Diagnostic yield and outcome of transrectal ultrasound-guided prostate biopsy in Sri Lanka

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Abstract

Introduction: The study was aimed to determine the diagnostic yield and outcome of transrectal ultrasound-guided prostate biopsy (TRUSPB) in a cohort of Sri Lankan men.

Methods: A prospective study was conducted among 333 (median age: 70 years, range: 48-88) men from a single urology unit. All patients underwent TRUSPB for persistently elevated serum prostate specific antigen (PSA) ≥4.00 ng/mL or suspicious rectal examination.

Results: The prostate cancer (PCa) detection rate was 57.7%. The PCa detection rate for PSA levels of 4.00 to <10, 10.00 to <20, 20.00 to <40, 40.00 to <100 and ≥100.00 ng/mL were 15/43 (34.9%), 23/88 (26.1%), 41/72 (56.9%), 51/63 (81.0%) and 60/62 (96.8%) respectively. Ten patients required further biopsies for rising PSA despite a first benign biopsy and three had PCa. Mild complications were identified in 6.9% (n=23).

Conclusions: The high PCa detection rate probably reflects the difference in our policy to perform biopsies only when serum PSA level is persistently elevated. TRUSPB appears to have a satisfactory yield with acceptable level of complications in the Sri Lankan resource limited setting.

Introduction

According to the National Cancer Registry of Sri Lanka in 2019, prostate cancer (PCa) is the 5th most common cancer in Sri Lankan men [1]. PCa incidence is rising in Sri Lanka, similar to other Asian countries, although the incidence is much lower than the Western world [2, 3]. Apart from a true increase in incidence, improved awareness and diagnosis, and better data collection, may have also contributed to this increase [3]. There is no nationally accepted serum prostate specific antigen (PSA)-based screening programme for PCa in Sri Lanka [4].

Transrectal ultrasound-guided prostate biopsy (TRUSPB) is the key diagnostic method used to confirm the presence of PCa among men in Sri Lanka. However, the data regarding the diagnostic yield and outcome of TRUSPB is limited in Sri Lanka [5]. The available single study is based on pathology reports, and is lacking clinical data as well as follow-up outcome. Therefore, this study was aimed to determine the diagnostic yield and outcome of TRUSPB in a cohort of Sri Lankan men.

Methods

A prospective study was conducted among men who underwent TRUSPB at the urology unit of Colombo South Teaching Hospital (CSTH), Sri Lanka from 1-Jan-2017 to 31-Dec-2019. Approval was obtained from the Ethics Review Committee of the CSTH. The inclusion criteria were all men with a clinically suspicious prostate with any PSA value or a clinically benign prostate with persistently high (≥4 ng/dl) serum PSA level. The exclusion criteria were patients with a past history of prostate biopsy, prostatic surgery or pelvic irradiation.

When the initial serum PSA level was ≥4 ng/dl and the prostate gland was clinically benign on digital rectal examination (DRE), the patient was given a 28-day course of levofloxacin 500 mg once daily and the serum PSA level was repeated. If the second serum PSA was higher, it was considered a persistently elevated serum PSA. Those with

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a benign histology after first TRUSPB were followed up until their serum PSA level became normal or plateaued. If the serum PSA continued to rise despite a benign histology, the patient was subjected to a repeat biopsy (Figure 1).

All patients had clinical evaluation of the prostate gland by a DRE performed by the urological surgeon. All patients underwent an abdominal ultrasound scan to assess the prostate. Multiparametric-magnetic resonance imaging (MRI) was not performed due to resource constraints. All TRUSPB were done by experienced radiologists using an 18-G biopsy needle. All patients underwent a standard systematic 12-core biopsy. The antibiotic regimen used was intravenous co-amoxiclav 1.2 g and intravenous metronidazole 500 mg given 2 hours before biopsy and oral co-amoxiclav 625 mg eight hourly and oral metronidazole 400 mg eight hourly for five days post-biopsy.

Patients with no immediate complications were discharged following a few hours of observation after advising to return to hospital if they develop urinary retention, fever, persisting haematuria or rectal bleeding. All patients were reviewed after 3 weeks as outpatients to discuss the histology and to identify post-procedural complications. All data in relation to clinical findings, ultrasonography, histology, complications and follow-up serum PSA were recorded.

Bivariate statistical analyses were performed to look for statistical associations. Chi-square test was used to determine associations between two categorical variables. Specificity, sensitivity, positive predictive value and negative predictive value were calculated. A p-value of less than 0.05 was deemed statistically significant [6].

Results

The study included 333 (median age: 70 years, range: 48-88) men. The median ultrasonographic volume of prostate was 40 ml (range: 10-150, IQR: 30-56.25). The median PSA level was 26 ng/mL (IQR:14-66). Around 71.2% (n=237) had lower urinary tract symptoms and 31.8% (n=106) had a history of acute urinary retention. Around 11.4% (n=38) had bone pain and 11.7% (n=39) had haematuria. DRE was clinically malignant among 29.4% (n=98). Ten patients who continued to have rising serum PSA levels after an initial benign biopsy underwent a second biopsy, and three had PCa. Two patients required a third biopsy for continuously rising serum PSA and one had PCa. A total of 196 (57.7%) patients had biopsies positive for PCa (Figure 1).

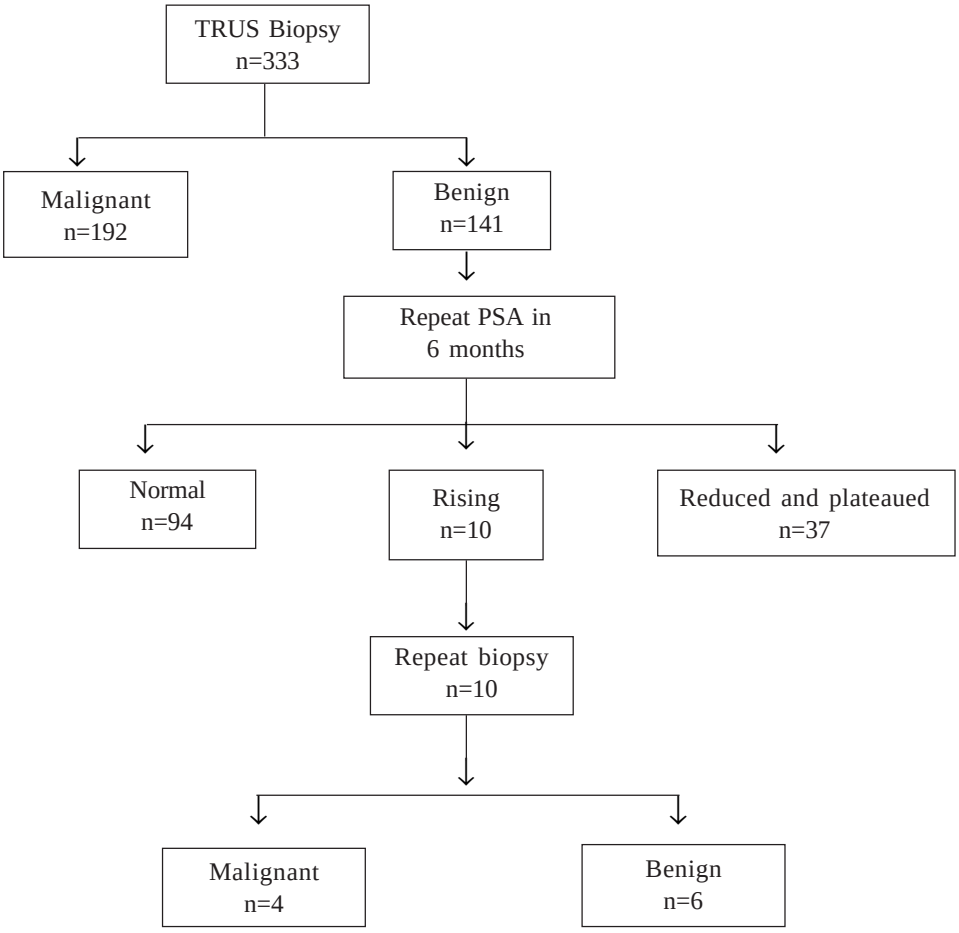

Figure 1. **: Flow chart showing the patient management pathways.**

The mean age of men with PCa was 71.4 ± 7.8 years, compared to 69.9 ± 7.0 years (p=0.09) in the benign group. The median serum PSA value was higher in men with PCa (50.9 ng/mL, IQR: 22-100 ng/mL) compared to those with a negative biopsy (15.8 ng/mL, IQR: 10-25 ng/mL, p<0.001). Malignant prostates had a lower median prostate volume (37, IQR: 30-50 ml vs. 50, IQR: 32-72 ml, p=0.002). The median PSA density was higher among malignant prostates (1.26 ng/ml^2, IQR: 0.5-2.7 vs. 0.34 ng/ml^2, IQR: 0.21-0.58, p<0.001). The likelihood of PCa was higher among those with clinically malignant DRE (76.5% vs. 49.8%, p < 0.001).

The serum PSA level was available in 330 patients. Table 1 shows the PCa detection rate with each PSA categories. Clinical assessment through DRE had minimal ability to predict PCa in all PSA categories. Table S1 shows rate of PCa in patients aged below and above 70 years. The Gleason score (ISUP grade) was compared with the PSA subgroups (Table 2). Sampling inadequacy precluded ISUP grading in 15 patients. Men with serum PSA of ≥40 ng/dl had a greater proportion of high-grade tumours (Table 3). Table 4 summarizes the sensitivity, specificity, positive predictive value, and negative predictive value of PSA levels in predicting PCa.

Of the benign causes, isolated benign prostatic hyperplasia (BPH) was seen among 23.2% (n=77) and coexistence of BPH and chronic prostatitis was seen among 13.5% (n=45). Other findings were isolated chronic prostatitis (3.6%, n=12) and non-caseating granulomatous prostatitis (1.2%, n=4). Twenty-three (6.9%) patients had complications after TRUSPB (urosepsis: 4.8%, n=16, acute urinary retention: 0.9%, n=3, and bleeding: 2.4%, n=8). Four patients with bleeding and fever required no intervention (Clavien-Dindo Grade-I). Nineteen patients needed interventions such as antibiotics, tranexemic acid for bleeding and urethral catheterisation (Clavien-Dindo Grade-II). None developed Clavien-Dindo Grade-III-V complications.

Table 1. Correlation between PSA level, DRE and rate of cancer detection

PSA levels (ng/ml)	*Patients (N)*	*Cancer detection*		*Malignant DRE*			*Clinically benign DRE*			*P value*
		N	*%*	*Total (N)*	*Cancer detection* N	%	*Total (N)*	*Cancer detection* N	%	
<4.00	2	2	100.0%	2	2	100.0%	0	0	0.0%	-
4.00 to <10	43	15	34.9%	6	2	33.3%	37	13	35.1%	0.93
10.00 to <20	88	23	26.1%	14	6	42.9%	74	17	23.0%	0.12
20.00 to <40	72	41	56.9%	16	11	68.8%	56	30	53.6%	0.28
40.00 to <100	63	51	81.0%	21	19	90.5%	42	32	76.2%	0.17
≥100.00	62	60	96.8%	37	35	94.6%	25	25	100.0%	0.23

Table 2. Correlation between PSA levels and ISUP grading in malignant prostates

PSA levels (ng/ml)	*Total (N)*	*ISUP Grade 1*		*ISUP Grade 2*		*ISUP Grade 3*		*ISUP Grade 4*		*ISUP Grade 5*		*Not available*	
		N	%	N	%	N	%	N	%	N	%	N	%
<4.00	2	1	50.0%	0	0.0%	0	0.0%	0	0.0%	1	50.0%	0	0.0%
4.00 to <10	15	5	33.3%	2	13.3%	1	6.7%	1	6.7%	5	33.3%	1	6.7%
10.00 to <20	23	6	26.1%	3	13.0%	1	4.3%	5	21.7%	5	21.7%	3	13.0%
20.00 to <40	41	17	41.5%	5	12.2%	1	2.4%	5	12.2%	10	24.4%	3	7.3%
40.00 to <100	51	12	23.5%	5	9.8%	4	7.8%	6	11.8%	21	41.2%	3	5.9%
≥100.00	60	10	16.7%	5	8.3%	2	3.3%	13	21.7%	25	41.7%	5	8.3%

Table 3. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) with 95% confidence internal (CI) based on the PSA levels

PSA levels (ng/ml)	*Sensitivity (95% CI)*	*Specificity (95% CI)*	*PPV (95% CI)*	*NPV (95% CI)*
≥4.00	99 (96.3-99.9)	0.0 (0.0-2.6)	57.9 (57.6-58.3)	0.0 (0.0-0.0)
≥10.00	91.1 (86.2-94.8)	20.3 (13.9-30.0)	61.4 (59.1-63.6)	62.2 (48.4-74.3)
≥20.00	79.2 (72.7-84.7)	67.4 (58.9-75.1)	77.2 (72.4-81.3)	69.9 (63.3-75.8)
≥40.00	57.8 (50.5-64.9)	89.9 (83.6-94.3)	88.8 (82.6-93.0)	60.5 (56.3-64.6)
≥100.00	31.2 (24.8-38.3)	98.6 (94.9-99.8)	96.8 (88.2-99.2)	50.7 (48.3-53.2)

Table S1. Comparison of age, PSA category and clinical findings with cancer detection rate

Age category (years)	*PSA category (ng/ml)*	*Total*	*PCa rate*		*P value*	*Clinically malignant DRE*			*Benign DRE*			*P value*
			N	*%*		*Total*	*PCa rate N*	*%*	*Total*	*PCa rate N*	*%*	
70 or less	10 or less	27	5	18.5%	<0.001	3	0	0.0%	24	5	20.8%	0.381
	More than 10.00	137	83	60.6%		36	29	80.6%	101	54	53.5%	0.004
More than 70	10 or less	18	13	66.7%	0.581	5	4	80.0%	13	8	61.5%	0.457
	More than 10.00	148	91	62.2%		52	42	80.8%	96	50	52.1%	0.001

Table S2. Comparison of cancer detection rates in similar studies from Sri Lanka and India

Study (Year), Country	*N*	*PCa detection rate*	*PCa detection rate at various PSA levels (ng/mL)*			
			<4	4.00- <10	10.00- <20	≥20.00
Present study (2020), Sri Lanka	333	196 (57.7%)	2/2 (100%)	15/43 (34.9%)	23/88 (26.1%)	152/197 (77.2%)
Lokuhetty (2009), Sri Lanka	749	264 (35.2%)	1/21 (4.8%)	55/137 (40.1%)	>10.00:	196/489 (40.1%)
Laddha A (2020), Kochi, India	853	382 (44.8%)	3/23 (13%)	62/282 (21.9%)	86/226 (38.1%)	231/322 (71.7%)
Patil (2017), Mumbai, India	235	60 (25.5%)	1/10 (10%)	5/84 (6.0%)	10/76 (13.2%)	44/65 (67.7%)
Sinha (2011), Hyderabad, India	119	29 (24.4%)	NA	2/28 (7%)	3/24 (7%)	24/56 (52%)
Chavan (2009), Mumbai, India	440	38 (8.7%)	NA	4/171 (2.3%)	3/118 (2.5%)	70/143 (49.0%)

Discussion and conclusion

In our study, the prevalence of PCa was considerably high (57.7%). We found that the mean PSA in men with PCa was significantly higher than benign prostatic diseases. Furthermore, the median prostate volume in PCa was significantly lower and the PSA density was significantly higher in the malignant prostates compared to the benign group. Clinical findings were not reliable in predicting PCa in all categories of PSA levels.

Comparison of previous studies are shown in table S2 which had a PCa rate of 8.7-44.8% [5, 7-10]. In a previous study from Sri Lanka, the prevalence of PCa in 749 symptomatic males subjected to TRUSPB was 35.2%, which was lower than the current study [5]. Comparatively, our study sample had a higher proportion of malignancies. This variability in proportion of malignant histology is likely to be related to policies of relevant units as to indications for biopsy rather than differences in prevalence rates. Our policy is to perform biopsies when serum PSA level is persistently elevated. Such a policy would avoid unnecessary biopsies in the presence of benign prostates but high initial serum PSA level due to varying causes. This policy has not missed any malignancies as follow-up PSA values of such patients have remained normal in our study.

At present, there is a tendency towards replacing TURSPB with transperineal biopsy due to high incidence of sepsis and missing malignancies in countries where PCa is highly prevalent and screening is practiced widely. Our urosepsis rate was 4.8% which was similar to Western data (2-6%) [11]. All of them settled with oral or intravenous antibiotics without any organ dysfunction or requiring intensive care. Only 10 patients required a second biopsy and two patients a third biopsy due to rising PSA levels after the initial negative histology. Out of them, only four (1.2%) were positive for malignancy. This is much lower than the missed malignancy rate in the West (8.5%), probably due to the lower prevalence of PCa in Sri Lanka [12]. It appears that in the Sri Lankan setting where prevalence of PCa is low and PSA based screening is not nationally accepted, TRUSPB appears to be an acceptable option and there seems to be no necessity at present to embrace transperineal biopsy as the preferred mode of prostate biopsy.

A cut-off value of 4 ng/mL for serum PSA in the diagnosis of PCa had a sensitivity of 99.0. indicating it as a suitable cut-off point to perform TRUSPB. Nearly one third (34.9%) of patients with a serum PSA level of 4-10 ng/ mL had PCa, and the ISUP grading in this group was either 4 or 5 among 40% which is clinically significant. The high proportion of high grade tumours among Sri Lankan men with PCa has been highlighted before [13]. Furthermore, clinical assessment with a DRE was not accurate to differentiate between benign and malignant prostates (33.3% vs. 35.1% respectively, p=0.93). Therefore, persistently elevated serum PSA above 4 ng/ mL should be an indication for prostate biopsy in order to use resources optimally while not missing any malignancy. In our study, the proportion of cancers in the serum PSA 4-10 ng/ mL group was 34.9%. About 68% (13/19) patients older than 70 years and having a serum PSA of 4-10 ng/ mL had PCa (Table 2). This challenges the notion that the cut off level of normal serum PSA rises with advancing age. Therefore, clinicians should be aware of this possibility and monitor the serum PSA level closely even in those above 70 years whose serum PSA is less than 10 ng/ mL.

Author contributions

UJ, SW and AA contributed to concept and design of study, acquisition of data, analysis, interpretation of data, drafting the article and final approval of the version to be published. SV, SM, VS, KE and MA: contributed to acquisition of data, interpretation of data, drafting the article and final approval of the version to be published. AA is the senior author and guarantor of this paper.

Declaration

Competing interests

The authors declare that they have no competing interests.

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Ethics approval

Ethics approval was obtained from the Ethics Review Committee of the CSTH.

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None declared.

Abbreviations

TRUSPB : Transrectal ultrasound-guided prostate biopsy
PSA : Prostate specific antigen
PCa : Prostate cancer
CSTH : Colombo South Teaching Hospital
DRE : Digital rectal examination
MRI : Multiparametric-magnetic resonance imaging
IQR : Interquartile range
ISUP : International Society of Urological Pathology
BPH : Benign prostatic hyperplasia

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