The Initial Application of MRI Based Prostate Volume-Adjusted Prostate-Specific Antigen In The Diagnosis of MRI-Positive Prostate Cancer Patients

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Research Article

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Abstract

Purpose: To identify the value of prostate-specific antigen density (PSAD) and prostate-specific antigen density of the transition zone (PSADTZ) in improving the sensitivity and specificity of the prostate multiparameter magnetic resonance imaging (mp-MRI), for the purpose of predicting prostate cancer (PCa) and grade reclassification in men with prostate-specific antigen (PSA) between 4 and 20 ng/mL to reduce unnecessary prostate biopsies.

Patients and Methods: Between 2018 and 2020, we retrospectively identified 283 consecutive men in Shanghai Jiao Tong University Affiliated Sixth People's Hospital who had mp-MRI and PSA test within 3 months before prostate biopsies. Total prostate volume (TPV) and transition zone volume (TZV) were measured on mp-MRI. PSA, PSAD, and PSADTZ were compared to improve the sensitivity and specificity of positive biopsy cores and pathological stage by univariate analyses and through the receiver operating curve (ROC). We were focused primarily on the MRI-positive patients with PSA levels of 4-20ng/ml who were most likely subjected to unnecessary repeated prostate biopsies.

Results: Of the 283 patients, 138 (48.8%) had PCa and in 145 (51.2%) a benign prostate disease was diagnosed. PSA, PSAD, and PSADTZ were significantly related to biopsy, and equally able to predict higher pathological stage. The receiver operating curve (AUC) for predicting the presence of PCa in all patients was 58.06 for PSA, 72.13 for PSAD and 78.28 for PSADTZ. In addition, the AUC for predicting higher pathological stage in PCa patients was 65.71 for PSA, 65.46 for PSAD and 69.81 for PSADTZ. For 228 MRI-positive patients, the AUC for predicting the presence of PCa was 61.31 for PSA, 74.00 for PSAD and 80.13 for PSADTZ. No difference among the PSA, PSAD, and PSADTZ was found in 55 MRI-negative patients. **Conclusion:** The determination of PSADTZ had higher diagnostic accuracy for PCa than that based on PSA or PSAD. For MRI-positive patients, PSADTZ promote a more effective and simple method for PCa detection, and may be useful for decreasing the burden of surveillance prostate biopsies.

Background

Prostate cancer (PCa) is the second most prevalent malignancy and the fifth reason for mortality caused by cancer in men around the world [1, 2]. Although the incidence of PCa in Asia is lower than that in Northern America, Oceania, and Northern Europe, it has been increasing rapidly. In the recent 5 years, with the wide application of serum prostate-specific antigen (PSA) examination, China has an increasing trend in the incidence of PCa (2.6%/yr)[1]. PSA, multiparameter MRI (mp-MRI), and transrectal prostate ultrasound (TRUS) all play essential roles in PCa screening and in the selection of appropriate candidate for biopsy[3]. For the prostate biopsy is invasive[4] and costly[5], it's necessary for doctors to make accurate judgment. PSA screening has been mostly used for early PCa detection. When the PSA level is higher than 20 ng/ml, the serum PSA test got significantly higher accurate (largest to 87.2%[6]) in predicting PCa[7, 8]. However, serum PSA is not disease specific. Not only prostate cancer can cause the increase of PSA, Benign prostate diseases, such as benign prostatic hyperplasia and prostatitis may also cause PSA elevation. In prostatic hyperplasia, the number of prostate cells and the prostate volume

increases, resulting in increased secretion of PSA, thereby increase the serum PSA[9]. According to the literatures, however, the false-positive rate was up to 69.93% in patients with PSA levels of 4–20 ng/mL[10, 11]. As two most commonly imaging examinations, TRUS and mp-MRI can partly improve the positive diagnostic rate of PCa, but also go with insufficient sensitivity and specificity, especially when the PSA ranges from 4–20ng/mL[8, 12]. New biomarkers, such as Prostate-specific antigen isoform 2 (p2PSA) and Prostate Health Index (PHI) have not yet universal[13]. Therefore, MRI-positive patients with PSA levels of 4-20ng/mL are most likely subjected to unnecessary repeated prostate biopsies.

The increase of PSA caused by prostatic hyperplasia is related to the increase of prostate volume. The increase of PSA caused by prostate cancer is less related to the volume of prostate. Therefore, the serum PSA per prostate volume of prostate cancer may be higher than that of normal or BPH people. Some studies found that the use of PSAD in the diagnosis of prostate cancer which has a positive significance. And other studies have further found that the effect of PSA density of the transition zone (PSADTZ) on prostate cancer and prostatic hyperplasia was better than that of simply using PSAD for[14]. The purpose of this study was to compare the performance of PSAD, PSADTZ and PSA in the detection of PCa and risk stratification while particularly focusing on MRI-positive patients with PSA serum levels of 4~20 ng/mL.

Patients And Methods

Study population

This retrospective study was approved by local ethics committee, and given the retrospective design, the requirement for written consent was waived. From January 2018 to June 2020, a total of 941 patients, who had a systematic biopsy at Shanghai Jiao Tong University Affiliated Sixth People's Hospital, were retrospectively investigated. Patients underwent TRUS-guided transperineal prostate biopsy, served as the reference standard[15]. We excluded men with (1) absence of clinical information within 3 months before biopsy (n=103); (2) PSA level <4ng/ml (n=63) or >20ng/ml (n=274); (3) absence of mp-MRI within 3 months before biopsy (n=197); (4) age <50 (n=1) or >84 (n=16); (5) a history of treatments for benign prostate hyperplasia or PCa (n=4); (6) PSA elevation with urinary tract infection.

Clinical and pathologic characteristics of patients, including age, PSA testing, and Gleason score, were obtained from pathology reports. The biopsy samples were analysed and reported on the basis of the International Society of Urological Pathology (ISUP) 2014 modified Gleason score grading system[16]. PI-RADS scores (version 2), prostate volume and transition zone volume were also obtained from MRI reports. The final study enrolled 283 patients, including 138 PCa patients and 145 patients without any histologic evidence of cancer. $PSAD = \text{total PSA (ng / mL)} / \text{prostate volume (cm}^3\text{)}$. The unit is $\text{ng / mL} \cdot \text{cm}^{-3}$. $PSAT = \text{total PSA (ng / mL)} / \text{prostate transition zone volume}$. The unit is $\text{ng / mL} \cdot \text{cm}^{-3}$.

MRI Examination and Images Analysis

All images were acquired with a 3-T MRI scanner (MAGNETOM Skyra, Siemens Healthcare), and a phased-array 18-channel body coil in combination with an integrated 32-channel spine coil was used for signal reception. The imaging protocol followed the standard of the European Society of Urology Radiology guidelines, and included T1-weight Imaging (T1WI), T2-weighted Imaging (T2WI), diffusion-weighted imaging (DWI) with b values of 50, 1000, and 1500 s/mm² and dynamic contrast-enhanced imaging (DCE). Two dedicated radiologists blinded to both clinical and pathological information analyzed prostate mp-MRI images in consensus. According to the PI-RADSv2 criteria, all images and suspicious lesions were scored. When multiple suspicious lesions were detected, an index lesion considered as the one with the highest score was a representative PI-RADSv2 score of a patient in the study. PI-RADS score 1-2 is MRI negative, and PI-RADS score 3-5 is MRI positive.

TPV was calculated for each patient by using an open-source software (Sante DICOM Viewer Free, v4.0.14, <https://www.santesoft.com/index.html>). Two over five-year prostate MRI-experienced radiologists independently measured the anteroposterior, transverse and longitudinal maximum diameters of entire prostate and TPZ on T2WI images. Both readers were blinded to PSA levels and biopsy results. Subsequently, TPV and TZV were estimated through ellipsoid formulas: (maximum anteroposterior dimension) × (maximum transverse dimension) [both placed on the axial T2-WI] × (maximum longitudinal dimension) [placed on the sagittal T2-WI] × 0.52 [17].

Statistical analyses

GraphPad Prism software (ver. 8.0.2, Inc., CA, USA) was used for analysis, and Shapiro-Wilk test was used to assess the normal distribution of continuous variables. An unpaired t test was used to assess normally distributed continuous variables. The Mann–Whitney U test was used to assess non-normally distributed continuous variables. The ROC (Receiver Operating Characteristics) curve was employed to graphically demonstrate the sensitivities and specificities of the different diagnostic tests. The areas below the ROC curve (global accuracy) were also calculated and compared in pairs, through Medcalc software (ver. 19.7, Mariakerke, Belgium) as described by Delong [18]. Medcalc was also used to demonstrate the best cut-off point for each diagnosis test (PSA, PSAD and PSADTZ) as well as to calculate its respective positive predictive values (PPV), negative predictive values (NPV), sensitivities and specificities to predict PCa. All statistical analysis was performed considering $p < 0.05$ statistically significant and with a 95% trust interval.

Results

Patient characteristics.

In this study, 941 men underwent prostate biopsy, among whom 283 patients were included in the final analysis. Based on the results of the initial biopsy, 138 patients were PCa-positive and 145 were PCa-negative, resulting in a detection rate of 48.8%. Demographic and clinical characteristics, as well as MRI findings of the entire study cohort, are summarized in Table 1. The median time between mp-MRI and the histopathological examination was 22 days (range 3-90 days). The analyzed parameters except age did

not follow normal distribution and thus, are summarized with median and IQR. The mean age was 70 years (range 51-84 years). The median PSA level, median TPV, median TZV, median TZV/TPV, median PSAD, and median PSADTZ of 283 patients were 10.00ng/ml (IQR 7.00-13.59ng/mL), 56.84ml (IQR 41.61-80.21mL), 26.27mL (IQR 15.37-45.59mL), 0.47 (IQR 0.37-0.56), 0.17ng/mL/mL(IQR 0.11-0.25ng/mL/mL) and 0.36 ng/mL/mL (IQR 0.21-0.62ng/mL/mL). Patients with PCa in ISUP grade 1-5 were 30 (21.7%), 36 (26.1%), 41 (29.7%), 13 (9.4%) and 18 (13.0%) respectively.

Table 1

The characteristics of MRI-positive patients and MRI-negative patients, and comparison of PCa patients and non-PCa patients.

Characteristic	Overall	Patients without PCa	Patients with PCa	<i>P</i>
All				
N	283	145	138	
Mean age (95% CI), years	70 (69-71)	69 (68-70)	70 (69-71)	0.1628
Median PSA level (IQR), ng/ml	10.00 (7.00-13.59)	9.08 (6.71-12.44)	11.19 (7.71-14.04)	0.0192
Median TPV (IQR), ml	56.84 (41.61-80.21)	69.44 (49.96-90.67)	49.31 (33.97-62.28)	<0.0001
Median TZV (IQR), ml	26.27 (15.37-45.59)	36.06 (23.61-55.84)	17.82 (12.44-29.38)	<0.0001
Median TZV/TPV (IQR)	0.47 (0.37-0.56)	0.53 (0.45-0.63)	0.40 (0.33-0.49)	<0.0001
Median PSAD (IQR), ng/ml/ml	0.17 (0.11-0.25)	0.13 (0.09-0.19)	0.21 (0.14-0.33)	<0.0001
Median PSADTZ (IQR), ng/ml/ml	0.36 (0.21-0.62)	0.25 (0.17-0.40)	0.53 (0.33-0.91)	<0.0001
MRI PI-RADSv2, n				
Negative	55	37	18	
Positive	228	108	120	
3	74	47	27	
4	120	55	65	
5	34	6	28	
ISUP grade (Gleason score), n (%)				
grade 1(≤6)		/	30 (21.7)	
grade 2(3+4)		/	36 (26.1)	
grade 3(4+3)		/	41 (29.7)	
grade 4(8)		/	13 (9.4)	
grade 5(9,10)		/	18 (13.0)	
MRI-positive patients				
N		108	120	

Characteristic	Overall	Patients without PCa	Patients with PCa	<i>P</i>
Mean age (95% CI), years		70 (68-71)	71 (70-72)	0.0793
Median PSA level (IQR), ng/ml		8.61 (6.32-11.93)	11.13 (7.87-14.22)	0.0032
Median TPV (IQR), ml		66.98 (48.86-88.08)	48.27 (32.94-57.39)	<0.0001
Median TZV (IQR), ml		34.81 (23.52-53.28)	16.77 (12.20-26.90)	<0.0001
Median TZV/TPV (IQR)		0.53 (0.44-0.63)	0.39 (0.33-0.48)	<0.0001
Median PSAD (IQR), ng/ml/ml		0.13 (0.09-0.19)	0.23 (0.14-0.33)	<0.0001
Median PSADTZ (IQR), ng/ml/ml		0.25 (0.16-0.40)	0.61 (0.34-0.97)	<0.0001
MRI PI-RADSv2, n (%)				
3		47 (43.5)	27 (22.5)	
4		55 (50.9)	65 (54.2)	
5		6 (5.6)	28 (23.3)	
ISUP grade (Gleason score), n (%)				
grade 1(≤6)		/	23 (19.2)	
grade 2(3+4)		/	32 (26.7)	
grade 3(4+3)		/	38 (31.7)	
grade 4(8)		/	13 (10.8)	
grade 5(9,10)		/	14 (11.7)	
MRI-negative patients				
<i>N</i>		37	18	
Mean age (95% CI), years		69 (66-71)	67 (64-70)	0.3041
Median PSA level (IQR), ng/ml		9.71 (7.66-14.93)	11.26 (7.04-12.17)	0.5907
Median TPV (IQR), ml		79.00 (52.52-100.80)	61.98 (39.71-73.27)	0.0258
Median TZV (IQR), ml		46.00 (23.91-58.65)	30.29 (16.49-41.82)	0.0212

Characteristic	Overall	Patients without PCa	Patients with PCa	<i>P</i>
Median TZV/TPV (IQR)		0.53 (0.47-0.59)	0.49 (0.40-0.58)	0.0786
Median PSAD (IQR), ng/ml/ml		0.15 (0.09-0.19)	0.18 (0.12-0.20)	0.0803
Median PSADTZ (IQR), ng/ml/ml		0.27 (0.17-0.39)	0.33 (0.28-0.50)	0.0630

Diagnostic performance of clinical characteristics and mp-MRI in the detection of prostate cancer

As shown in Table 1, there were no significant differences in the mean patient age between PCa group and non-PCa group ($P = 0.1628$). The PSA level (11.19 vs 9.08, $P=0.0192$), PSAD (0.21 vs 0.13, $P<0.0001$) and PSADTZ (0.53 vs 0.25, $P<0.0001$) were significantly higher in the PCa group than in the non-PCa group, but the TPV (49.31 vs 69.44, $P<0.0001$), TZV (17.82 vs 36.06, $P<0.0001$) and TZV/TPV (0.40 vs 0.53, $P<0.0001$) was significantly lower in the PCa group than in the non-PCa group. To examine the diagnostic efficacy of PSA, PSAD and PSADTZ, ROC curves of these three classifiers for predicting PCa were drawn (Figure 1). The AUC values of PSA, PSAD and PSADTZ were 0.5806, 0.7213 and 0.7828, and every two of three parameters showed significant differences ($P<0.0001$), which means PSADTZ is a better index for predicting PCa when the PSA levels of patients are 4~20 ng/ml.

Among the 138 patients with confirmed PCa, 120 were positive on mp-MRI and 18 were negative. Of the 145 patients with benign diagnoses, 108 were positive on mp-MRI and 37 were negative. The patient-based sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and likelihood ratio of mp-MRI were 86.96% (95% CI 80.32-91.59%), 25.52% (95% CI 19.12-33.18%), 52.63% (95% CI 46.16-59.02), 67.27% (95% CI 54.10-78.19%) and 1.167 respectively (Table 2).

Table 2
Diagnostic performance of mpMRI in the detection of prostate cancer.

	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)	Likelihood Ratio	<i>P</i>
mpMRI	86.96% (80.32-91.59)	25.52% (19.12-33.18)	52.63% (46.16-59.02)	67.27% (54.10-78.19)	1.167	0.0080

Comparing the efficiency of PSA, PSAD and PSADTZ in the detection of risk stratification.

Based on the differences of prognosis, 138 PCa patients were divided into lower-risk group (Gleason score ≤ 6) and higher-risk group (Gleason score ≥ 7). Table 3 showed the clinical parameters of two groups. As we can see, the age and PV of two groups made no difference. Higher-risk group got lower TZV (15.89 vs 23.44, $P=0.0195$ and TZV/TPV (0.39 vs 0.43, $P=0.03681$), but the PSA level (11.56 vs 8.70, $P=0.0082$), PSAD (0.23 vs 0.16, $P=0.0093$) and PSADTZ (0.63 vs 0.37, $P=0.0008$) of them were much

higher. ROC curves of PSA, PSAD and PSADTZ for predicting prognosis of PCa patients and the comparison between these three parameters were shown in Figure 2. The AUC value of PSA, PSAD and PSADTZ were 0.6571, 0.6546 and 0.6981 respectively, however, there was no significant difference among them.

Table 3
Comparison of patients' characteristics with higher and lower pathological stage.

Characteristic	Gleason score ≤ 6	Gleason score ≥ 7	<i>P</i>
<i>N</i>	30	108	
Median age (IQR), years	71 (65-76)	71 (66-74)	0.6835
Median PSA level (IQR), ng/ml	8.70 (6.94-11.87)	11.56 (7.98-14.45)	0.0082
Median TPV (IQR), ml	52.92 (40.56-69.83)	48.27 (32.06-58.80)	0.1557
Median TZV (IQR), ml	23.44 (16.33-31.72)	15.89 (11.71-28.67)	0.0195
Median TZV/TPV (IQR)	0.43 (0.36-0.50)	0.39 (0.31-0.48)	0.0368
Median PSAD (IQR), ng/ml/ml	0.16 (0.10-0.24)	0.23 (0.15-0.34)	0.0093
Median PSADTZ (IQR), ng/ml/ml	0.37 (0.23-0.61)	0.63 (0.34-0.98)	0.0008

Comparison of PSA, PSAD and PSADTZ between non-PCa group and PCa group when the mp-MRI exam is positive.

For the specificity of mp-MRI in our study was only 25.52%, we divided patients into MRI-positive group and MRI-negative group to make further comparison. Demographic and clinical characteristics of MRI-positive patients were shown in Table 1. There were no significant differences in the mean patient age between PCa group and non-PCa group ($P = 0.0793$). The PSA level (11.13 vs 8.61, $P = 0.0032$), PSAD (0.23 vs 0.13, $P < 0.0001$) and PSADTZ (0.61 vs 0.25, $P < 0.0001$) were significantly higher in the PCa group than in the non-PCa group, but the TPV (48.27 vs 66.98, $P < 0.0001$), TZV (16.77 vs 34.81, $P < 0.0001$) and TZV/TPV (0.39 vs 0.53, $P < 0.0001$) was significantly lower in the PCa group than in the non-PCa group. ROC curves of PSA, PSAD and PSADTZ for predicting PCa in MRI-positive patients were shown in Figure 3, and the comparison between these three parameters was shown in Table 4. The AUC value of PSADTZ (0.8013) was higher than PSA (0.6131) and PSAD (0.7400). When we chose the best cut-off values of PSA, PSAD, PSADTZ (11.24, 0.2277 and 0.3844, respectively) for predicting PCa, the sensitivities were 50.00%, 52.50% and 70.83%, respectively and the specificities were 72.22%, 87.96% and 74.07%, respectively.

Table 4

The difference comparison between AUCs of PSA, PSAD and PSADTZ for predicting PCa in MRI-positive patients, and the cut-off points that have produced the best sensibility and specificity rates.

Characteristic	AUC (95% CI)	Z statistic	P	Cut-off point	Sensitivity	Specificity
PSA	0.6131 (0.5397 - 0.6865)		0.0032	11.24	0.5000	0.7222
PSAD	0.7400 (0.6765 - 0.8034)		<0.0001	0.2277	0.5250	0.8796
PSADTZ	0.8013 (0.7452 - 0.8574)		<0.0001	0.3844	0.7083	0.7407
PSA ~ PSAD	/	3.808	0.0001			
PSA ~ PSADTZ	/	4.918	<0.0001			
PSAD ~ PSADTZ	/	4.029	<0.0001			

Comparison of PSA, PSAD and PSADTZ between non-PCa group and PCa group when the mp-MRI exam is negative.

As shown in the bottom of Table 1, the TPV (61.98 vs 79.00, $P=0.258$) and TZV (30.29 vs 46.00, $P=0.212$) were lower in the PCa group than in the non-PCa group, but there were no significant differences in age ($P=0.3041$), PSA ($P=0.5907$), TZV/TPV ($P=0.0786$), PSAD ($P=0.0803$) and PSADTZ ($P=0.0630$) between PCa group and non-PCa group. As matter of fact that few MRI-negative patients accepted prostate biopsy, no further comparison was made.

Discussion

PCa is one of the most common malignant tumors in the urological system, and it is the sixth leading cause of cancer death (7.4% of deaths) among men worldwide[19]. It is usually suspected in cases of increased serum PSA levels and/or abnormal digital rectal examination (DRE). In these patients, the standard method to diagnose PCa is prostate biopsy. But any prostate biopsy is associated with a risk of infection (1–8%) and an increased risk of life-threatening sepsis (1–4%), as a consequence of increasing antibiotic resistance[20, 21]. Other associated morbidities include dysuria, hematospermia, haematuria, rectal bleeding, vasovagal episodes and urinary retention[21, 22]. These drawbacks of prostate biopsy limit the willingness of physicians and patients to perform and undergo potentially unnecessary biopsies. The estimated false-negative rate of systematic biopsy for any cancer is 25–40% [23].

PSA was considered as tumor marker of PCa, but BPH may also cause PSA elevation. In view of this, Benson et al[24] think that PSA combined with prostate volume can be more accurate to evaluate prostate cancer risk than PSA alone. That is PSA density (PSAD), which is the ratio of serum total PSA to

total prostate volume. Studies have shown that PSAD can increase the sensitivity of serum PSA in the diagnosis of prostate cancer, especially when serum PSA is low[Sci Rep. 2020 Mar 20;10(1):5157]. Lodeta et al[25] analysis 125 cases of PSA patients at the 4-10ng/ml level, the results showed that PSA was not statistically significant between non-PCa and PCa groups, but differences of PSAD was significant between the two groups($P=0.002$), and with $PSAD \geq 0.15$ ng/ml/ml as cutoff point, the sensitivity is 86.7%. BPH mainly occurs in the transitional zone, while prostate cancer mostly occurs in the peripheral zone. The PSA level enhancement is mainly related to the size of the transitional zone. Therefore, someone proposed PSADTZ should be used to identify BPH and PCa. Kalish et al[26] analyze 21 cases PCa and 38 cases BPH in PSA range 4-10ng/ml, found that PSADTZ had statistical significance between the two groups, while PSA and PSAD between the two groups was not statistically significant. They get conclusion that PSADTZ is more accurate to distinguish the prostate cancer than the PSA and PSAD. Kikuchi et al[27] got the similar conclusion and found that PSADTZ has the largest AUC in the PSA gray area, which can avoid unnecessary prostate biopsy (68/117). Tang et al[28] found that PSADTZ can increase the detection rate of prostate cancer in the Chinese population of PSA 4-10ng/ml and 10.1-20ng/ml. Our current results found that the AUC values of PSA, PSAD and PSADTZ were 0.5806, 0.7213 and 0.7828, and every two of three parameters showed significant differences ($P<0.0001$), indicating that PSADTZ was a better index for predicting PCa when the PSA levels of patients were 4~20 ng/mL. Additionally, we discovered that the AUC value of PSA, PSAD and PSADTZ were no significant difference between the lower-risk and higher-risk Pca groups, which may be attributed to the fewer samples and need to be explored in the future study.

Multiparametric prostate MRI (mp-MRI) is the combination of anatomic (traditional) MRI with functional MRI techniques and is useful imaging modality for interrogating the prostate gland. It is an emerging imaging modality for diagnosis, characterization, staging, and treatment planning of PCa. The technique, results reporting, and its role in clinical practice have been the subject of significant development over the last decade. Even so, mp-MRI still has false positive and false negative results. Therefore, our main purpose is to reduce unnecessary biopsy by combining serum PSA with mp-MRI measurement parameters. The Prostate Imaging Reporting and Data System version 1(PI-RADS v1) was created to address the need for a universal system when performing, interpreting, and reporting prostate mpMRI for tumor identification, risk stratification, and to guide image-guided biopsy in 2012. It changes the diagnosis of MRI from a descriptive to an objective diagnosis. PI-RADS v2 was developed in 2015 in order to address the aforementioned limitations of PI-RADS v1. The aims of PI-RADS v2 were to optimize interdisciplinary communication and decrease variability in describe. Increased serum PSA levels and PI-RADS score ≥ 3 are indications of prostate biopsy, but there are still negative results in these patients. In this study, the proportion reached 47.4%. Therefore, it is needful to reduce unnecessary biopsy. According to MRI imaging of prostate zonal anatomy, the prostate comprises a peripheral zone (PZ), a transition zone (TZ), a central zone, and an anterior fibromuscular stroma[29]. The density parameters, such as PSAD and PSADTZ, are ratios obtained by dividing PSA level by total prostate and transition zone volume. Both parameters have been introduced to improve the diagnostic accuracy in prostate cancer detection and predict prostate cancer stage[6, 30], however, the suggested cut-off data is still highly

debated[31] and no study have reported these parameters on both MRI-negative and MRI-positive Pca patients[30]. In our study, the mean differences in PSA, PSAD, PSADTZ between the non-PCa group and the PCa group in the MRI-positive patients have statistic significance. The determination of PSADTZ had higher diagnostic accuracy for PCa than that based on PSA or PSAD. Therefore, PSADTZ promote a more effective and simple method for PCa detection, and may be useful for decreasing the burden of surveillance prostate biopsies for MRI-positive patients.

The present study had some limitations. It was a retrospective, single-center study and the sample size of our study was small especially in patients with negative MRI. Multicenter studies will be carried out to further validate these results. Despite these limitations, the findings of this study may impact current clinical practice.

Conclusion

The determination of PSADTZ had higher diagnostic accuracy for PCa than that based on PSA or PSAD. For MRI-positive patients, PSADTZ promote a more effective and simple method for PCa detection, and may be useful for decreasing the burden of surveillance prostate biopsies, the AUC for predicting the presence of PCa was 61.31 for PSA, 74.00 for PSAD and 80.13 for PSADTZ.

Declarations

Ethics approval and consent to participate

This study was carried out following relevant guidelines and regulations (Declaration of Helsinki). Ethical approval of the manuscript was obtained from The Shanghai Jiaotong University Affiliated Sixth People's Hospital Research Ethics Committee (approval no. 2020-062). The requirement for informed consent was exempted by The Shanghai Jiaotong University Affiliated Sixth People's Hospital Research Ethics Committee.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Availability of Data and Materials

The data analysed during the current study are available from the corresponding author on reasonable request.

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Nailong Cao: Provision of study materials or patients, Manuscript writing, Final approval of manuscript

Baojun Gu: Administrative support , Provision of study materials or patients, Manuscript writing, Final approval of manuscript

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Figures

Characteristic	AUC (95% CI)	<i>P</i>
PSA	0.5806 (0.5136 - 0.6475)	0.0192
PSAD	0.7213 (0.6624 - 0.7802)	<0.0001
PSADTZ	0.7828 (0.7302 - 0.8354)	<0.0001

Comparison between the accuracy of characteristics	Z statistic	<i>P</i>
PSA ~ PSAD	4.493	<0.0001
PSA ~ PSADTZ	5.521	<0.0001
PSAD ~ PSADTZ	4.216	<0.0001

Figure 1

Receiver operating characteristic(ROC) curve and the difference comparison between areas under ROC curves of PSA, PSAD and PSADTZ in the detection of prostate cancer

Characteristic	AUC (95% CI)	<i>P</i>
PSA	0.6571 (0.5573 - 0.7569)	0.0086
PSAD	0.6546 (0.5440 - 0.7652)	0.0097
PSADTZ	0.6981 (0.5937 - 0.8026)	0.0009

Comparison between the accuracy of characteristics	Z statistic	<i>P</i>
PSA ~ PSAD	0.0545	0.9566
PSA ~ PSADTZ	0.776	0.4375
PSAD ~ PSADTZ	1.855	0.0636

Figure 2

ROC curve and the difference comparison between AUCs of PSA, PSAD and PSADTZ in the detection of higher pathological stage

Figure 3

ROC curve of PSA, PSAD and PSADTZ in the MRI-positive patients for predicting PCa