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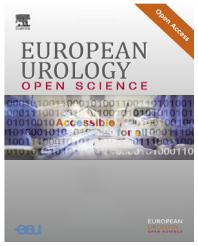

European Association of Urology

Prostate Cancer

The Impact of Prostate Volume on Prostate Cancer Detection: Comparing Magnetic Resonance Imaging with Transrectal Ultrasound in Biopsy-naïve Men

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Abstract

Background and objective: This study aimed to determine the difference in prostate volume (PV) derived from transrectal ultrasound (TRUS) and multiparametric magnetic resonance imaging (mpMRI), and to further investigate the role of TRUS prostate-specific antigen density (PSAD) and mpMRI-PSAD in prostate cancer (PCa) detection in biopsy-naïve men.

Methods: Patients who underwent an initial prostate biopsy within 3 mo after mpMRI between January 2016 and December 2021 were analyzed retrospectively. The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of both TRUS-PSAD and mpMRI-PSAD for PCa detection were calculated and compared. The Pearson correlation coefficient, Bland-Altman plot, and receiver operating characteristic curve were also utilized to explore the interests of this study.

Key findings and limitations: The median prostate-specific antigen level of 875 patients was 9.79 (interquartile range [IQR]: 7.09–13.50) ng/ml. The median mpMRI-PV and TRUS-PV were 41.92 (IQR: 29.29–60.73) and 41.04 (IQR: 29.24–57.27) ml, respectively, demonstrating a strong linear correlation (r = 0.831, 95% confidence interval: 0.809, 0.850; $p < 0.01$) and sufficient agreement. No significant difference was observed in terms of the sensitivity, specificity, PPV, and NPV between TRUS-PSAD and mpMRI-PSAD for any PCa and clinically significant PCa (csPCa) detection. The overall discriminative ability of TRUS-PSAD for detecting PCa or non-PCa, as well as csPCa and non-csPCa, was comparable with that of mpMRI-PSAD, and similar results were also observed in the subsequent analysis

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stratified by mpMRI-PV quartiles, prostate-specific antigen level, and age. The limitations include the retrospective and single-center nature and a lack of follow-up information.

Conclusions and clinical implications: TRUS-PV and MRI-PV exhibited a strong linear correlation and reached sufficient agreement. The efficiency of TRUS-PSAD and mpMRI-PSAD for PCa detection was comparable. TRUS could be used for PV estimation and dynamic monitoring of PSAD, and TRUS-PSAD could effectively guide clinical decision-making and optimize diagnostic strategies.

Patient summary: In this work, prostate volume (PV) derived from transrectal ultrasound (TRUS) exhibited a strong linear correlation with the PV derived from multiparametric magnetic resonance imaging (mpMRI). The efficiency of TRUS prostate-specific antigen density (PSAD) and mpMRI-PSAD for the detection of prostate cancer was comparable. TRUS could be used for PV estimation and TRUS-PSAD could help in clinical decision-making and optimizing diagnostic strategies.

1. Introduction

Prostate cancer (PCa) remains the most common newly diagnosed tumor among men worldwide, with an estimated new 34 700 deaths in 2023 in the USA [1,2]. The traditional diagnostic pattern is performing transrectal ultrasound (TRUS) guided ten- to 12-core systematic biopsy to confirm the presence of PCa in patients with elevated prostate-specific antigen (PSA) or abnormal digital rectal examination. However, the inherent limitations, including the inevitable sampling errors of a biopsy and the poor accuracy of TRUS, affect the detection efficiency of PCa severely [3]; thus, more accurate tools are warranted.

Currently, the utilization of multiparametric magnetic resonance imaging (mpMRI) has expanded dramatically the traditional diagnostic pathway for PCa, improved greatly the detection efficiency for clinically significant PCa (csPCa), and prevented a certain number of unnecessary biopsies [4–7]. An MRI-guided fusion biopsy has been reported to be able to identify more csPCa cases than the standard ultrasound-guided biopsy, posing superior sensitivity and specificity [8,9]. Moreover, in the era of mpMRI and its related fusion biopsy, more patients with low- and intermediate-risk PCa are able to be identified, and for these patients, focal therapy may be a promising alternative modality with promising midterm oncological results, avoiding some side effects of radical surgery [10]. However, the limitations about the low positive predictive value (PPV) and high negative predictive value (NPV) of mpMRI may account for the omission of several csPCa cases in the subsequent guided biopsy [11,12]; therefore, complementary parameters of mpMRI with the ability to compensate for the above deficiencies are needed urgently.

As a key factor, PSA has long been used in clinical practice for PCa screening [4]. Owing to its noncancer specificity nature and interference from other benign diseases, such as benign prostatic hyperplasia, PSA is characterized by poor specificity and low diagnostic efficacy; thus, its role in PCa detection is weakened further [13]. However, PSA density (PSAD), originated from serum PSA concentration and prostate volume (PV), has preliminarily presented the promising potential in predicting csPCa, prostate biopsy decision-making and individual treatment adjustment such as differentiating active surveillance (AS) and immediate interventions [14,15]. In the era of MRI, a 0.15 ng/ml/ml cut-off of PSAD was adopted extensively to stratify patients with positive mpMRI (Prostate Imaging Reporting and Data System [PI-RADS] $\geq$3) and guide a prompt biopsy [16,17]. In addition, our previous work demonstrated that PSAD <0.20 ng/ml/ml can be a potential criterion for safe exemption from unnecessary biopsies in the negative mpMRI Chinese population (PI-RADS <3) [18].

The PSAD value fluctuates with inaccurate PV estimates [19,20], interfering with scientific clinical decision-making and leading to the unreasonable formulation of personalized treatment plans. Generally, TRUS is the preferred method for estimating PV, but the use of TRUS-originated PV and subsequent PSAD is limited greatly by low interoperator agreement, poor intraoperator reproducibility, and underestimated tendency [21–23]. According to the recommendation of the European Association of Urology guidelines, mpMRI is considered the most accurate and reliable imaging method for PV evaluation [24,25]. However, although several studies have compared the difference between TRUS-PV and mpMRI-PV [22,26,27], the evidence about the preferred method for PV estimation and the application of subsequent PSAD still remain unclear. Moreover, the sample size of the above studies greatly limited the extrapolation of findings.

Therefore, with the advantage of the large single-center cohort, we conducted a retrospective study with the aim of determining the difference between TRUS-PV and mpMRI-PV, and further investigated the role of TRUS-PSAD and mpMRI-PSAD in PCa detection.

2. Patients and methods

Our study was approved by the Research Ethics Committee of the West China Hospital of Sichuan University (Chengdu,

China; no. 2019-869), and due to the retrospective design, anonymous data, and confidential information of included patients, this study was allowed to be conducted under waiver of informed consent by the local institutional review board. Initially, 6419 patients who underwent a prostate biopsy between January 2016 and December 2021 at West China Hospital of Sichuan University were retrieved retrospectively from the West China Hospital database. Patients with PSA level of 3–20 ng/ml who underwent prebiopsy mpMRI were ultimately included. We excluded those with unavailable TRUS- or mpMRI-estimated PV, and we also excluded those who had a previous prostate biopsy or medical therapy for PCa or benign prostate hyperplasia (eg, 5-alpha reductase inhibitors or surgical intervention). Patients who did not undergo a prostate biopsy within 3 mo of mpMRI were also excluded from the present study. Finally, 875 patients were included in the analysis. The specific screening flow chart is presented in Supplementary Figure 1.

All patients underwent prostate MRI through a 3.0 T MRI system (ie, Skyra; Siemens, Germany, or GE Healthcare, USA). All MRI results (≥200 scans per year) were interpreted by radiologists who had at least 3 yr of subspecialty experience and were unaware of TRUS-PV. One sonologist and one urologist performed TRUS with PV measurements at the time of biopsy. Urologists with a minimum of 3 yr of biopsy experience performed a TRUS-guided transperineal prostate biopsy. Systematic 12-core biopsies were obtained using a 16-gauge needle, and the template used for the transperineal systematic biopsies has been reported elsewhere [28]. If the positive MRI lesion was located within the coverage of the systematic biopsy scheme, a 12-core systematic biopsy was performed, and an average of three fusion-targeted biopsy cores were added for a suspicious lesion when systematic cores failed to reach the index targets on the basis of a transperineal systematic biopsy, especially for positive lesions in the anterior or apex of the prostate [29,30]. PV information was extracted from sonography and radiology reports. Both of these were estimated using the ellipsoid formula. TRUS-PSAD and mpMRI-PSAD were calculated by the ratio of serum total PSA to PV derived from TRUS and mpMRI, respectively.

Demographic and clinical information was extracted from medical records. The number of total biopsy cores, number of positive cores for PCa, and Gleason score for each patient were obtained from pathology reports. Clinically significant PCa was defined as Gleason 7 (3 + 4) and higher (grade group ≥2) [31]. We conducted a paired-cohort study to compare PVs estimated by mpMRI versus TRUS in the included patients, and subsequently, to evaluate the association of mpMRI- and TRUS-derived PSAD with the detection of any PCa and csPCa. PV estimated by MRI was treated as a continuous variable and by quartiles.

The data were expressed as mean (standard deviation) or median (interquartile range [IQR]). We compared differences between groups (non-csPCa vs csPCa) using the Student t test (continuous variables) and the chi-square or Fisher exact test (categorical variables) when appropriate. The linear association between TRUS- and MRI-based PVs was assessed through a Pearson correlation coefficient, and the agreement between these was evaluated by the Bland-Altman plot. Receiver operating characteristic (ROC) curves were generated for the mpMRI-PSAD and csPCa in PSA subgroups (PSA <10 and >10) separately, and the optimal cutoff values of PSAD of the two groups were also calculated with the highest Youden's index. Based on the cutoff of PSAD, the sensitivity, specificity, PPV, NPV, and confidence intervals (CIs) of both TRUS-PSAD and MRI-PSAD for PCa detection were calculated and compared to demonstrate the clinical impact of each measurement method. Then, we estimated the diagnostic performance of PSAD (mpMRI and TRUS derived) for PCa detection according to the ROC curve and the area under the curve (AUC) for each model, and compared using the DeLong test. Finally, we compared the differences among the different MRI-PV groups (MRI-PV quartiles), PSA groups, and age groups using MRI-PV as a reference.

A two-tailed p value of <0.05 was considered to indicate statistical significance. An analysis was performed using the software package R (http://www.R-project. org; the R Foundation, Boston, MA, USA) and EmpowerStats (http://www.empowerstats.com; X and Y Solutions, Inc., Boston, MA, USA).

3. Results

Overall, 875 patients were ultimately included in this study; the median age was 67 (IQR: 60–73) yr. The median (IQR) PSA level was 9.79 (7.09–13.50) ng/ml. The median PVs measured by MRI and TRUS were 41.92 (IQR: 29.29–60.73) and 41.04 (IQR: 29.24–57.27) ml, respectively. A paired t test showed that the PV measured by MRI was significantly higher than that measured by TRUS in every patient (p < 0.05; Supplementary Fig. 2). Subsequently, PSAD derived from TRUS-PV and MRI-PV were 0.23 (IQR: 0.15–0.35) and 0.22 (IQR: 0.15–0.35) ng/ml/ml, respectively. The detection rates of any PCa and csPCa were 43.66% (382/875) and 33.71% (295/875), respectively. When stratified by MRI-PV quartiles, there were 153 (70.2%), 109 (49.8%), 65 (29.7%), and 55 (25.1%) patients with any PCa, and 132 (60.3%), 85 (38.8%), 47 (21.5%), and 31 (14.2%) patients with csPCa in the first, second, third, and fourth quartiles of MRI-PV, respectively. Compared with those without a diagnosis of csPCa, those diagnosed with csPCa tended to be significantly older, have higher PSA and PSAD levels, and have a lower PV detected by both MRI and TRUS (all p < 0.001). The detailed clinicopathological characteristics are given in Table 1.

PV calculated by TRUS showed a strong positive correlation with that calculated by mpMRI within 3 mo of MRI to biopsy (r = 0.831, 95% CI: 0.809, 0.850; p < 0.01; Fig. 1). A Bland-Altman plot confirmed that there was sufficient agreement between TRUS-PV and mpMRI-PV (Supplementary Fig. 3). A comprehensive breakdown of statistical analyses, including sensitivity, specificity, PPV, NPV, and CIs for each diagnostic test (TRUS and mpMRI), was also performed to understand the diagnostic accuracy of TRUS-PSAD and mpMRI-PSAD. Given that MRI-PV showed a better correlation with prostatectomy specimen volume than TRUS-PV [32], we chose mpMRI-PV to estimate the optimal cutoff

Table 1 – Patient demographics and biopsy results

Characteristic	All patients (n = 875)	Non-csPCa patients (n = 580)	csPCa patients (n = 295)	p value
Age (yr), median (IQR)	67.00 (60.00–73.00)	65.50 (59.00–72.00)	69.00 (63.00–75.00)	<0.001
PSA (ng/ml), median (IQR)	9.79 (7.09–13.50)	9.14 (6.62–12.53)	11.34 (8.37–15.02)	<0.001
PV (ml), median (IQR)				<0.001
TRUS	41.04 (29.24–57.27)	47.18 (34.03–63.62)	31.89 (24.70–41.71)	
mpMRI	41.92 (29.29–60.73)	49.41 (33.54–67.04)	31.30 (22.90–42.47)	
PSAD (ng/ml^2), median (IQR)				<0.001
TRUS	0.23 (0.15–0.35)	0.19 (0.13–0.27)	0.33 (0.22–0.52)	
mpMRI	0.22 (0.15–0.35)	0.18 (0.12–0.26)	0.34 (0.22–0.50)	
PCa, n (%)				<0.001
Yes	382 (43.66)	87 (15.00)	295 (100.00)	
No	493 (56.34)	493 (85.00)	0 (0.00)	
csPCa, n (%)				<0.001
Yes	295 (33.71)	0 (0.00)	295 (100.00)	
No	580 (66.29)	580 (100.00)	0 (0.00)	

csPCa = clinically significant prostate cancer; IQR = interquartile range; mpMRI = multiparametric magnetic resonance imaging; PCa = prostate cancer; PV = prostate volume; PSA = prostate-specific antigen; PSAD = prostate-specific antigen density; TRUS = transrectal ultrasound.

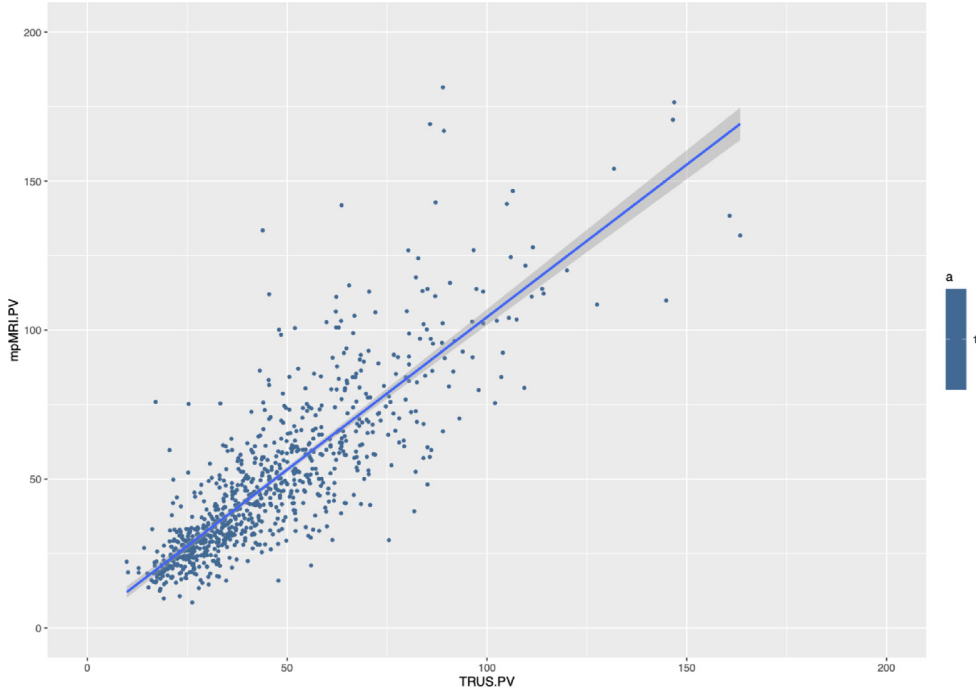

Fig. 1 – Prostate volumes measured by TRUS versus prostate volumes measured by mpMRI. mpMRI = multiparametric magnetic resonance imaging; PV = prostate volume; TRUS = transrectal ultrasound.

value of PSAD for PCa detection. As Supplementary Figure 4 shows, the optimal PSAD threshold for predicting PCa was established as 0.192 and 0.329 ng/ml/ml to achieve the maximum diagnostic accuracy in patients with PSA <10 and >10 ng/ml, respectively. According to the above cutoff values, the sensitivity, specificity, PPV, NPV, and CIs of TRUS-PSAD and MRI-PSAD for any PCa and csPCa detection were calculated in PSA subgroups and are shown in Table 2. For patients with PSA <10 ng/ml, mpMRI-PSAD showed better sensitivity, specificity, PPV, and NPV for both any PCa detection and csPCa detection than TRUS-PSAD. For patients with PSA >10 ng/ml, all indexes were higher in mpMRI-PSAD for any PCa detection, which was contrary to csPCa detection. However, none of above differences was statistically significant.

Moreover, the overall discriminative performance of two models with TRUS-PSAD and mpMRI-PSAD about PCa and csPCa detection was also assessed. The Delong test indicated that no significant difference was found between TRUS-PSAD and MRI-PSAD for detecting any PCa as well as csPCa (AUC = 0.727 vs 0.741, p = 0.712, and 0.770 vs 0.777, p = 0.609, respectively; Fig. 2). Furthermore, MRI-PV data were stratified by quartiles, and the Delong test indicated that there was no significant difference for either any PCa detection (AUC = first quartile, 0.717 vs 0.714, p = 0.476; second quartile, 0.717 vs 0.710, p = 0.443; third quartile 0.588 vs 0.617, p = 0.688; and fourth quartile, 0.573 vs 0.547, p = 0.339; Supplementary Fig. 5A–D) or csPCa detection between different MRI-PV quartiles (AUC: first quartile, 0.694 vs 0.691, p = 0.471; second quartile,

Table 2 – Sensitivity, specificity, positive predictive values, and negative predictive values of both TRUS-PSAD and MRI-PSAD for PCa detection in PSA subgroups

	TRUS-PSAD value (95% CI)	mpMRI-PSAD value (95% CI)	*p* value
PSA between 4 and 10			
Any PCa			
Sensitivity	0.58 (0.50, 0.65)	0.61 (0.53, 0.68)	0.576
Specificity	0.66 (0.60, 0.72)	0.71 (0.66, 0.77)	0.177
Positive predictive value	0.49 (0.42, 0.57)	0.55 (0.47, 0.62)	0.159
Negative predictive value	0.73 (0.67, 0.78)	0.76 (0.70, 0.81)	0.459
csPCa			
Sensitivity	0.68 (0.58, 0.76)	0.72 (0.63, 0.80)	0.477
Specificity	0.66 (0.61, 0.71)	0.71 (0.66, 0.76)	0.212
Positive predictive value	0.41 (0.34, 0.48)	0.46 (0.39, 0.54)	0.198
Negative predictive value	0.85 (0.80, 0.89)	0.88 (0.83, 0.91)	0.579
PSA between 10 and 20			
Any PCa			
Sensitivity	0.68 (0.61, 0.74)	0.69 (0.62, 0.75)	0.918
Specificity	0.75 (0.68, 0.80)	0.77 (0.71, 0.83)	0.564
Positive predictive value	0.74 (0.67, 0.80)	0.76 (0.69, 0.82)	0.612
Negative predictive value	0.69 (0.62, 0.75)	0.70 (0.64, 0.76)	0.928
csPCa			
Sensitivity	0.75 (0.68, 0.81)	0.73 (0.66, 0.79)	0.717
Specificity	0.73 (0.67, 0.78)	0.73 (0.67, 0.78)	0.919
Positive predictive value	0.67 (0.59, 0.73)	0.66 (0.59, 0.73)	0.901
Negative predictive value	0.80 (0.74, 0.85)	0.79 (0.73, 0.84)	0.921

csPCa = clinically significant prostate cancer; CI = confidence interval; mpMRI = multiparametric magnetic resonance imaging; MRI = magnetic resonance

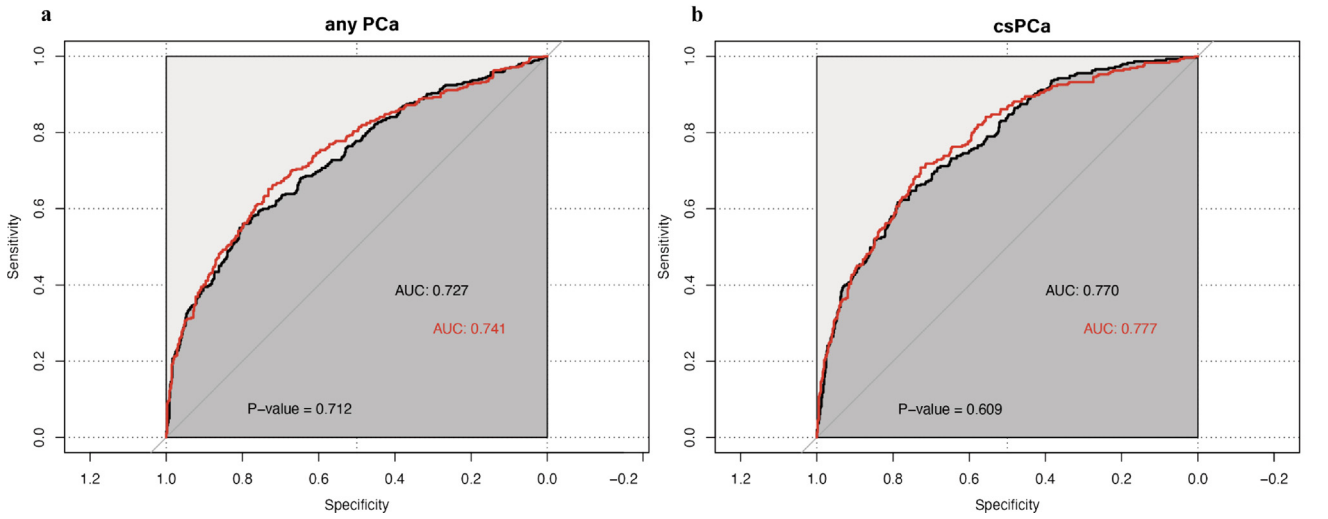

Fig. 2 – ROC curve analysis of the AUC used to assess the predictive accuracy of PSAD detected by TRUS (black line) and mpMRI (red line) for (A) any PCa and (B) csPCa. AUC = area under the curve; csPCa = clinically significant prostate cancer; mpMRI = multiparametric magnetic resonance imaging; PCa = prostate cancer; PSAD = prostate-specific antigen density; ROC = receiver operating characteristic; TRUS = transrectal ultrasound.

0.760 vs 0.751, p = 0.426; third quartile 0.640 vs 0.664, p = 0.66; and fourth quartile, 0.651 vs 0.585, p = 0.197; Supplementary Fig. 6A–D).

Additionally, patients were also stratified according to serum PSA level or age. There was no significant difference in the AUCs of PSAD values derived from TRUS and MRI in the PSA <10 ng/ml group (PCa, 0.665 vs 0.688, p = 0.737, Supplementary Fig. 5E; csPCa, 0.733 vs 0.744, p = 0.627, Supplementary Fig. 6E). Similar results were found for patients with PSA ≥10 ng/ml (PCa, 0.783 vs 0.787, p = 0.551, Supplementary Fig. 5F; csPCa, 0.803 vs 0.794, p = 0.376, Supplementary Fig. 6F). According to our subgroup analysis adjusted by age, nonsignificant improvements were observed in AUC (MRI vs TRUS) for detecting any PCa (≤60, 0.711 vs 0.618, p = 0.544; >60 and ≤70, 0.754 vs 0.773, p = 0.694; and >70, 0.757 vs 0.771, p = 0.636; Supplementary Fig. 5G–I) and csPCa (≤60, 0.769 vs 0.773, p = 0.527; >60 and ≤70, 0.788 vs 0.795, p = 0.578; and >70, 0.798 vs 0.807, p = 0.587; Supplementary Fig. 6G–I).

4. Discussion

Our research revealed a strong linear correlation and sufficient agreement between TRUS-PV and MRI-PV by a retrospective cohort with the largest sample size. No significant difference was detected in terms of the sensitiv-

ity, specificity, PPV, and NPV between TRUS- and MRI-derived PSAD values for any PCa and csPCa detection. Furthermore, the overall discriminative ability of TRUS-PSAD for detecting PCa or non-PCa, as well as csPCa and non-csPCa, was comparable with that of mpMRI. Therefore, TRUS is a potentially reliable tool for PV estimation and dynamic monitoring of PSAD, and TRUS-PSAD could effectively guide clinical decision-making and optimize diagnostic strategies.

PV was calculated by the prolate elliptical formula in our study, which is the most widely applied formula among studies, and the median TRUS-PV and MRI-PV were 41.92 and 41.04 ml, respectively. Differently, the PVs recorded in other studies were much greater than those in our study. Martins et al [33] reported median volumes of 54.9 ml evaluated by TRUS and 49.9 ml evaluated by MRI within 6 mo prior to radical prostatectomy. Additionally, the median TRUS-PV was 49.2 ml, and the median MRI-PV was 54.1 ml in a study by Choe et al [27]. A possible explanation for this discrepancy might be the various ethnic proportions of the population included in these studies, as we have noticed that the Asian race accounted for 3.8% of the population in the study by Choe et al [27]. In addition, this discrepancy might also be attributed to the inherent limitation of the elliptical formula for nonuniform shapes mainly for the prostate median lobe. Interestingly, we observed significant differences in PVs between the non-csPCa (47.18 for TRUS and 49.40 for mpMRI) and csPCa (31.89 for TRUS and 31.30 for mpMRI) groups. Therefore, the relatively high proportion (33.7%, 295/580) of patients diagnosed with csPCa might lead to the low median PV in our study, as we found a lower proportion (28%) in Choe et al's [27] study.

Our study unmasked a strong positive correlation and sufficient agreement between TRUS-PV and MRI-PV, which was consistent with the findings of previous studies. Martins et al [33] reported high agreement between PVs evaluated by MRI and TRUS, with a correlation coefficient of 0.924. Paterson and coworkers [32] also found a strong correlation between TRUS-PV and MRI-PV, and further explored the association between these PVs and the final pathological PV. They proposed that TRUS and MRI were both of great value in the PV estimation, whereas MRI revealed a better correlation with pathological PV. In addition, Choe et al [27] suggested that MRI provided more accurate volume estimates for final pathological PV than TRUS (correlation coefficient: 0.913 vs 0.878). Despite the high agreement, a significant difference was still observed between the paired TRUS-PV and MRI-PV in each patient, which was also reported in previous studies [32]. However, little attention has been paid to the subsequent impact of differences between PVs estimated by TRUS and mpMRI.

To visualize the clinical implications of differences between the estimated PVs, we then tested the diagnostic performance of subsequent PSAD in detecting any PCa and csPCa by AUC models. Our study showed that no significant difference was observed in the diagnostic performance of TRUS-PSAD and MRI-PSAD for the detection of both any PCa and csPCa. Furthermore, this association did not change significantly in the subsequent analysis stratified by mpMRI-PV, PSA level, and patient age. Our findings were in accordance with those of a study by Choe et al [27], and the comparison of AUCs between mpMRI-PSAD and TRUS-PSAD presented no statistically significant difference for csPCa (0.732 vs 0.722, $p = 0.20$) but a marginal improvement for any PCa (0.689 vs 0.675, $p = 0.05$). Therefore, the difference in PV between TRUS and MRI would not be a source of heterogeneity in the predictive power of PSAD for either PCa or csPCa.

In addition, the sensitivity, specificity, PPV, and NPV of TRUS-PSAD and MRI-PSAD for any PCa and csPCa detection in PSA subgroups were also compared, and no significant difference was observed in terms of any index. In the era of targeted biopsies, MRI-targeted biopsies, due to their excellent ability to identify csPCa and non-csPCa cases, have played an increasingly important role in the diagnostic pathway of PCa. Previous studies attempting to improve the predictive accuracy of the PCa (csPCa or non-csPCa) before a biopsy have suggested the use of the combination of MRI (PI-RADS) and PSAD. Boesen et al [17] proposed that performing a biopsy only in patients with PI-RADS >3 or PSAD $\geq$0.15 ng/ml/ml successfully reduced 41% of unnecessary biopsies and 45% of overdiagnostic non-csPCa cases at the cost of missing only 5% of csPCa cases. In addition, Schoots and Padhani [20] incorporated five studies with 3006 biopsy-naïve men and developed risk-adapted strategies for patient biopsy selection by combining MRI and PSAD. However, our study failed to report the clinical impact of the combination of mpMRI and PSAD; thus, further studies are warranted.

Currently, AS has become a standard option of care management for patients diagnosed with low-risk PCa as approximately 50% of eligible low-risk PCa patients in the USA received AS strategy at the time of initial diagnosis [25,34]. PSAD is often used as a key criterion in determining patients' eligibility for AS and necessity for additional treatments [35–37]. Our findings proposed that the difference between PVs estimated by TRUS and mpMRI was statistically significant, whereas the difference between PSAD values was not clinically significant. Therefore, owing to the rapidity, low cost effectiveness, and reproducibility of TRUS, its value in monitoring PSAD for low-risk PCa patients might have been underestimated before, which means that TRUS is a reliable tool for monitoring disease and decision-making, in terms of PSAD, for low-risk PCa patients who are in AS. Owing to the significant difference between TRUS-PV and mpMRI-PV, tailoring an appropriate TRUS-PSAD threshold is a prerequisite for the wide application of TRUS during the follow-up of patients undergoing AS; thus, well-designed future studies with large sample size and excellent external validation results are needed urgently to tailor the TRUS-PSAD cutoff geographically or ethnically. Moreover, considering that our study investigated only the effect of PV differences on PSAD of PCa prediction and failed to explore the effect of PV differences on other aspects, the unfinished task should also be a very interesting research direction in the future, which is crucial to improve the application of TRUS for PV measurement in clinical practice.

Our results should be interpreted in the context of a number of limitations. First are the limitations inherent to

its retrospective and single-center nature, including the difficulty of extrapolation and the instability of the results. Second, the lack of follow-up information in this study prevented further exploration of the survival affected by mpMRI and TRUS. Third, internal variation or interobserver heterogeneity between the numbers of urologists, radiologists, and pathologists may affect the stability of findings, even if blinding is used between departments; however, it was exactly the features of real-world practice, with extensive experience and assessment in accordance with the guidelines ensuring the reliability of the results. In addition, the diagnosis of any PCa and csPCa in the present study was based on the reference specimen from prostate biopsy but not from radical prostatectomy, which could introduce some changes and biases when assessing the precision of our findings in external validation due to the inconsistent pathological results between prostate biopsy and prostatectomy specimens [38,39].

5. Conclusions

TRUS-PV showed a strong linear correlation and sufficient agreement with mpMRI-PV. A significant difference between paired TRUS-PV and mpMRI-PV was observed in each patient, whereas the diagnostic performance of subsequent TRUS-PSAD and mpMRI-PSAD for PCa detection was comparable. TRUS could be used for PV estimation and dynamic monitoring of PSAD, and TRUS-derived PSAD could effectively guide PSAD-dominated clinical decision-making and optimize diagnostic strategies for patients with suspected PCa and low-risk PCa patients in AS.

***Author contributions*:** Yige Bao had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Ye, Wei, Bao.
Acquisition of data: Zheng, Zhang, Ye.
Analysis and interpretation of data: Zheng, Zhang, Ye.
Drafting of the manuscript: All authors.
Critical revision of the manuscript for important intellectual content: Tu, Bao, Wei.
Statistical analysis: Ye, Zhang, Zheng.
Obtaining funding: Bao.
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***Data sharing statement*:** The data that support the findings of this study are available from the corresponding author upon reasonable request.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.euros.2024.04.001.

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