

Diagnostic Performance of Age-Volume Ratio versus Prostate-Specific Antigen Density for Prostate Cancer Detection in a Rural Chinese Biopsy Cohort: a Retrospective Study

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Abstract

Background

PSAD improves risk stratification for PCa over total tPSA, yet its reliability depends on prostate volume measurement and overlooks age. AVR combining age and prostate volume, has shown promising diagnostic performance in northwestern Chinese populations but lacks validation in rural eastern coastal cohorts. This study compared the diagnostic performance of AVR with PSAD for PCa detection, with a focus on the PSA gray zone (tPSA 4–10 ng/mL) and the PSAD gray zone (0.15–0.30 ng/mL²).

Methods

This single-center retrospective study enrolled 111 patients who underwent prostate biopsy (52 PCa, 59 non-PCa) between January 2023 and January 2026. AVR (age/prostate volume) and PSAD (tPSA/prostate volume) were calculated. Receiver operating characteristic (ROC) curves were constructed with biopsy pathology as the reference standard; areas under the curve (AUC) with 95% confidence intervals (CIs) were estimated by 2,000 bootstrap resamples, and optimal cut-offs were determined by the Youden index. AUCs were compared using the DeLong test. Serial and parallel combination strategies of AVR and PSAD were evaluated using the McNemar test.

Results

In the whole cohort, the AUCs of AVR, PSAD, and tPSA were 0.753 (95% CI 0.658–0.841), 0.808 (95% CI 0.724–0.884), and 0.755 (95% CI 0.662–0.840), respectively. In the PSA gray zone (n = 58), AVR and PSAD showed comparable AUCs (0.779 vs. 0.773, DeLong P = 0.883), both superior to tPSA (0.589). In the PSAD gray zone (n = 37), AVR yielded a higher AUC than PSAD (0.740 vs. 0.631, P = 0.270), with sensitivity 81.2% and specificity 71.4% at the cut-off of 1.428. The serial strategy (AVR ≥ 1.428 and PSAD ≥ 0.188) improved specificity to 74.6% (11.9 percentage points over AVR alone) and reached 81.0% in the PSAD gray zone. When clinically significant PCa (ISUP grade group ≥ 2) was the endpoint, AVR's AUC decreased to 0.660, below PSAD (0.767).

Conclusions

PSAD remained the best-performing derivative in the unstratified cohort. AVR was non-inferior to PSAD in the PSA gray zone and retained discrimination in the PSAD gray zone, serving as a complementary tool. The serial combination of AVR and PSAD improved specificity, potentially reducing unnecessary biopsies.

Background

Prostate cancer (PCa) has become one of the most rapidly increasing malignancies among Chinese men. According to the latest national cancer registry estimates, China reported approximately 134,000 new cases and 47,000 deaths from prostate cancer in 2022, and the disease now ranks sixth in incidence among male cancers in China [1]. Prostate cancer is the most frequently diagnosed male malignancy worldwide, with an estimated 1.4 million new cases annually [2], and PSA-based screening has been demonstrated to reduce disease-specific mortality in the European Randomized Study of Screening for Prostate Cancer (ERSPC) at 16-year follow-up [3]. Unlike their counterparts in Europe and North America, Chinese patients are frequently diagnosed at advanced stages, with only about one-third presenting with localized disease; the National Guidelines for Diagnosis and Treatment of PCa in China (2022) therefore emphasize that early detection through PSA-based screening is critical, recommending PSA testing for well-informed males over 50 years of age [4]. However, serum total PSA (tPSA) has limited specificity. When tPSA falls within the gray zone of 4–10 ng/mL, a multicenter real-world study of 2,426 Chinese patients reported a biopsy positivity rate of only 25.8% [5], leaving clinicians with a difficult decision regarding whether to proceed with prostate biopsy. To address this uncertainty, prostate-specific antigen density (PSAD), which normalizes tPSA by prostate volume, has been incorporated into the 2022 Chinese National Guidelines, with $PSAD > 0.15 \text{ ng/mL}^2$ listed as a biopsy indication, and the guidelines further advocate the combined use of multiple PSA-derived indices for risk stratification [4]. A meta-analysis by Huang et al. demonstrated that the free/total PSA ratio (f/tPSA) and PSAD have comparable diagnostic performance within the PSA gray zone [6]. Notably, the same multicenter study reported an overall biopsy positivity rate of 47.6% in Chinese biopsy-naïve patients [5], indicating that the Chinese biopsy population is characterized by “older age, higher PSA, and a non-negligible positivity rate.”

Nevertheless, the reliability of PSAD hinges on accurate prostate volume measurement, and Asian men typically have smaller prostates than Caucasian populations—a finding confirmed by the REDUCE trial, in which Asian participants had a mean prostate volume of 35.0 mL versus 43.5 mL in Caucasians ($P < 0.001$) [7]. A 2025 review further highlighted that smaller prostate volumes in Asian populations amplify the impact of measurement errors when converting to density, while PSAD fails to account for age as an independent risk factor [8]. Yang et al. [9] therefore proposed the age/prostate volume ratio (AVR), introducing an age dimension beyond volume correction, and reported that its diagnostic performance was comparable to PSAD and superior to tPSA in a northwestern Chinese cohort. Lu et al. [10] similarly combined age and prostate volume in the PSA-AV index, demonstrating a marked improvement in gray-zone cancer detection. However, AVR has not yet been validated in rural eastern coastal Chinese populations. We therefore retrospectively analyzed clinical data from patients undergoing prostate biopsy at our institution, comparing the diagnostic performance of AVR and PSAD across different clinical scenarios—including the PSA gray zone, the PSAD gray zone, and the endpoint of clinically significant PCa—to provide localized evidence for non-invasive risk stratification.

Methods

Study Population

This single-center retrospective study enrolled patients who underwent prostate biopsy at the Department of Urology, Jinshan Branch of Shanghai Sixth People's Hospital, between January 2023 and January 2026. All biopsies were ultrasound-guided transperineal procedures following a systematic 10-core protocol, and biopsy pathology served as the diagnostic reference standard. The transperineal route was chosen in light of its substantially lower infectious complication rate compared with the transrectal approach, as highlighted by the TREXIT 2020 initiative [11] and confirmed by a systematic review of 113,944 men showing infection-related complications of only 0.15% [12]. A multicenter real-world study also demonstrated comparable cancer detection rates between transperineal and transrectal routes in patients with gray-zone PSA [13]. Inclusion criteria were: (i) a definitive pathological diagnosis obtained from prostate biopsy; (ii) no prior endocrine therapy, radiotherapy, or prostate surgery before biopsy. Patients were excluded if they met any of the following: (i) biopsy not performed or pathological result unavailable; (ii) missing prostatic dimensions on MRI precluding volume calculation; (iii) missing serum tPSA records, making PSAD incalculable; (iv) concurrent acute prostatitis, acute urinary retention, or other conditions that may distort PSA levels; (v) previously confirmed PCa.

A total of 123 patients were initially collected. Three were excluded (two did not undergo biopsy and one lacked a pathology result), leaving 120. One patient was missing all three MRI dimensions, and eight had tPSA values recorded only as exceeding 100 ng/mL (exact values unavailable). To ensure that every indicator could be computed on the same set of patients, these nine were removed, yielding a final cohort of 111: 52 with PCa (46.8%) and 59 without. The study was approved by the institutional ethics committee of our hospital (approval No. [jszxxy202618]), and informed consent was waived owing to the retrospective design.

Variables and Group Definitions

All patients underwent multiparametric MRI (mpMRI; including T2-weighted imaging and diffusion-weighted imaging) prior to biopsy. Scanner models and field strengths were not fully standardized across the cohort, as some examinations were performed at outside hospitals. Three prostatic dimensions, namely length (L), width (W), and height (H), were taken from radiology reports; when a dimension was missing, the investigator reviewed the MRI images and supplemented the measurement. Prostate volume (PV, in mL) was estimated using the prolate ellipsoid formula:

$$PV = \pi/6 \times L \times W \times H$$

This method shows excellent agreement with surgical specimen weight when measured on MRI [14], with only minor deviations compared with transrectal ultrasound [15]. PSAD was calculated as tPSA divided by PV, and AVR was calculated as age (years) divided by PV. Patients were grouped into PCa and non-PCa according to biopsy pathology. The PSA gray zone was defined as tPSA 4–10 ng/mL; one

patient whose initial tPSA exceeded 10 ng/mL but dropped below 10 ng/mL on repeat testing was also included in this subgroup. The PSAD gray zone was defined as PSAD 0.15–0.30 ng/mL² [4].

Statistical Analysis

All analyses were performed in Python 3.13 (SciPy 1.18, NumPy 2.4). Continuous variables were expressed as the mean $\pm$ standard deviation (SD), and between-group differences were assessed with the Mann-Whitney U test. Receiver operating characteristic (ROC) curves were plotted for each indicator, with biopsy pathology as the reference standard. Areas under the curve (AUC) were reported with 95% confidence intervals (CIs) derived from 2,000 bootstrap resamples. Optimal cut-off values were identified by maximizing the Youden index (sensitivity + specificity – 1). Pairwise AUC comparisons used the DeLong test [16]. Clinically significant PCa was defined as ISUP grade group ≥ 2 (Gleason score $\geq 3 + 4$), according to the 2014 ISUP consensus classification [17]. For the combined strategies, differences in sensitivity and specificity against the single-indicator approach were evaluated with the McNemar test. To keep the comparison consistent, the cut-off for each indicator in the combination analysis was fixed at its Youden-derived value from the entire cohort (AVR ≥ 1.428 , PSAD ≥ 0.188). A two-sided $P < 0.05$ was considered statistically significant.

Use of Artificial Intelligence

During the preparation of this manuscript, the authors used generative artificial intelligence (AI) tools to assist with language editing and formatting. All AI-assisted suggestions were reviewed, edited, and verified by the authors, who take full responsibility for the content of this manuscript.

Results

Baseline Characteristics

Baseline characteristics of the two groups are shown in Table 1. Patients in the PCa group were older (74.27 ± 7.47 vs. 67.88 ± 7.43 years, $P < 0.001$), had higher tPSA (18.56 ± 13.77 vs. 9.15 ± 4.85 ng/mL, $P < 0.001$), higher PSAD (0.55 ± 0.44 vs. 0.21 ± 0.16 ng/mL², $P < 0.001$), and higher AVR (2.25 ± 0.90 vs. 1.60 ± 0.99 , $P < 0.001$) than those without cancer. Prostate volume was smaller in the PCa group (37.73 ± 13.73 vs. 55.04 ± 26.26 mL, $P < 0.001$), and %fPSA was lower ($13.79 \pm 8.24\%$ vs. $15.36 \pm 5.98\%$, $P = 0.044$). The mean prostate volume of 37.73 mL in the PCa group (well below the 55.04 mL in non-PCa patients) is consistent with the observation that smaller glands are more likely to harbor cancer. These between-group differences in age, tPSA, and prostate volume are the very components of AVR and PSAD, so it is expected that both indicators discriminate well; this is a property inherent to diagnostic studies and does not imply causation. The lower %fPSA in the PCa group also accords with the established understanding that a low free-to-total PSA ratio favors malignancy.

Table 1
Comparison of baseline characteristics between the PCa and non-PCa groups (mean $\pm$ SD)

Variable	PCa group (n = 52)	Non-PCa group (n = 59)	P value
Age (years)	74.27 $\pm$ 7.47	67.88 $\pm$ 7.43	< 0.001
tPSA (ng/mL)	18.56 $\pm$ 13.77	9.15 $\pm$ 4.85	< 0.001
fPSA (ng/mL)	2.23 $\pm$ 1.48	1.36 $\pm$ 0.84	0.003
%fPSA (%)	13.79 $\pm$ 8.24	15.36 $\pm$ 5.98	0.044
PV (mL)	37.73 $\pm$ 13.73	55.04 $\pm$ 26.26	< 0.001
PSAD (ng/mL ²)	0.55 $\pm$ 0.44	0.21 $\pm$ 0.16	< 0.001
AVR	2.25 $\pm$ 0.90	1.60 $\pm$ 0.99	< 0.001
<i>Note: fPSA and %fPSA were available in 47 PCa and 53 non-PCa cases. P values from the Mann-Whitney U test.</i>			

Diagnostic Performance in the Whole Cohort

ROC analysis of all 111 patients is summarized in Table 2 and Fig. 1. PSAD achieved the highest AUC at 0.808 (95% CI 0.724–0.884). AVR (0.753, 95% CI 0.658–0.841) and tPSA (0.755, 95% CI 0.662–0.840) were nearly identical (DeLong P = 0.977). Although both fell below PSAD, neither difference reached statistical significance (AVR vs. PSAD, P = 0.188; tPSA vs. PSAD, P = 0.118). %fPSA, available in 100 patients, produced an AUC of only 0.617 (95% CI 0.501–0.729), offering limited diagnostic value.

Table 2
ROC analysis of each indicator for PCa diagnosis in different cohorts

Cohort	Indicator	AUC (95% CI)	Optimal cut-off	Sensitivity (%)	Specificity (%)
Whole cohort (n = 111)	AVR	0.753 (0.658–0.841)	1.428	82.7	62.7
	PSAD	0.808 (0.724–0.884)	0.188	84.6	66.1
	tPSA	0.755 (0.662–0.840)	9.740	75.0	72.9
PSA gray zone (n = 58)	AVR	0.779 (0.644–0.896)	1.391	92.9	61.4
	PSAD	0.773 (0.648–0.883)	0.155	92.9	59.1
	tPSA	0.589 (0.401–0.769)	8.290	57.1	65.9
PSAD gray zone (n = 37)	AVR	0.740 (0.565–0.896)	1.428	81.2	71.4
	PSAD	0.631 (0.443–0.804)	0.188	68.8	61.9
<i>Note: AUC, area under the curve; CI, confidence interval. Cut-offs were determined by maximizing the Youden index. PSA gray zone: tPSA 4–10 ng/mL. PSAD gray zone: 0.15–0.30 ng/mL².</i>					

PSA Gray Zone Subgroup

58 patients fell within the PSA gray zone (14 with PCa, a positivity rate of 24.1%). Here AVR and PSAD performed comparably, with AUCs of 0.779 (95% CI 0.644–0.896) and 0.773 (95% CI 0.648–0.883), respectively (DeLong P = 0.883). tPSA dropped to an AUC of 0.589 (95% CI 0.401–0.769), below both, but the differences did not reach significance (P = 0.140 and 0.068), likely a consequence of the limited sample size in this subgroup. At the cut-off of 1.391, AVR achieved a sensitivity of 92.9% with 61.4% specificity.

PSAD Gray Zone Subgroup

37 patients had PSAD values between 0.15 and 0.30 ng/mL² (16 with PCa, positivity rate 43.2%). In this clinically challenging interval, AVR yielded a higher AUC than PSAD (0.740, 95% CI 0.565–0.896 vs. 0.631, 95% CI 0.443–0.804), though the difference was not statistically significant (DeLong P = 0.270) (Fig. 2). At the cut-off of 1.428, AVR reached a sensitivity of 81.2% and specificity of 71.4%, both exceeding PSAD's 68.8% and 61.9%. The diminished discrimination of PSAD in this range can be partly explained by a range-restriction effect: the standard deviation of PSAD within the gray zone shrank to

0.043, only 12.0% of the whole-cohort value (0.361), whereas AVR retained 60.2% of its variability (0.599 vs. 0.995).

Combined Strategies of AVR and PSAD

Used alone at an AVR cut-off of ≥ 1.428 , AVR achieved 82.7% sensitivity and 62.7% specificity. The serial strategy—both AVR ≥ 1.428 and PSAD ≥ 0.188 positive—raised specificity to 74.6%, an 11.9 percentage-point gain over AVR alone, with sensitivity at 75.0%. The parallel strategy (either indicator positive) pushed sensitivity to 92.3% but dropped specificity to 54.2% (Table 3). McNemar testing confirmed that the specificity improvement of the serial approach over AVR alone was statistically significant ($P = 0.016$), while the sensitivity change was not ($P = 0.250$).

In the PSAD gray zone ($n = 37$), the whole-cohort cut-offs happened to coincide with the subgroup’s Youden-optimal values. AVR alone showed 81.2% sensitivity and 71.4% specificity; the serial strategy yielded 62.5% sensitivity and 81.0% specificity, with only four false positives; the parallel strategy achieved 87.5% sensitivity and 52.4% specificity. Within this interval where PSAD’s discrimination is constrained, serial testing raised specificity to 81.0%, a 9.6 percentage-point increase over AVR alone (McNemar $P = 0.500$, possibly limited by small sample size), underscoring the added value of combined strategies in gray-zone risk stratification.

Table 3
Diagnostic performance of different combination strategies of AVR and PSAD ($n = 111$)

Strategy	Sensitivity (%)	Specificity (%)	Accuracy (%)	Missed (n)	False positive (n)
AVR alone (≥ 1.428)	82.7 (71.4–92.2)	62.7 (50.0–74.5)	72.1 (64.0–80.2)	9	22
PSAD alone (≥ 0.188)	84.6 (73.2–93.9)	66.1 (53.7–77.6)	74.8 (66.7–82.9)	8	20
Serial (AVR and PSAD)	75.0 (62.7–86.0)	74.6 (63.0–84.9)	74.8 (66.7–82.0)	13	15
Parallel (AVR or PSAD)	92.3 (84.4–98.2)	54.2 (41.0–66.2)	72.1 (63.1–80.2)	4	27
<i>Note: Cut-offs were fixed at the Youden-optimal values from the whole-cohort ROC analysis (AVR ≥ 1.428, PSAD ≥ 0.188). Serial: both indicators positive; Parallel: either indicator positive. Values in parentheses are 95% CIs from 2,000 bootstrap resamples.</i>					

Sensitivity Analysis Using Clinically Significant PCa as the Endpoint

Among the 52 cancer cases, 35 (67.3%) were Gleason 3 + 3 (ISUP grade group 1), and 17 were ISUP grade group ≥ 2 (Gleason score $\geq 3 + 4$), defined as clinically significant prostate cancer (csPCa). When the ROC analysis was repeated with csPCa as the endpoint (Table 4), the AUC of AVR in the whole cohort

fell to 0.660, below PSAD (0.767) and tPSA (0.771). In the PSAD gray zone (only 5 csPCa events), AVR and PSAD produced AUCs of 0.656 and 0.775, respectively. Shifting the endpoint from all PCa to csPCa thus attenuated AVR’s discriminatory power.

Table 4
ROC analysis with clinically significant PCa (ISUP grade group ≥ 2) as endpoint

Cohort	AVR	PSAD	tPSA
Whole cohort (n = 111, csPCa = 17)	0.660	0.767	0.771
PSAD gray zone (n = 37, csPCa = 5)	0.656	0.775	0.619
<i>Note: csPCa defined as Gleason score $\geq 3 + 4$ (ISUP grade group ≥ 2). The PSAD gray zone subgroup had only 5 csPCa events.</i>			

Discussion

This study provides what is, to our knowledge, the first head-to-head comparison of AVR and PSAD in a rural eastern Chinese biopsy cohort. The principal findings are: in the unstratified cohort, PSAD performed best (AUC 0.808); within the PSA gray zone, AVR matched PSAD (0.779 vs. 0.773, $P = 0.883$); within the PSAD gray zone, AVR retained discriminatory power (0.740 vs. 0.631, $P = 0.270$); and serial combination of the two raised specificity from 62.7% to 74.6%, reaching 81.0% in the PSAD gray zone.

PSAD remains the preferred derivative in the unstratified cohort

Wang et al. [18] systematically reviewed 39 studies and reported pooled sensitivities of 0.74 and specificities of 0.61 for PSAD at the 0.15 ng/mL² threshold in detecting clinically significant PCa. This accords with the earlier meta-analysis by Feng et al. [19], which pooled 11 studies of 1,821 participants and reported a sensitivity of 0.73, a specificity of 0.64, and an AUC of 0.77 for PSAD in detecting PCa. Since Benson et al. [20] introduced PSAD in 1992, the concept of normalizing PSA by prostate volume has gained broad acceptance as a practical improvement over raw tPSA. Our whole-cohort AUC of 0.808 for PSAD, exceeding both AVR (0.753) and tPSA (0.755), is in line with this literature. Song et al. [21] reported a PSAD AUC of 0.627 for PCa detection in 5,220 patients from 18 Chinese hospitals (Chinese Prostate Cancer Consortium), with 88.7% sensitivity at the 0.10 ng/mL² cut-off, providing the largest Chinese multicenter benchmark for PSAD performance. In a recent BMC Urol. study of 671 patients with 981 PI-RADS 3 lesions, Franz et al. [22] confirmed PSAD as the strongest predictor of both PCa and csPCa, while prostate volume was inversely associated with cancer risk, in keeping with our finding that smaller glands are more likely to harbor malignancy. Peng et al. [23] similarly identified PSAD as the only independent predictor in 318 BPH patients with elevated PSA and negative MRI (AUC 0.848), recommending a higher threshold of 0.30 ng/mL² for this specific population. Yusim et al. [24] reported a PSAD AUC of 0.78 for clinically significant PCa in 992 men undergoing TRUS-guided biopsy, further

supporting the central role of PSAD in pre-biopsy risk stratification. For an unselected biopsy population, then, PSAD remains the first-line PSA derivative; replacing it with AVR is not supported by our data.

AVR is non-inferior to PSAD in the PSA gray zone

The tPSA range of 4–10 ng/mL represents the most common clinical dilemma. In our cohort, the gray-zone positivity rate was 24.1%, close to the 25.8% reported by Xu et al. [5] in a multicenter Chinese study of 2,426 patients, and to the 26% positivity rate documented by the Chinese Prostate Cancer Consortium survey of 13,904 biopsies performed across 33 member hospitals [25]. Within this range, tPSA itself nearly loses all discriminatory ability (AUC 0.589), while both AVR and PSAD recover discrimination through volume correction, yielding AUCs of 0.779 and 0.773, respectively (DeLong $P = 0.883$). This finding is consistent with Yang et al.'s northwestern Chinese cohort [9] and the meta-analysis by Huang et al. [6] on gray-zone PSA derivatives. Lin et al. [26] previously demonstrated in a two-center Chinese cohort of 461 men that PSAD outperforms tPSA within the 2.5–10.0 ng/mL range, with an optimal cut-off of 0.15 ng/mL² (matching the threshold adopted in the Chinese national guidelines [4] and consistent with our PSAD gray-zone definition). Although that meta-analysis also suggested some utility for %fPSA in the gray zone [6], our %fPSA AUC was only 0.617, and fPSA testing incurs additional cost. Liu et al. [27] developed multivariable predictive models incorporating age, prostate volume, f/tPSA ratio, and PSAD for patients with PSA in the gray zone, achieving sensitivity of 75.4% and specificity of 75.8%, suggesting that combining multiple readily available clinical variables benefits gray-zone decision-making. AVR, which can be calculated from age and prostate volume alone, may therefore substitute for PSAD in risk stratification.

AVR retains discrimination in the PSAD gray zone

A PSAD of 0.15–0.30 ng/mL² sits in the “middle ground” between the biopsy threshold and the highly suspicious range—the most difficult interval for clinical decision-making. Among our 37 patients in this zone, 43.2% had cancer, yet PSAD's AUC dropped to 0.631. A range-restriction effect offers a partial explanation: the standard deviation of PSAD within the gray zone shrank to 0.043, only 12.0% of the whole-cohort value (0.361), compressing the indicator into a narrow band that diminishes its discriminatory capacity. AVR, whose numerator is age rather than tPSA, is not subject to the same constraint and retained 60.2% of its variability (0.599 vs. 0.995), producing an AUC of 0.740 ($P = 0.270$ vs. PSAD) with 81.2% sensitivity and 71.4% specificity at an AVR cut-off of 1.428. Lu et al. [10] similarly demonstrated that incorporating age and volume into the PSA-AV index raised the gray-zone detection rate from 36% to 81%, suggesting that the age dimension compensates for the limitations of volume-only correction. When PSAD falls within its own gray zone and discrimination wanes, AVR can serve as an auxiliary decision-making tool.

Clinical value of the serial strategy

Used alone at an AVR cut-off of ≥ 1.428 , AVR achieved 82.7% sensitivity and 62.7% specificity. The serial approach—both $\text{AVR} \geq 1.428$ and $\text{PSAD} \geq 0.188$ positive—lifted specificity to 74.6% (an 11.9 percentage-point gain, McNemar $P = 0.016$) with sensitivity at 75.0%, potentially cutting false-positive biopsies by

roughly one-third. The benefit was more pronounced in the PSAD gray zone: specificity reached 81.0% (up from 71.4%), with only six missed cancers and four false positives. Notably, the whole-cohort Youden cut-offs happened to match the PSAD gray zone's own optimal values, so no cohort mismatch arises when applying them to this subgroup. In the PSA gray zone, however, applying the whole-cohort cut-offs reduced the serial strategy's sensitivity to 64.3%, suggesting that PSA-gray-zone patients may need separately calibrated thresholds. Dong et al. [28] recently proposed a biopsy strategy based on PSAD and prostate volume for Chinese patients with tPSA > 10 ng/mL and PI-RADS 1–3, demonstrating that 66.5% of biopsies could be safely avoided while missing only 1.7% of csPCa. This finding reinforces the principle that volume-based indices, when combined with imaging assessment, can meaningfully reduce overdiagnosis, a conclusion consistent with the specificity gain of our serial strategy. For centers with limited access to MRI, this “screen-then-confirm” two-step approach is operationally feasible and consistent with the combined-indicator strategy advocated by the Chinese national guidelines [4].

AVR's limited ability to distinguish clinically significant PCa

When csPCa (ISUP grade group ≥ 2) replaced all PCa as the endpoint, AVR's AUC fell from 0.753 to 0.660, below both PSAD (0.767) and tPSA (0.771). This suggests that AVR preferentially identifies low-grade tumors (Gleason 3 + 3) rather than aggressive ones—a limitation rooted in its composition: older age and smaller glands are indirect surrogates, not direct measures of tumor burden, whereas the numerators of PSAD and tPSA more directly reflect cancer-driven PSA secretion. AVR is therefore better positioned as a triage and stratification tool for reducing unnecessary biopsies, not as an indicator of aggressiveness. Patients positive for AVR should still undergo mpMRI and PI-RADS assessment to identify clinically significant disease. Jahnen et al. [29] reported that age and PSAD are independent predictors of csPCa in a cohort of 677 patients, yet even together they remain subordinate to MRI findings, supporting the view that no single blood-based index can replace imaging for csPCa identification. The PI-RADS v2.1 system demonstrates csPCa detection rates ranging from 3% (PI-RADS 1) to 83% (PI-RADS 5) across assessment categories [30], and a recent meta-analysis of 117 studies confirmed its high sensitivity (96% at PI-RADS ≥ 3) for csPCa detection [31]. Wang et al. [32] developed a diagnostic model combining PSAD and PI-RADS score from 1,807 patients across three Chinese hospitals, achieving excellent discrimination for csPCa with risk thresholds of 0.05 and 0.60. Their model's reliance on PSAD rather than age-based indices for csPCa prediction further supports the notion that AVR is better suited for triage than for aggressiveness assessment. Our csPCa sample was limited, and this conclusion warrants validation in larger cohorts.

Localization significance

Chinese men have distinctly smaller prostates than Western populations [7, 8]. In our cohort, the mean PV in the PCa group was only 37.73 mL, and the median AVR reached 2.15 (IQR 1.60–2.63), higher than the 1.84 (IQR 1.48–2.27) reported by Yang et al. [9] in northwestern China, suggesting that the “older age, smaller gland” profile of rural eastern coastal populations may give AVR greater applicability. The overall positivity rate of 46.8% in our cohort is consistent with the $\sim 47.6\%$ reported by Xu et al. [5] and with the 41.0% from a recent community-based screening of 17,198 residents in suburban Shanghai [33],

indicating that our study population is reasonably representative. Of note, AVR cut-offs are highly population-dependent: our Youden-optimal value was 1.428, whereas Yang et al. [9] derived 0.89 at approximately 90% sensitivity (in a cohort with tPSA 4–20 ng/mL). Establishing population-specific reference ranges will require multicenter data with larger samples.

Limitations

Several limitations should be acknowledged. First, the single-center retrospective design and modest sample size mean that cut-off derivation and performance estimation come from the same dataset, introducing potential optimistic bias; prospective multicenter external validation is needed. Second, eight patients with tPSA values recorded only as exceeding 100 ng/mL (exact values unavailable) were all in the PCa group; their exclusion may have inflated AVR's AUC. A sensitivity analysis including these cases ($n = 119$) produced an AVR AUC of 0.717, directionally consistent with the main analysis, and none fell within the PSA or PSAD gray zones, so core conclusions are unaffected. Third, mpMRI was acquired across different periods and scanners (including outside-hospital examinations), and PI-RADS v2.1 scoring was not uniformly applied; we therefore could not evaluate AVR's incremental value over imaging or adjust for imaging-suspicion-driven selection bias. Although MRI-based volume estimation is more accurate than TRUS [15], this heterogeneity precludes a head-to-head comparison of AVR with imaging-based risk stratification, for which PI-RADS v2.1 now provides a robust framework [30, 31]. AVR's calculation depends only on age and prostate volume, so PI-RADS availability does not affect between-group comparisons; however, %fPSA data were partially missing. Future prospective studies will standardize image assessment (PI-RADS v2.1) and test AVR's incremental value combined with imaging. Fourth, csPCa comprised only 17 cases (5 in the PSAD gray zone), limiting the precision of csPCa-specific analyses.

Conclusions

In this rural eastern Chinese biopsy cohort, PSAD remained the best-performing PSA derivative for the unstratified population. AVR was non-inferior to PSAD in the PSA gray zone and retained discrimination in the PSAD gray zone, where PSAD's own discriminatory power is constrained. The serial combination of AVR and PSAD improved specificity and may help reduce unnecessary prostate biopsies. AVR cut-offs are population-dependent, and multicenter studies with larger samples are warranted to establish reference values appropriate for Chinese populations.

Abbreviations

AVR

Age-Volume Ratio

AUC

Area Under the Curve

BPH

Benign Prostatic Hyperplasia

CI

Confidence Interval

CPCC

Chinese Prostate Cancer Consortium

csPCa

Clinically Significant Prostate Cancer

ERSPC

European Randomized Study of Screening for Prostate Cancer

fPSA

Free Prostate-Specific Antigen

%fPSA

Free/Total PSA Ratio

IQR

Interquartile Range

ISUP

International Society of Urological Pathology

mpMRI

Multiparametric Magnetic Resonance Imaging

MRI

Magnetic Resonance Imaging

PCa

Prostate Cancer

PI-RADS

Prostate Imaging Reporting and Data System

PSA

Prostate-Specific Antigen

PSAD

Prostate-Specific Antigen Density

PV

Prostate Volume

REDUCE

Reduction by Dutasteride of Prostate Cancer Events

ROC

Receiver Operating Characteristic

SD

Standard Deviation

tPSA

Total Prostate-Specific Antigen

TRUS

Transrectal Ultrasound

Declarations

Ethics approval and consent to participate

This retrospective study was approved by the Ethics Committee of Jinshan Branch of Shanghai Sixth People's Hospital (approval No. [jszxxy202618]). Clinical trial number not applicable. Written informed consent was waived by the ethics committee due to the retrospective nature of the study, which used routinely collected clinical data. All patient data were anonymized prior to analysis.

Consent for publication

Not applicable. No individual person's data (including individual details, images, or videos) are presented in this manuscript.

Availability of data and materials

The datasets analyzed during the current study are not publicly available due to patient privacy protection requirements, but are available from the corresponding author (Wenpu Chen, Email: cwp305@163.com) upon reasonable request. The Python code used for statistical analysis is available from the corresponding author upon reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

CY [Chengshuai Yu] contributed to the study design, data collection, statistical analysis, and manuscript drafting. HH [Hengda Hu] contributed to data collection and data cleaning. WM [Weixiong Ma] contributed to data collection and literature review. WC [Wenpu Chen] contributed to study supervision, data interpretation, and critical revision of the manuscript for important intellectual content. All authors read and approved the final manuscript.

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Figures

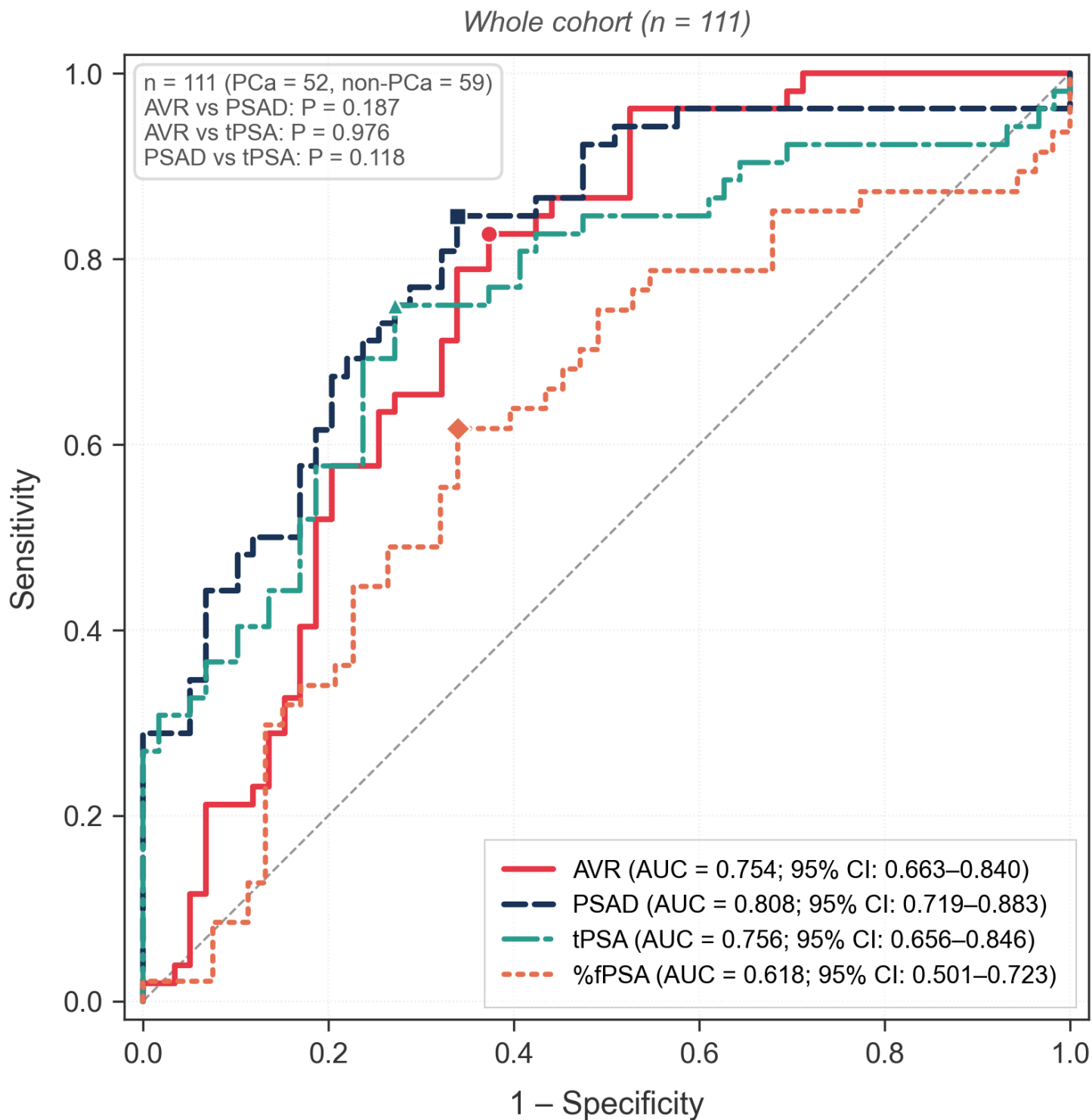


Figure 1

Receiver operating characteristic (ROC) curves of AVR, PSAD, and tPSA for prostate cancer detection in the whole cohort (n = 111). Areas under the curve (AUCs) with 95% confidence intervals are shown for each indicator. The diagonal dashed line represents the reference line (AUC = 0.5). AVR, age-volume ratio; PSAD, prostate-specific antigen density; tPSA, total prostate-specific antigen; AUC, area under the curve; CI, confidence interval.

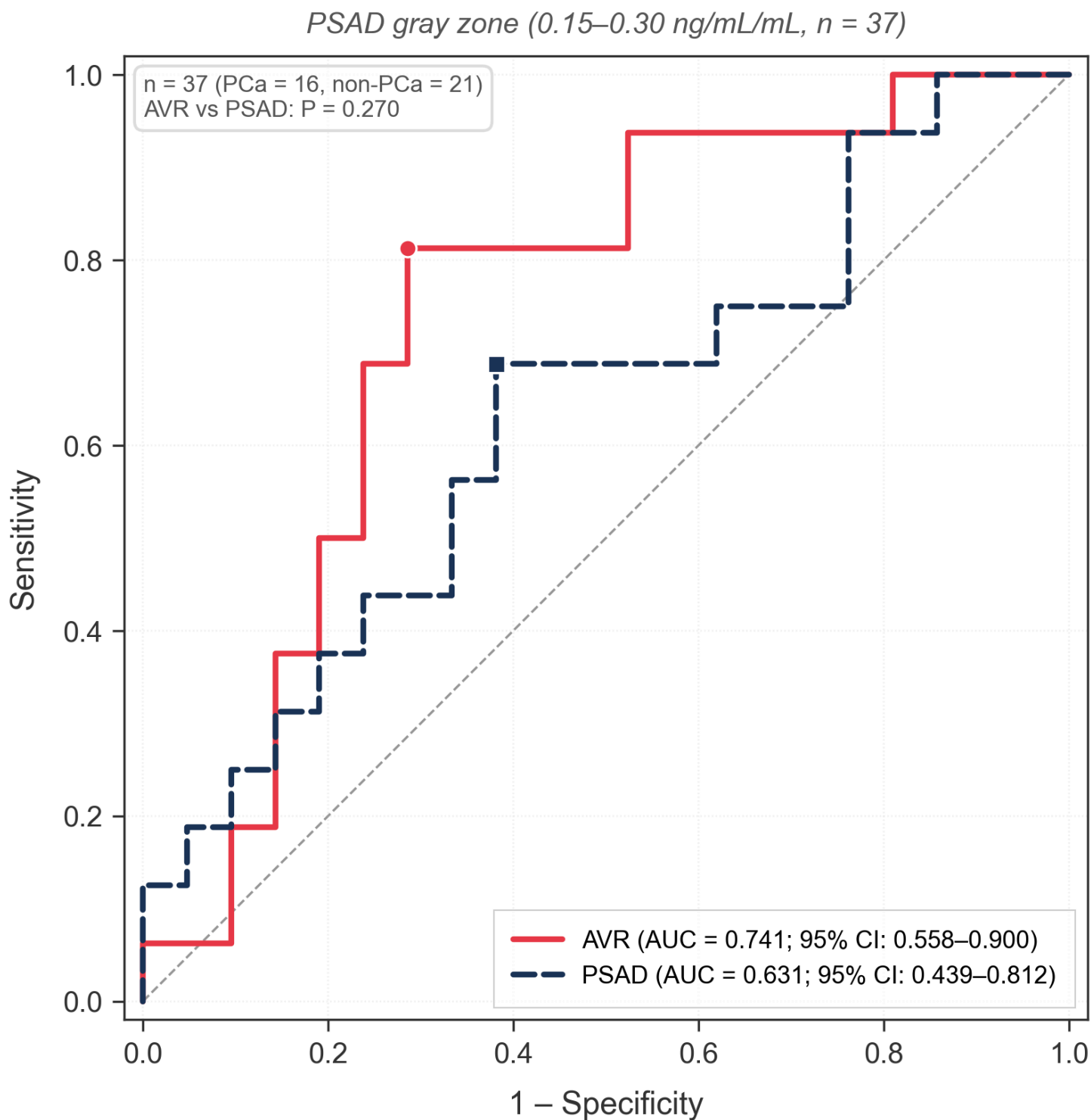


Figure 2

Receiver operating characteristic (ROC) curves of AVR and PSAD in the PSAD gray zone subgroup (n = 37, PSAD 0.15–0.30 ng/mL²). AUCs with 95% confidence intervals are shown. Despite the narrow range of PSAD values in this subgroup, AVR retained discriminatory power. AVR, age-volume ratio; PSAD, prostate-specific antigen density; AUC, area under the curve; CI, confidence interval.