Original Article

JHSMR Journal of Health Science and Medical Research

Cancer Detection Yield of TRUS-Guided Biopsy in Nepalese Men in the Fusion Biopsy Era

Ajit Khadga, M.S.[1], Mahesh Bahadur Adhikari, FNUH[1], Bipin Maharjan, FCPS[1], Ravi Kiran Gautam, FCPS[1], Prashant Mishra, M.S.[1], Birodh Basnet, MBBS[1], Deepak Kumar Yadav, M.S.[1], Kricha Pande, M.D.[2]

[1]Department of Urology and Kidney Transplant, Nepal Mediciti Hospital, Nakhkhu Patan, Karyabinayak 44600, Nepal.
[2]Department of Pathology, Nepal Mediciti Hospital, Nakhkhu Patan, Karyabinayak 44600, Nepal.

Received 4 November 2024 ● Revised 30 December 2024 ● Accepted 4 January 2025 ● Published online 28 April 2025

Abstract:

Objective: Transrectal ultrasound (TRUS)-guided biopsy of the prostate is performed to obtain a histopathological diagnosis of prostate cancer and has been the mainstay of urological practice for years. In the era of fusion biopsy this study aimed to investigates the relevance of TRUS-guided biopsy and its role in cancer detection rates, particularly in resource-limited settings.

Material and Methods: This retrospective study was carried out in a tertiary care institute. All symptomatic patients who underwent TRUS-guided biopsy for indication of raised serum prostate-specific antigen (PSA) level (>4 ng/mL) or suspicious digital rectal examination (DRE) findings (nodule, irregularity, hard consistency) from January 2021 to December 2023 were included. The data obtained were entered in statistics package for social sciences (SPSS). Statistical analyses used were Chi-square test and Spearman's rank correlation analysis.

Results: Out of the 77 patients included in the study, 24 were diagnosed with malignancy, resulting in an overall cancer detection rate of 31.16%. The detection rates for PSA levels of 4-10 ng/mL and 10-20 ng/mL were low, at 14.81% and 18.18%, respectively, while the rate exceeded 50% for PSA levels greater than 30 ng/mL. Additionally, 13 patients (16.88%) had post-biopsy complications, with one requiring hospital admission for fever.

Conclusion: Despite advancements in fusion biopsy, TRUS-guided biopsy remains an essential diagnostic tool for prostate cancer. This study emphasizes the technique's ongoing significance, especially where access to advanced imaging modalities is limited, underscoring its crucial role in clinical decision-making.

Contact: Ajit Khadga, M.S.
Department of Urology and Kidney Transplant, Nepal Mediciti Hospital,
Nakhkhu Ukalo Road, Nakhkhu Patan, Karyabinayak 44600, Nepal.
E-mail: itsmeguies@gmail.com

J Health Sci Med Res
doi: 10.31584/jhsmr.20251194
www.jhsmr.org

Keywords: cancer detection rate, prostate cancer, serum PSA, TRUS-guided biopsy

Introduction

Prostate cancer (PCa) is the most frequently diagnosed cancer in men (excluding skin cancer). It is the fifth leading cause of male cancer-related deaths worldwide[1]. Asia has the lowest incidence of PCa, but it varies significantly among different countries[2]. Although PCa is a major cause of morbidity and mortality in the Nepalese population[3], there are few studies determining the association between prostate-specific antigen (PSA) levels and the risk of PCa.

A transrectal ultrasound guided (TRUS-guided) biopsy is a procedure used to obtain tissue samples from the prostate for the diagnosis of prostate cancer. It is often performed when serum prostate-specific antigen (PSA) levels are elevated or when there are other indications, such as abnormal findings from a digital rectal examination (DRE).

In developed nations, advanced techniques such as magnetic resonance imaging (MRI)-guided biopsies have enhanced the detection of clinically significant prostate cancer while minimizing unnecessary interventions compared to resource-limited settings like Nepal where we primarily rely on TRUS-guided biopsies due to their accessibility and cost-effectiveness. TRUS-guided biopsy have been used for detecting PCa since the early 1990s[4]. The reported cancer detection rates for TRUS-guided biopsy vary significantly, with reported yields of 30% among Western countries[5] and a slightly lower range in Asian populations.

Complication rates associated with TRUS-guided biopsies range from 20% to 50% globally, with infectious complications, such as bacteriuria and sepsis, affecting 1–4% of patients[6]. While these rates are well-documented in resource-rich countries, data from Nepal and other low-resource settings remain scarce, making it difficult to evaluate the risks and benefits of this diagnostic approach in such populations.

This study aims to address the significant gap in knowledge regarding prostate cancer detection in the Nepalese population. Specifically, it evaluates the cancer detection rate of TRUS-guided biopsies in patients without prostatitis and explores the sensitivity, specificity, and predictive values (positive and negative) of PSA cutoff levels and suspicious DRE findings. The findings of this study will provide valuable insights into the utility of TRUS-guided biopsies in resource-limited settings and inform clinical practice in Nepal and similar contexts.

Material and Methods

This is a retrospective analysis done in 77 patients at a single tertiary referral hospital, who underwent TRUS-guided biopsy from January 2021 to December 2023. Ethical approval was obtained from the Institutional Review Committee of the Nepal Mediciti Hospital (IRC-RC-081/82-05), and informed consent was documented for all patients prior to the procedure.

Patients were included if they underwent TRUS-guided biopsy for one or more of the following indications: elevated serum PSA levels (>4 ng/mL), suspicious DRE findings (e.g., nodules, irregularities, or hard consistency), or a multiparametric MRI (mpMRI) Prostate Imaging Reporting and Data System (PIRADS) score of 3 or higher.

Patients with a recent history of urinary tract infection, prostatitis, catheterization, or prostate instrumentation were excluded from the study. Prostatitis was excluded based on clinical history, patient-reported symptoms, and laboratory

results where available. Additionally, patients taking 5-alpha reductase inhibitors were excluded in order to avoid potential PSA suppression effects.

Procedure details

Serum PSA was estimated using a fully automated chemiluminescent immunoassay method. Prostate volume was calculated using the formula:

Prostate Volume=Length x Width x Height x $\pi/6$

All patients received an enema 4 hours before the procedure and were administered prophylactic intravenous amikacin (500 mg) 30 minutes prior to the biopsy. The procedure was conducted using an 18-gauge disposable core biopsy gun and a 7.5 MHz end-firing biplanar transrectal ultrasonography probe. Patients were placed in the Sims position, and the perianal region was disinfected with betadine solution. Local anesthesia (5 mL of 2% lignocaine) was infiltrated bilaterally into the prostatic capsule.

A standard 12-core biopsy was performed, with tissue samples obtained from predefined locations: right base lateral, right base medial, left base medial, left base lateral, right mid-gland lateral, right mid-gland medial, left mid-gland medial, left mid-gland lateral, right apex lateral, right apex medial, left apex medial, and left apex lateral. Targeted biopsies were also conducted for patients with PIRADS ≥3 lesions identified on mpMRI. MRI was utilized systematically for patients with ambiguous clinical findings or persistently elevated PSA despite prior negative investigations.

The procedures were performed by urologists with at least 5 years of experience in prostate biopsies, ensuring consistent expertise in sample collection and interpretation. Biopsy specimens were preserved in 10% formalin for histopathological evaluation. Post-procedure, patients were monitored for 2 hours before discharge with a prescription for ciprofloxacin (500 mg twice daily for 5 days) and instructions to return in case of complications.

Statistical analysis

Data analysis was performed using SPSS software version 25.0. Descriptive statistics were used to compare the mean age, prostate size, and PSA levels between patients with malignant and benign findings. Chi-square tests were applied to assess the distribution of suspicious versus normal DRE findings and the cancer detection rates (CDRs) across different PSA groups. To analyze the correlation between PSA levels and Gleason scores, Spearman's rank correlation coefficient was employed, and confidence intervals (95%) were calculated for diagnostic metrics such as sensitivity, specificity, and predictive values. A p-value of <0.05 was considered statistically significant.

Results

Baseline characteristics

A total of 77 patients were included in the study, with 24 (31.16%) diagnosed with a malignant disease and 53 (68.83%) with a benign disease. The baseline characteristics of patients are summarized in Table 1.

Detection rates (CDRs) by PSA levels and DRE findings

The overall CDR was 31.16%. PSA levels and DRE findings significantly influenced detection rates, as shown in Table 2.

The CDRs for PSA ranges 4–10 ng/mL and 10–20 ng/mL were relatively low (14.81% and 18.18%, respectively). Detection rates exceeded 50% for PSA levels >30 ng/mL, peaking at 71.42% for PSA levels of 50–100 ng/mL. Suspicious DRE findings increased CDRs within PSA ranges of 30–100 ng/mL, with statistically significant differences (p-value<0.01).

Diagnostic performance of DRE findings

The overall sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of suspicious DRE findings for detecting prostate cancer were 46.87%, 79%, 62.5%, and 66.66%, respectively. Diagnostic performance across PSA ranges is detailed in Table 3.

A receiver operating characteristic (ROC) curve was generated from simulated PSA scores and patient classification labels. The curve evaluates the trade-off between sensitivity (True Positive Rate) and specificity (False Positive Rate) across various thresholds. The AUC: area under the curve, a measure of model accuracy is shown in Figure 1.

Table 1 Patients characteristics and distribution of serum PSA levels & DRE findings

Characteristic	All patients (n=77)	Malignant disease (n=24)	Benign disease (n=53)
Age (years)	66.35 (53–84)	73.16 (63–82)	63.30 (53–84)
Prostate size (grams)	43.34 (22–165)	38.95 (20–75)	45.33 (22–165)
PSA (ng/mL)	33.11 (4.01–447)	66.65 (7.2–447)	17.73 (4.01–140)

PSA=prostate specific antigen, DRE=digital rectal examination

Table 2 Cancer detection rates (CDRs) by PSA range and DRE findings

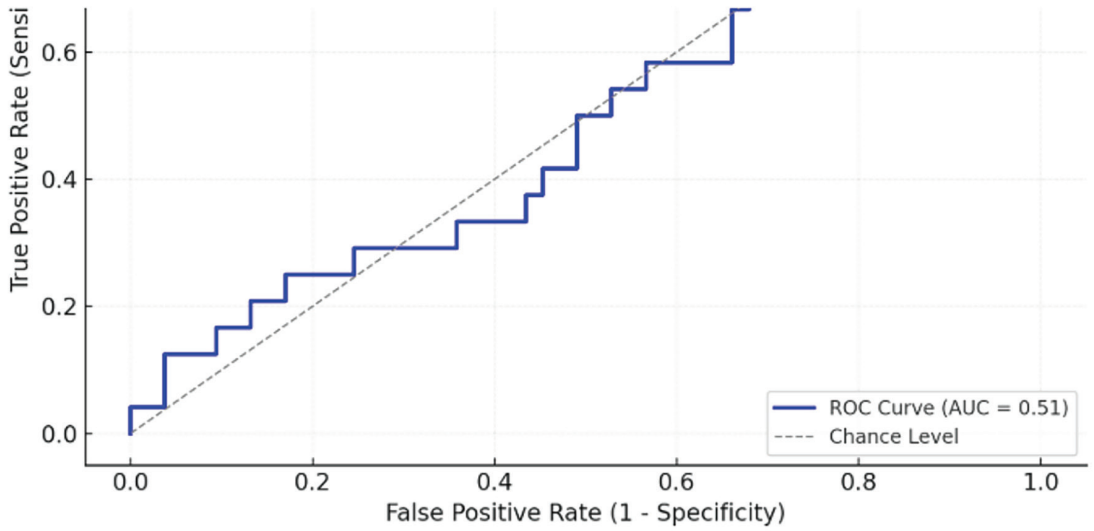
PSA range (ng/mL)	Total patients	Malignant cases	CDR (%) [95% CI]	Suspicious DRE CDR (%)	Normal DRE CDR (%)	p-value
4–10	27	4	14.81 [6.6–28.5]	20.00	13.61	–
10–20	22	4	18.18 [7.3–38.5]	33.33	12.50	–
20–30	9	4	44.44 [18.9–72.4]	42.85	50.00	–
30–50	8	5	62.50 [30.6–86.3]	60.00	66.66	<0.01
50–100	7	5	71.42 [38.1–90.9]	80.00	50.00	<0.001
>100	4	2	50.00 [15.3–84.7]	50.00	–	–

PSA=prostate specific antigen, CDR=cancer detection rate, DRE=digital rectal examination, CI=confidence interval

Table 3 Diagnostic performance metrics of PSA ranges

PSA range (ng/mL)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Overall	46.87	79	62.50	66.66
4–10	20.00	86.36	25.00	82.60
10–20	33.33	87.50	50.00	77.77
20–30	42.85	80	75.00	20.00
30–50	60.00	33.33	60.00	33.33
50–100	80.00	50.00	80.00	50.00
>100	50.00	–	100.00	–

Sensitivity, specificity, positive predictive values and negative predictive values for suspicious DRE in different PSA ranges.
PSA=prostate specific antigen, PPV=positive predictive value, NPV=negative predictive value, DRE=digital rectal examination



Illustrates the trade-off between sensitivity and specificity of PSA values in malignancy detection, with area under the curve (AUC) noted. ROC=receiver operating characteristic, PSA=prostate specific antigen

Figure 1 ROC curve for PSA in predicting prostate cancer detection

Correlation between PSA and Gleason's grade

A moderate positive correlation was observed between serum PSA levels and Gleason's grade in patients with adenocarcinoma (ρ=0.51; p-value<0.05). Gleason's grades among positive cases were distributed as follows: Grade ≤6 (n=2), 3+4 (n=2), 4+3 (n=5), 8 (n=7), and 9–10 (n=8).

Complications

A total of 13 patients (16.88%) experienced complications following the TRUS-guided biopsy. The complications, categorized by severity using the Clavien-Dindo classification, are summarized in Table 4.

One patient required hospitalization for a febrile urinary tract infection and was successfully treated with intravenous antibiotics. Other complications were self-limiting and managed conservatively.

Table 4 Post-biopsy complications categorized by clavien-dindo classification

Complication	Number of cases (n=13)	Clavien-Dindo grade
Hematuria	9	I
Hematospermia	1	I
Hematochezia	1	I
Fever (self-limiting)	1	II
Fever (hospitalized)	1	IIIa

Summarizes the number and severity grade complications following TRUS-guided biopsy

Discussion

In 1989, TRUS-guided biopsy was first described by Hodge and colleagues[7]. The group reported that the technique used a spring-loaded gun to target any ultrasound-visible lesions. In a study of 136 consecutive men with abnormal DRE exam, a 6-core, 1.5 cm TRUS-

guided biopsy produced a CDR of 62%, representing a significant improvement in CDR.

The number of cores in TRUS-guided biopsy increased to 10-12, becoming the standard of care[8,9]. Despite its widespread adoption, TRUS-guided biopsy has a reported underdiagnosis rate of 25–30% of clinically significant tumors[10]. This could occur either due to the under-sampling of lesions or the complete omission of lesions, as demonstrated in repeated biopsy studies[7]. The PROMIS trial highlighted the clinical role of mpMRI for men with suspected prostate cancer prior to biopsy[11]. The authors reported a PPV of mpMRI at 90%, compared to 51% for conventional TRUS-guided biopsy without pre-biopsy imaging [OR 8.2; 95% CI: 4.7–14.3; p-value<0.0001][7].

MRI-TRUS fusion technique is the newest among common methods for detecting prostate cancer. It includes in-bore MR-guided biopsy, cognitive registration, and software registration-based fusion. Fusion biopsy is the diagnostic method of choice for prostate cancer, particularly in patients with previous negative biopsies with suspicious findings[12].

A case study of 2 patients with suspicious DRE findings, mpMRI PIRADS V scores, and PSA levels greater than 100 ng/mL underscores the clinical significance of fusion techniques. These patients underwent a TRUS-guided biopsy at our center twice without detecting any malignancy. Upon referral to India for MRI-TRUS fusion biopsy, they were confirmed positive for prostate cancer, highlighting how fusion biopsy improves diagnostic accuracy.

Recent innovations in prostate cancer diagnosis include the use of transperineal biopsies combined with 3D MRI fusion-guided technology. This approach minimizes infection risks compared to traditional transrectal biopsies and provides more accurate imaging for targeting suspicious areas in the prostate. This technology may improve detection rates and allow procedures to be performed under local anesthesia, further enhancing patient safety and comfort[13].

In a study comparing CDRs between TRUS guided and MRI-targeted biopsy (MRI-TBX), according to PSA level in biopsy-naïve patients, the TRUS-Bx and MRI-TBX groups showed overall CDRs of prostate cancer at 41.4% versus 55.4% (p-value=0.003), and clinically significant prostate cancer at 30.1% versus 42.8% (p-value=0.005). PI-RADS scores of 4 and 5 were associated with higher rates of prostate cancer and clinically significant prostate cancer[14].

Comparative Detection Rates: South Asia and Resource-Limited Settings

Analysis of TRUS-guided biopsy yields varies by region:

- Taiwan: Reported a 14.6% TRUS-guided biopsy yield, attributed to excluding inflammatory prostatic changes and limited PSA ranges[15].
- China: TRUS-guided biopsy yields were 47%[16], though lower among men with PSA levels <20 ng/m.
- Iran and Israel: TRUS-guided biopsy yields of 32.4%[17] and 29%[18], respectively, align closely with global averages.
- Hong Kong: A study by Teoh et al. reported yields of 13.4%, 21.8%, 41.7%, and 85.2% for serum PSA ranges of 4-20, 10-20, 20-50, and 50-100 ng/mL, respectively[19], which aligns with our findings.
- Japan: A single study reported a TRUS-guided biopsy yield of 54.3%[20].
- North America: Orozco et al. reported yields of over 35%, despite employing only 6-core biopsies[21].
- India: Cancer detection rates were 24.37%[22] and 57.5%[23] depending on specific studies.
- Nepal: Reported an unusually high overall TRUS-guided biopsy detection rate of 80% for biopsies ranging between 6 and 12 cores. This finding is significantly higher than others in the global literature[24].

These findings suggest significant geographical variability in cancer detection rates. One explanation is genetic predisposition, which may lead to regional

differences in cancer prevalence. Another critical factor is healthcare access, particularly in resource-limited settings, where delayed diagnostics or access to advanced imaging (MRI/fusion biopsy) might influence the detection rates.

Current evidence highlights the importance of PSA thresholds in guiding biopsy decisions. For example, research demonstrates higher detection rates with PSA >10 ng/mL, yet biopsies at lower thresholds could still result in missed cases of clinically significant prostate cancer. These observations suggest the need to redefine biopsy criteria in order to improve efficiency, ensuring early detection.

While TRUS-guided biopsies are widely utilized, their limitations are well-documented. TRUS-guided biopsy is notably less sensitive than MRI-guided fusion biopsies in detecting clinically significant prostate cancers, particularly in men with prior negative biopsies or in regions of the prostate not adequately sampled by ultrasound alone. These limitations underscore the need for advanced imaging-guided biopsy techniques to supplement traditional TRUS methods, particularly in high-risk cases.

Conclusion

TRUS-guided biopsy is a safe daycare procedure with increasing cancer detection rates at higher PSA levels. However, optimizing PSA cutoffs remains uncertain. Nepalese clinicians should adopt individualized approaches and consider integrating cost-effective advanced imaging techniques to improve diagnostic accuracy. Further population-specific studies are needed in order to establish evidence-based guidelines.

Consent for publication

This study is a retrospective analysis; hence, written consent for publication was not obtained. However, all patients provided informed consent prior to undergoing the procedure.

Research registration number

ERB Protocol No: IRC-RC-081/82-05.

Acknowledgement

We extend our sincere appreciation to the entire urology staff and all our colleagues in the Pathology Department for their invaluable insights into the histopathological findings.

Conflict of interest

None.

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