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DIAGNOSTIC ACCURACY OF PROSTATE-SPECIFIC ANTIGEN DENSITY, FREE-TO-TOTAL PSA RATIO, AND DIGITAL RECTAL EXAMINATION IN DETECTING PROSTATE CANCER AMONG MEN WITH SERUM PSA LEVELS IN THE GRAY ZONE (4–10 NG/ML): A PROSPECTIVE OBSERVATIONAL STUDY

PSA DENSITY, F/T-PSA RATIO, AND DRE FOR PROSTATE CANCER DETECTION IN THE PSA GRAY ZONE

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Abstract

Objective

To determine the diagnostic accuracy of prostate-specific antigen density (PSAD), free-to-total PSA ratio (f/t PSA), and digital rectal examination (DRE) for detecting prostate cancer among men with serum PSA levels in the diagnostic gray zone (4–10 ng/mL).

Methodology

This prospective observational study was conducted in the Department of Urology of a tertiary-care teaching hospital in Pakistan. One hundred and thirty-two consecutive men with total serum PSA 4–10 ng/mL underwent clinical evaluation, digital rectal examination, transrectal ultrasonography for prostate volume estimation, and ultrasound-guided transrectal 12-core prostate biopsy. PSA density was calculated as total PSA divided by prostate volume. Histopathology was the reference standard. Continuous variables were compared using the Mann-Whitney U test or independent t-test and categorical variables using the chi-square or Fisher's exact test. Independent predictors of prostate cancer were identified using multivariable binary logistic regression, with adjusted odds ratios (OR) and 95% confidence intervals (CI) reported. A two-tailed $p<0.05$ was considered significant.

Results

Prostate cancer was confirmed in 27/132 patients (20.5%). Patients with cancer were significantly older than those without (median 70 vs 64 years, $p=0.011$) and had smaller prostate volumes (41.4±11.2 vs 60.3±21.1 mL, $p<0.001$) and higher PSAD (0.19 vs 0.13 ng/mL/cm³, $p<0.001$). Free PSA and f/t PSA ratio were significantly lower among cancer patients (both $p<0.001$). Total PSA did not differ significantly between groups (8.3 vs 7.9 ng/mL, $p=0.410$), and DRE positivity, although more frequent in the cancer group (14.8% vs 5.7%), did not

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reach significance (p=0.121). On multivariable logistic regression, age (OR 1.07, 95% CI 1.01–1.14, p=0.030) and PSAD (OR per unit increase 3.4×10^{5}, 95% CI $512–2.3\times10^{8}$, p<0.001) were independent predictors of prostate cancer, whereas total PSA was not (OR 0.96, p=0.745). Among the 27 cancer patients, 16 (59.3%) had clinically significant disease (Gleason score ≥7); the percentage of positive biopsy cores independently predicted clinically significant cancer (OR 1.08 per 1% increase, 95% CI 1.02–1.14, p=0.007).

Conclusion

PSA density was the strongest independent predictor of prostate cancer among men with gray-zone PSA values, while total PSA alone showed limited discriminatory value. Incorporating PSAD, together with age, free PSA/f-t-PSA ratio, and digital rectal examination, into routine assessment may improve patient selection for prostate biopsy and reduce unnecessary invasive procedures, particularly in resource-limited settings.

Introduction

Prostate cancer is the second most common cancer diagnosed in men worldwide, with an estimated 1.47 million new cases in 2022.[1] Although age-standardized incidence is highest in North America, Europe, and Australia, its burden is rising in South Asia, including Pakistan, as life expectancy increases, PSA testing becomes more widespread, and lifestyles become increasingly westernized. In Pakistan, reported incidence remains lower than in Western populations; however, patients frequently present with locally advanced or metastatic disease, which adversely affects long-term outcomes.[1,6]

Serum prostate-specific antigen (PSA) transformed early detection of prostate cancer and remains the cornerstone of screening. Its principal limitation is poor specificity: elevated concentrations may reflect benign prostatic hyperplasia, prostatitis, urinary tract infection, or recent prostatic manipulation rather than malignancy. The greatest diagnostic uncertainty occurs when total PSA lies between 4 and 10 ng/mL — the so-called "PSA gray zone" — where only a minority of biopsies confirm cancer, yet transrectal biopsy carries recognized risks of bleeding, infection, urinary retention, pain, and psychological distress.

Several inexpensive adjunctive parameters have been proposed to improve patient selection in this range. PSA density (PSAD), calculated by dividing serum PSA by prostate volume, corrects for the PSA contribution of benign glandular enlargement and has repeatedly shown better specificity than total PSA alone.[2–4] The free-to-total PSA ratio (f/t PSA) exploits the observation that malignant tissue releases a greater proportion of complexed PSA, lowering the free fraction.[5] Digital rectal examination (DRE), although operator-dependent, remains a simple bedside test capable of identifying suspicious induration or nodularity before any biochemical testing is available. PSAD cut-off values derived from one population may not directly translate to another, as cross-population studies have shown variation in optimal thresholds.[1,7]

Advanced tools such as multiparametric MRI, the Prostate Health Index, the 4Kscore, and genomic panels have improved diagnostic accuracy in high-resource settings,[6] but their cost and limited availability restrict routine use in low- and middle-income countries. Liu et al. similarly demonstrated, in a Chinese cohort of 235 men with gray-zone PSA, that PSAD and prostate volume were independent predictors of both prostate cancer and clinically significant disease, and that a multivariable clinical-parameter model outperformed multiparametric MRI alone.[7] Comparable findings from Korean and Middle Eastern cohorts further support the diagnostic value of PSAD-based parameters in gray-zone populations.[8–11] However, prospective data evaluating these low-cost parameters in Pakistani patients remain scarce, despite likely differences

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in prostate volume, PSA kinetics, and healthcare access compared with the populations described above. Emerging serum metabolomic biomarkers have also shown potential to distinguish malignant from benign disease within the PSA gray zone, although prospective validation remains limited.[21]

This prospective observational study was therefore designed to evaluate the diagnostic accuracy of PSAD, f/t PSA ratio, and DRE for predicting histopathologically confirmed prostate cancer among men with serum PSA between 4 and 10 ng/mL, and to identify the clinical parameters independently associated with both overall and clinically significant prostate cancer in this population.

Materials and Methods

Study Design and Setting

This prospective observational study was conducted in the Prostate Clinic, Department of Urology, at a tertiary-care teaching hospital in Pakistan. The study was conducted in accordance with the ethical principles of the Declaration of Helsinki[10] and is reported according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.[11]

Sample Size and Sampling

The sample size was estimated using an anticipated prostate cancer prevalence of 5.3% among Pakistani men with gray-zone PSA, a 95% confidence level, and a 2% margin of error, yielding a target enrolment of 132 participants, which constituted the final study population. A non-probability consecutive sampling technique was used: all eligible patients attending the clinic during the recruitment period were enrolled until the target was reached.

Eligibility Criteria

Men were eligible if they presented with total serum PSA between 4 and 10 ng/mL and underwent transrectal ultrasound-guided prostate biopsy after clinical evaluation. Patients were excluded if they had a PSA outside this range, clinical evidence of acute prostatitis, recent urethral catheterization or lower urinary tract instrumentation, prior prostate surgery, current treatment with 5-alpha reductase inhibitors, or incomplete clinical/histopathological records. Age, PSAD, f/t PSA ratio, and DRE findings were treated as study variables rather than enrolment criteria, so that their diagnostic performance could be assessed across the full range of values observed in an unselected gray-zone population (age range 50–85 years).

Study Procedure

After written informed consent, demographic data and lower urinary tract symptoms were recorded. Serum total and free PSA were measured before any prostate manipulation. Digital rectal examination was performed by an experienced consultant urologist and classified as suspicious or non-suspicious for malignancy based on nodularity, asymmetry, induration, or obliteration of the median sulcus. Transrectal ultrasonography was then performed to estimate prostate volume, and PSA density was calculated as:

$$PSAD\ (ng/mL/cm^3) = Total\ serum\ PSA\ (ng/mL) \div Prostate\ volume\ (cm^3)$$

All participants subsequently underwent ultrasound-guided transrectal prostate biopsy under local anaesthesia using an 18-gauge biopsy needle, following a systematic 12-core protocol with additional targeted cores where sonographic abnormalities were identified. Histopathological examination was the reference standard for the diagnosis of prostate cancer, and Gleason grading was used to classify clinically significant prostate cancer (CSPCa) as Gleason score ≥7, consistent with prior gray-zone PSA studies.[7]

Study Variables and Outcomes

Independent variables were age, total PSA, free PSA, f/t PSA ratio, PSAD, prostate volume, and DRE findings. The primary outcome was histopathologically confirmed prostate cancer. Secondary outcomes were the diagnostic performance of PSAD, f/t PSA ratio, and DRE; the independent predictors of prostate cancer on multivariable analysis; and, among patients with confirmed cancer, the clinical and pathological correlates of clinically significant disease (CSPCa,

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Gleason ≥7), including the percentage of positive biopsy cores.

Statistical Analysis

Data were entered in Microsoft Excel and analysed using IBM SPSS Statistics (IBM Corp., Armonk, NY, USA). Normality of continuous variables was assessed using the Shapiro-Wilk test and histogram inspection. Normally distributed variables are presented as mean ± standard deviation and compared using the independent-samples t-test; non-normally distributed variables are presented as median (interquartile range, IQR) and compared using the Mann-Whitney U test. Categorical variables are presented as frequencies and percentages and compared using the chi-square test or Fisher's exact test where expected cell counts were fewer than five. Variables significant on univariable analysis were entered into multivariable binary logistic regression models (stepwise, forward-conditional method) to identify independent predictors of (i) prostate cancer versus benign histopathology and (ii) clinically significant versus non-significant prostate cancer. Adjusted odds ratios with 95% confidence intervals are reported. A two-tailed p-value <0.05 was considered statistically significant throughout.

Ethical Considerations

Ethical approval was obtained from the Ethics Committee prior to patient recruitment. Written informed consent was obtained from all participants, and data were anonymized before analysis.

Results

Patient Characteristics

A total of 132 men with serum PSA 4–10 ng/mL underwent transrectal ultrasound-guided prostate biopsy. Histopathology confirmed prostate cancer in 27 patients (20.5%), giving an overall cancer detection rate of 20.5% in this gray-zone cohort (Table I). The median age of the overall cohort was 66 years (IQR 60–71). Patients with prostate cancer were significantly older than those with benign histopathology (median 70 vs 64 years, p=0.011) and had significantly smaller prostate volumes (41.4±11.2 vs 60.3±21.1 mL, p<0.001). Median total PSA did not differ significantly between men with and without cancer (8.3 vs 7.9 ng/mL, p=0.410), confirming the limited discriminatory ability of total PSA within the gray zone. In contrast, free PSA (1.1 vs 1.9 ng/mL, p<0.001), f/t PSA ratio (13.6% vs 25.5%, p<0.001), and PSAD (0.19 vs 0.13 ng/mL/cm³, p<0.001) were all significantly different between the two groups. DRE was suspicious in 4/27 (14.8%) cancer patients versus 6/105 (5.7%) of those without cancer; this difference did not reach statistical significance (p=0.121) (Table I).

Clinically Significant Prostate Cancer (CSPCa)

Among the 27 histopathologically confirmed cancers, 16 (59.3%) had Gleason score ≥7 (clinically significant disease, CSPCa) and 11 (40.7%) had Gleason score 6 (non-CSPCa). None of the routine clinical/biochemical parameters (age, prostate volume, total PSA, free PSA, f/t PSA ratio, PSAD, or DRE) differed significantly between the CSPCa and non-CSPCa subgroups (all p>0.05, Table I). However, the percentage of positive biopsy cores was markedly higher in patients with CSPCa than those with non-significant disease (median 66.6% vs 16.6%, p<0.001), reflecting greater tumour burden.

Multivariable Analysis – Predictors of Prostate Cancer

On multivariable binary logistic regression including age, total PSA, and PSAD, age (adjusted OR 1.07, 95% CI 1.01–1.14, p=0.030) and PSAD (p<0.001) were independent predictors of prostate cancer, whereas total PSA was not (adjusted OR 0.96, 95% CI 0.74–1.25, p=0.745) (Table II). Because PSAD is a continuous measure confined to a narrow biological range (approximately 0.05–0.40 ng/mL/cm³ in this cohort), its odds ratio per 1-unit increase is numerically very large (OR 3.4×10^5, 95% CI 512–2.3×10^8); expressed per clinically meaningful 0.1-unit increase in PSAD, this corresponds to an approximate 3.6-fold increase in the odds of prostate cancer, consistent with its identification as the strongest predictor

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in the model. Free PSA, f/t PSA ratio, and DRE, although significant on univariable comparison, were not retained in the final stepwise model, most likely reflecting shared variance with PSAD and total PSA rather than an absence of clinical relevance.

Multivariable Analysis – Predictors of Clinically Significant Disease

Among the 27 patients with confirmed prostate cancer, logistic regression identified the percentage of positive biopsy cores as an independent predictor of clinically significant disease (adjusted OR 1.08 per 1% increase, 95% CI 1.02–1.14, p=0.007) (Table III), indicating that greater biopsy tumour burden was associated with higher-grade disease, independent of the pre-biopsy clinical and biochemical parameters evaluated.

Table I. Baseline and comparative characteristics of the study population, stratified by prostate cancer status and, among cancer patients, by clinically significant disease (Gleason ≥7).

Parameter	Total (n=132)	PCa (n=27)	Non-PCa (n=105)	p-value*	Non-CSPCa mean±SD (n=11)	CSPCa mean±SD (n=16)	p-value †
Total, n (%)	132	27 (20.5%)	105 (79.5%)	<0.001	11 (40.7%)	16 (59.3%)	0.336
Age (years), median (IQR)	66 (60–71)	70 (67–73)	64 (60–70)	0.011	68.55 ± 6.94	68.50 ± 4.69	0.984
Prostate volume (mL), mean±SD	56.4 ± 20.9	41.44 ± 11.22	60.26 ± 21.05	<0.001	43.82 ± 11.30	39.81 ± 11.23	0.373
Total PSA (ng/mL), median (IQR)	8.2 (6.4–9.9)	8.3 (7.2–9.2)	7.9 (5.9–9.9)	0.410	8.02 ± 1.00	8.66 ± 1.63	0.259
Free PSA (ng/mL), median (IQR)	1.8 (1.1–2.6)	1.1 (0.95–1.73)	1.9 (1.3–2.8)	<0.001	1.32 ± 0.48	1.32 ± 0.63	0.989
f/t PSA (%), median (IQR)	22.6 (16.5–32.1)	13.6 (11.10–18.7)	25.5 (18.10–36.10)	<0.001	16.4 (11.6–18.7)	13.2 (10.9–20.9)	0.323
PSAD (ng/mL/cm³), median (IQR)	0.14 (0.11–0.20)	0.19 (0.16–0.23)	0.13 (0.10–0.19)	<0.001	0.20 (0.14–0.22)	0.21 (0.18–0.32)	0.150
DRE suspicious, n (%)	10	4 (14.8%)	6 (5.7%)	0.121	1 (9.1%)	3 (18.8%)	0.624
Positive biopsy cores (%), median (IQR)	—	53.8 (25–75)	—	—	16.6 (8.3–41.7)	66.6 (54.9–92.1)	<0.001

*PCa: prostate cancer; CSPCa: clinically significant prostate cancer (Gleason ≥7); non-CSPCa: Gleason score 6; PSAD: PSA density; DRE: digital rectal examination; SD: standard deviation; IQR: interquartile range. *PCa vs non-PCa. †Non-CSPCa vs CSPCa (among the 27 confirmed cancers).*

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Table II. Multivariable binary logistic regression analysis of clinical parameters predicting prostate cancer (n=132).

Variable	B	S.E.	p-value	Adjusted OR	95% CI (Lower–Upper)
Age (years)	0.070	0.032	0.030	1.072	1.007 – 1.142
Total PSA (ng/mL)	−0.044	0.134	0.745	0.957	0.735 – 1.246
PSA density (ng/mL/cm³)	12.738	3.316	<0.001	3.4×10^5	512 – 2.3×10^8
Constant	−7.908	2.408	0.001	—	—

Variables entered: age, total PSA, PSA density (stepwise, forward-conditional method). OR: odds ratio; CI: confidence interval; S.E.: standard error. The odds ratio for PSAD is expressed per 1 ng/mL/cm³ increase; given the narrow biological range of PSAD (0.05–0.40 ng/mL/cm³ in this cohort), this corresponds to an approximate 3.6-fold increase in the odds of prostate cancer per 0.1-unit increase in PSAD.

Table III. Multivariable binary logistic regression analysis of predictors of clinically significant prostate cancer among patients with confirmed malignancy (n=27).

Variable	B	S.E.	p-value	Adjusted OR	95% CI (Lower–Upper)
Positive biopsy cores (%)	0.075	0.028	0.007	1.078	1.021 – 1.138
Constant	−3.260	1.389	0.019	—	—

Variable entered: percentage of positive biopsy cores (stepwise, forward-conditional method); clinically significant prostate cancer defined as Gleason score ≥7. OR: odds ratio; CI: confidence interval; S.E.: standard error.

Discussion

In this prospective study of 132 men with PSA in the diagnostic gray zone, PSA density was the strongest independent predictor of prostate cancer, while total serum PSA alone did not discriminate between malignant and benign histopathology. Age, prostate volume, free PSA, and f/t PSA ratio also differed significantly between men with and without cancer, and, among patients with confirmed malignancy, the percentage of positive biopsy cores independently predicted clinically significant disease. These findings support incorporating simple, low-cost clinical parameters into the assessment of men with gray-zone PSA to guide biopsy decisions.

Total PSA Alone Has Limited Diagnostic Value

Total PSA did not differ significantly between men with and without prostate cancer in this cohort (p=0.410), consistent with the well-recognized overlap between benign prostatic hyperplasia and malignancy within the 4–10 ng/mL range. Liu et al. similarly reported no significant difference in total PSA between prostate cancer and non-cancer groups among 235 Chinese men with gray-zone PSA (P=0.824), underscoring the limited standalone value of total PSA in this population and the need for adjunctive markers.[7]

PSA Density Was the Strongest Predictor

PSAD was significantly higher in men with prostate cancer and remained the strongest independent predictor on multivariable analysis. This is biologically plausible: benign glandular enlargement increases PSA production roughly in proportion to gland volume, whereas malignant tissue secretes disproportionately more PSA per unit volume, so adjusting PSA for gland volume improves specificity. Liu et al. likewise found PSAD to be an independent predictor of both overall and clinically significant prostate cancer, with prostate volume and PSAD outperforming other single clinical parameters.[7] Lee et al. similarly reported that PSAD achieved better diagnostic performance than unadjusted PSA in men with gray-zone PSA (67.1% sensitivity, 71.7% specificity at a cut-off of 0.18 ng/mL/cm³),[8] and PSAD-based cut-offs have been shown to predict clinically significant disease across multiple populations.[2–4] Because transrectal ultrasound is inexpensive and widely

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available, routine calculation of PSAD represents a practical strategy for improving biopsy selection in resource-limited settings such as ours.

Free PSA and f/t PSA Ratio

Both free PSA and the f/t PSA ratio were significantly lower among men with prostate cancer, consistent with the established observation that malignant prostate tissue releases a greater proportion of protein-bound PSA into the circulation.[5] A meta-analysis of f/t PSA ratios in men with total PSA 4–10 ng/mL reported improved detection of prostate cancer compared with total PSA alone,[5] supporting our findings. Combining f/t PSA with PSAD has similarly been shown to improve sensitivity for reducing unnecessary biopsies beyond either parameter used alone.[18] However, neither free PSA nor f/t PSA ratio was retained in the final multivariable model in the present study, most likely because of shared variance with PSAD and total PSA rather than a true absence of independent predictive value; this should be interpreted with caution given the study's modest sample size, and larger cohorts may be needed to disentangle these correlated predictors.

Age and Prostate Volume

Increasing age was independently associated with prostate cancer, consistent with the known rise in incidence with age and its inclusion in established prostate cancer risk calculators such as those derived from the European Randomised Study of Screening for Prostate Cancer (ERSPC).[12] Prostate volume was significantly smaller among men with cancer, an association reported previously in ERSPC risk-calculator analyses[13] and attributed to the disproportionate contribution of benign glandular hyperplasia to gland enlargement; this relationship underlies the improved performance of PSAD relative to unadjusted PSA.

Digital Rectal Examination

DRE was more frequently suspicious among men with prostate cancer (14.8% vs 5.7%), but this difference did not reach statistical significance, likely reflecting the limited sample size and the low overall proportion of palpable disease in this gray-zone cohort. Comparable large studies have shown that DRE contributes modestly, but not always significantly, to detection when combined with PSA-based parameters,[14] suggesting DRE is best used as a complementary rather than standalone test in this setting.

Clinically Significant Disease

None of the pre-biopsy clinical or biochemical parameters distinguished clinically significant (Gleason ≥7) from non-significant cancer in this cohort, which may reflect the small number of confirmed cancers (n=27) available for this subgroup comparison. Only the percentage of positive biopsy cores — a post-biopsy pathological measure of tumour burden — was independently associated with clinically significant disease. This finding is consistent with previous work showing that biopsy core positivity correlates with grade and volume of disease,[7] but it also highlights that our pre-biopsy panel, while useful for deciding whether to biopsy at all, was not able to identify which of the biopsied men had higher-grade disease; larger studies incorporating multiparametric MRI or biomarker panels would be needed to address this specific question.

Clinical Implications

These findings have practical relevance for resource-limited healthcare systems. Multiparametric MRI, the Prostate Health Index, the 4Kscore, and genomic biomarkers improve diagnostic accuracy but remain costly and inaccessible in many centres.[6] PSAD, f/t PSA ratio, and DRE are inexpensive, widely available, and can be incorporated into routine outpatient evaluation. Using these parameters together — rather than total PSA alone — may improve patient selection for biopsy, reduce unnecessary invasive procedures, and lower healthcare costs without materially compromising cancer detection.

Strengths and Limitations

This study has several strengths: a prospective design that minimized recall bias; histopathological confirmation for every

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participant; simultaneous evaluation of multiple routinely available predictors with multivariable adjustment; and, to our knowledge, one of the first prospective evaluations of these parameters in a Pakistani gray-zone PSA population.

Several limitations should be acknowledged. First, this was a single-centre study, which may limit generalizability to other populations and healthcare settings. Second, the sample size, while adequate for the primary comparisons, yielded relatively wide confidence intervals for some estimates (notably the PSAD odds ratio) and limited statistical power for the CSPCa subgroup analysis (n=27); larger multicentre cohorts are needed to confirm these findings and to more precisely quantify effect sizes. Third, because all study variables — including PSAD, f/t PSA ratio, and DRE — were treated as measured predictors rather than enrolment gates, cancer prevalence in this cohort (20.5%) may not be directly comparable with series that pre-selected patients on the basis of abnormal findings in one or more of these parameters; this should be considered when comparing detection rates across studies. Fourth, newer biomarkers such as the Prostate Health Index, 4Kscore, PCA3, and multiparametric MRI were not evaluated and may further improve risk stratification when combined with the parameters studied here. Finally, long-term oncological follow-up of biopsy-negative patients was not available.

Future Directions

Future multicentre prospective studies with larger sample sizes should validate these findings and evaluate integrated prediction models combining PSAD, f/t PSA ratio, DRE, multiparametric MRI, and emerging molecular biomarkers. Radiomics-based nomograms[19] and PSMA PET/CT[20] have shown promising early results in refining risk stratification within the PSA gray zone and may warrant incorporation into future prediction models. Externally validated risk calculators incorporating these variables could further reduce unnecessary prostate biopsies while preserving detection of clinically significant disease.

Conclusion

Among men with serum PSA in the diagnostic gray zone (4–10 ng/mL), PSA density was the strongest independent predictor of prostate cancer and outperformed total PSA alone. Increasing age, smaller prostate volume, lower free PSA, and lower f/t PSA ratio were also significantly associated with biopsy-confirmed malignancy, whereas total PSA showed limited discriminatory ability. Incorporating PSAD, f/t PSA ratio, and DRE into routine assessment may improve patient selection for prostate biopsy and reduce unnecessary invasive procedures, particularly in resource-limited settings; larger multicentre studies are warranted to externally validate these findings.

Clinical Relevance

- PSA density should be routinely calculated in men with gray-zone PSA using widely available transrectal or transabdominal ultrasound.
- The free-to-total PSA ratio provides additional, though non-independent, diagnostic information and can support clinical decision-making.
- Digital rectal examination remains a useful, low-cost bedside adjunct, even though it was not independently predictive in this cohort.
- Combining these readily available parameters, rather than relying on total PSA alone, may reduce unnecessary biopsies without compromising cancer detection — an approach particularly relevant where multiparametric MRI and genomic testing are not routinely available.

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Conflict of Interest

The authors declare that they have no competing interests.

Data Availability Statement

The datasets generated and analysed during the current study are available from the corresponding author upon reasonable request and subject to institutional policy.

Ethical Approval

The study was approved by the Ethics Committee of the participating institution. All participants provided written informed consent before enrolment, and the study was conducted in accordance with the ethical principles of the Declaration of Helsinki.

Figure Legends

Figure 1. STROBE flow diagram of patient recruitment, biopsy outcomes, and classification into prostate cancer / non-prostate cancer and CSPCa / non-CSPCa subgroups.

Figure 2. Forest plot of adjusted odds ratios (95% CI) for age, total PSA, and PSA density from the multivariable logistic regression model predicting prostate cancer (Table II).

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