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Research Article

A Practical Algorithm for Evaluation of Men With persistently Raised PSA: Is the Role of DRE Underestimated?

Krishna Rao Gurugubelli[1], Bharat Kumar[1], Sachin Bhagwan Dhakare[1], Atul Vishwanath Domakuntla[1], Arun Kumar SM[2], Lal Darsan[3], H Krishna Moorthy[4]*

[1]DrNB Resident, Department Of Urology, Lourdes Hospital-Postgraduate Institute of Health Sciences and Research, Pachalam, Kochi, Kerala, India
[2]Consultant Radiologist, Lourdes Hospital-Postgraduate Institute of Health Sciences and Research, Pachalam, Kochi, Kerala, India
[3]MS (Surg), DNB (Surg), FMAS, Mch (Urology), Consultant Urologist, Department of Urology, Lourdes Hospital-Postgraduate Institute of Health Sciences and Research, Pachalam, Kochi, Kerala, India
[4]MS(Surg), DNB (Surg), Mch (Urology), DNB (Urology), MNAMS, Senior Consultant & Head of the Department, Department of Urology, Lourdes Hospital-Postgraduate Institute of Health Sciences and Research, Pachalam, Kochi, Kerala, India

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Correspondence to: Dr. H. Krishna Moorthy, MS(Surg), DNB (Surg), Mch (Urology), DNB (Urology), MNAMS, Senior Consultant & Head of the Department, Department of Urology, Lourdes Hospital-Postgraduate Institute of Health Sciences and Research, Pachalam, Kochi, Kerala, India. Email: dr.moorthy65@gmail.com

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Abstract

Background: Symptomatic men with elevated prostate-specific antigen (PSA) pose a diagnostic challenge due to overlap between benign and malignant conditions. A structured, algorithm-based approach integrating clinical examination, imaging, and appropriate biopsy modality may improve diagnostic accuracy while reducing unnecessary procedures.

Objective: To evaluate an algorithm-based diagnostic approach for symptomatic men with elevated PSA, stratified by clinical palpability, and to assess the diagnostic performance of finger-guided transrectal biopsy and multi parametric MRI-directed TRUS (trans rectal ultrasound) cognitive fusion biopsy.

Materials and Methods: This prospective observational study included 78 symptomatic men with persistently elevated PSA of >4ng/ml who underwent prostate biopsy. Patients were stratified based on digital rectal examination (DRE) into clinically palpable and non-palpable prostate groups. Patients with palpable lesions underwent finger-guided transrectal biopsy, while those with non-palpable prostates underwent multiparametric MRI (mpMRI), followed by TRUS-guided cognitive fusion biopsy for PI-RADS ≥ III lesions. Final diagnosis was confirmed by biopsy, TURP histopathology when performed, or serial PSA follow-up when treatment is inconclusive of malignancy.

Results: Among 56 patients with clinically palpable lesions, finger-guided biopsy detected carcinoma prostate in 36 patients, with one false-negative identified on TURP. Sensitivity, specificity, PPV, NPV, and diagnostic accuracy were 97.2%, 100%, 100%, 95%, and 98.2%, respectively. Among 22 patients with clinically non-palpable prostates and PI-RADS ≥ III lesions, TRUS-guided cognitive fusion biopsy detected malignancy in 13 patients, with 100% sensitivity, specificity, and diagnostic accuracy. No statistically significant difference in cancer detection was observed between groups (p = 1.00).

Conclusion: An algorithm-based approach integrating DRE, mpMRI, and tailored biopsy techniques provides excellent diagnostic accuracy in men with persistently elevated PSA. Finger-guided biopsy remains effective in clinically palpable lesions, while mpMRI-directed TRUS biopsy is highly reliable in clinically non-palpable cases.

Keywords: Prostate-Specific Antigen; Prostatic Cancer Diagnostic Algorithm; Digital Rectal Examination; Multiparametric MRI; TRUS-Guided Biopsy.

Introduction

Elevated prostate-specific antigen (PSA) levels in symptomatic men represent a frequent and complex diagnostic challenge in urological practice. Although PSA is widely used for prostate cancer detection, it lacks specificity and may be elevated in several benign conditions, including benign prostatic hyperplasia (BPH), prostatitis, acute urinary retention, and following urological instrumentation [1–3]. This diagnostic ambiguity is particularly relevant in symptomatic patients, where PSA elevation may not reliably indicate malignancy.

Digital rectal examination (DRE) remains a fundamental component of prostate cancer evaluation. Clinically palpable abnormalities detected on DRE are associated with a higher likelihood of malignancy and often represent more advanced disease [4,5]. However, a substantial proportion of prostate cancers—particularly clinically significant tumors—occur in men with a non-palpable prostate on DRE, limiting the sensitivity of clinical examination alone [6].

Multiparametric magnetic resonance imaging (mpMRI) has emerged as a valuable tool in the evaluation of men with elevated PSA, especially in those with clinically non-palpable prostates. mpMRI improves detection of clinically significant prostate cancer, facilitates lesion localization, and enables targeted biopsy approaches, thereby reducing unnecessary biopsies and detection of indolent disease [7–9]. The Prostate Imaging Reporting and Data System (PI-RADS) provides standardized risk stratification, with PI-RADS ≥ III lesions demonstrating an increased likelihood of malignancy [10].

Despite these advances, considerable variation exists in real-world diagnostic pathways, particularly in resource-limited settings where access to mpMRI may be selective and Asian populations, where differences in disease epidemiology and access to diagnostic modalities have been reported. There is a need for a practical, algorithm-based approach that integrates clinical palpability, PSA assessment, mpMRI findings, and appropriate biopsy techniques to optimize cancer detection while minimizing unnecessary interventions [11-14].

This study evaluates an algorithm-driven diagnostic strategy for symptomatic men with elevated PSA, stratified by clinical palpability, and assesses the diagnostic performance of finger-guided transrectal biopsy and mpMRI-directed TRUS cognitive fusion biopsy.

Materials and Methods

This prospective observational study was conducted at a tertiary care urology center after obtaining institutional ethics committee approval. Symptomatic men aged ≥50 years presenting with severe lower urinary tract obstructive symptoms and having persistently elevated serum PSA (>4 ng/mL) detected in 2 blood samples obtained at 1 month interval and no prior diagnosis of prostate cancer were evaluated. All patients underwent detailed clinical assessment, digital rectal examination (DRE), and serum PSA estimation. Based on DRE findings, patients with clinically palpable prostate lesions underwent finger-guided transrectal prostate biopsy, while patients with elevated PSA and clinically non-palpable prostates underwent multiparametric MRI (mpMRI), followed by TRUS-guided cognitive fusion biopsy for PI-RADS ≥ III lesions. Patients with negative biopsy results were followed with serial PSA measurements and/or underwent transurethral resection of the prostate (TURP) when clinically indicated. Final diagnosis was established based on biopsy histopathology, TURP histopathology, or sustained decline in PSA levels on follow-up. Statistical analysis was performed. Categorical variables were expressed as frequencies and percentages. Comparisons between patients with clinically palpable and clinically non-palpable prostate lesions were performed using Fisher's exact test due to small sample sizes. A p-value <0.05 was considered statistically significant.

Results

Out of the 78 symptomatic men with elevated PSA the patient distribution and diagnostic pathway is given in (Table 1).

The results of prostate biopsy being taken were as follows:

Table 1: Patient Distribution and Diagnostic Pathway.

Parameter	Number of Patients (n = 78)	Percentage
Clinically palpable lesions (DRE positive)	56	71.8%
Clinically non-palpable prostate (DRE negative)	22	28.2%
Finger-guided transrectal biopsy	56	71.8%
mpMRI followed by TRUS cognitive fusion biopsy	22	28.2%

Group 1: Clinically Palpable Lesions

All 56 patients underwent finger-guided transrectal biopsy.

- Malignancy detected on initial biopsy: 36 patients (64.28 %)
- Negative for malignancy: 20 patients (35.71%)

Among the 20 biopsy-negative patients:

- One patient was diagnosed with carcinoma prostate on final histopathology following TURP (5%).
- The remaining 19 patients showed benign histopathology on TURP or a sustained decrease in PSA on follow-up (95%).

Group 2: Clinically Non-Palpable Lesions

All 22 patients underwent mpMRI, and all were found to have PI-RADS ≥ III lesions. These patients underwent TRUS-guided cognitive fusion biopsy.

- Malignancy detected: 13 patients (59.09%)
- Negative for malignancy: 9 patients (40.90%)

All biopsy-negative patients were confirmed to have benign disease on TURP histopathology.

Histopathological outcomes are depicted in (Table 2). The diagnostic performance of biopsy techniques given in (Tables 3A, and 3B).

The overall Cancer Detection rates were as follows:

- Total carcinoma prostate diagnosed: 50 out of 78 patients (64.1%)
- Total carcinoma prostate diagnosed among the DRE positive lesions – 66.07 %
- Total carcinoma prostate diagnosed among the DRE negative lesions (but mp-MRI showing PIRADS >III lesions)– 59.09 %

This difference was **not statistically significant** (**Fisher's exact test, p = 1.00**). The false-negative rate was low in both groups, with **one false-negative case (1.8%)** identified in the finger-guided biopsy group and **no false-negative cases** in the TRUS cognitive fusion biopsy group. This difference was also **not statistically significant** (**p = 1.00**).

Table 2: Histopathological Outcomes.

Group	Biopsy Positive	Biopsy Negative	Final Benign	Final Malignant
Clinically palpable (Finger-guided biopsy)	36	20	19	37*
Clinically non-palpable (TRUS cognitive fusion biopsy)	13	9	9	13

*One malignancy detected on TURP after initial negative biopsy.

Table 3A: Finger-Guided Transrectal Biopsy (Clinically Palpable Lesions).

Parameter	Value
Sensitivity	97.2%
Specificity	100%
Positive Predictive Value	100%
Negative Predictive Value	95%
Diagnostic Accuracy	98.2%

Table 3B: TRUS-Guided Cognitive Fusion Biopsy (Clinically Non-Palpable Lesions).

Parameter	Value
Sensitivity	100%
Specificity	100%
Diagnostic Accuracy	100%

Discussion

The proposed diagnostic algorithm, as illustrated in (Figure 1), emphasizes a stepwise approach to the evaluation of men with persistently elevated PSA. A properly performed digital rectal examination serves as the pivotal initial stratification tool, dividing patients into clinically palpable and non-palpable groups, thereby guiding subsequent diagnostic pathways.

In patients with clinically palpable prostate lesions, immediate finger-guided transrectal biopsy forms the cornerstone of evaluation. Our findings demonstrated that this approach yielded excellent diagnostic performance, with a sensitivity of 97.2% and diagnostic accuracy of 98.2%. The algorithm therefore supports the continued relevance of DRE-directed biopsy in symptomatic patients, particularly in settings where advanced imaging may not be universally accessible. The single false-negative case identified only after TURP highlights the safeguard of clinical follow-up, ensuring malignancy detection even when initial biopsy is negative.

For patients with persistently elevated PSA and clinically non-palpable prostate, the algorithm prioritizes multiparametric MRI as the next diagnostic step. mpMRI facilitates lesion localization and risk stratification, allowing

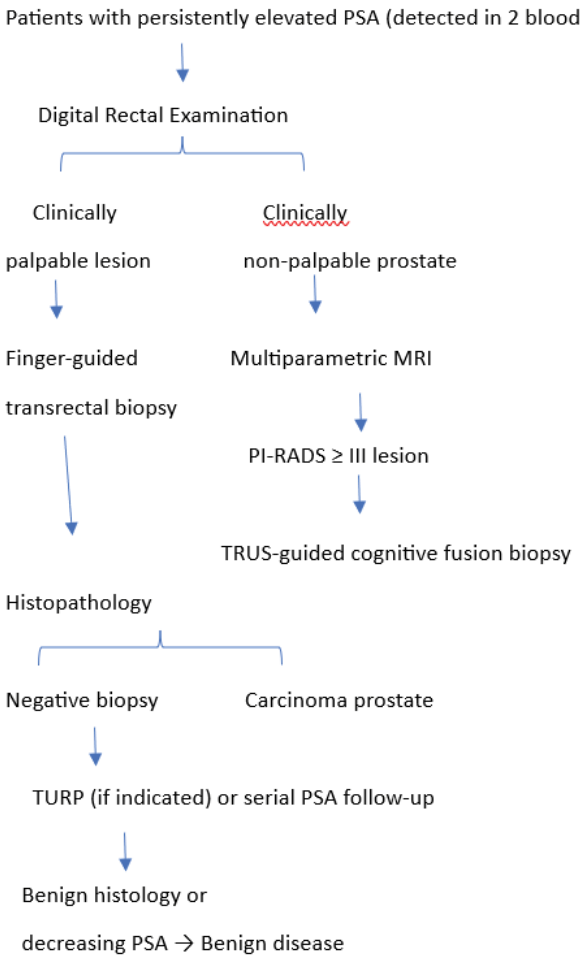

Figure 1: Algorithm for evaluation of men with persistently elevated PSA integrating DRE, mpMRI, and biopsy pathways.

selective biopsy of PI-RADS ≥ III lesions. In our cohort, TRUS-guided cognitive fusion biopsy following mpMRI achieved 100% sensitivity and specificity, underscoring the ability to accurately detect clinically significant disease in this subgroup while avoiding unnecessary biopsy in patients without high-risk imaging features.

A key strength of the algorithm lies in its integration of confirmatory endpoints beyond initial biopsy. Patients with negative biopsy results were not assumed to be disease-free but were taken up for TURP because of severe obstructive and serially followed up.

The lack of statistically significant differences in cancer detection and false-negative rates between the two pathways suggests that appropriate selection of biopsy technique based on clinical palpability and imaging findings is more important than the biopsy modality itself.

The algorithm provides a pragmatic balance between clinical examination, imaging, and histopathology. By aligning biopsy technique with clinical palpability and imaging risk, it optimizes cancer detection while minimizing invasive procedures. Such a structured pathway is particularly applicable in resource-variable healthcare settings and can be readily adapted to routine urological practice.

Conclusion

A clinically driven, algorithm-based approach effectively stratifies symptomatic men with elevated PSA and guides appropriate biopsy selection. Finger-guided transrectal biopsy remains reliable in clinically palpable lesions, while mpMRI-directed TRUS cognitive fusion biopsy offers excellent diagnostic accuracy in clinically non-palpable cases. This structured pathway optimizes prostate cancer detection and minimizes unnecessary invasive procedures.

Conflict of Interest

The authors declare that there are no conflicts of interest regarding the publication of this manuscript.

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