PET status. The x-axis represents 1-specificity, and the y-axis represents sensitivity. The diagonal line denotes the reference line of no discriminative power.