

Role of Prostate Specific Antigen, Digital Rectal Examination and Trans Rectal Ultra Sonography in the Diagnosis of Prostate Cancer in Patients with Lower Urinary Tract Symptoms

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Abstract: *The aim of this study is to compare the role of prostate specific antigen [PSA], digital rectal examination [DRE] and Trans rectal Ultrasonography [TRUS] in detection of prostate cancer among patients presenting with lower urinary tract symptoms [LUTS] and having International Prostate Symptoms Score [IPSS] not less than 7. This study was carried out in I.P.G.M.E.R and S.S.K.M Hospital, Kolkata, West Bengal, India, from March 2011 to March 2012. Sixty patients presenting with LUTS and with IPSS not less than 7, had been screened for prostate cancer using PSA estimation, DRE and TRUS. Trans rectal sextant prostate biopsy was performed in all patients. The PSA estimation revealed 85% sensitivity and 72.5% specificity for the patients with serum total PSA level >10 ng/ml. The positive predictive value [PPV] was 60.7%. If 4 ng/ml is taken as lower cut off value for serum total PSA, the sensitivity increases to 95% whereas specificity reduces to 46.66% and PPV becomes 50%. DRE alone showed 60% sensitivity, 92.5% specificity and 80% PPV for the diagnosis of carcinoma prostate. TRUS has got highest sensitivity [75%], highest specificity [85%]. But the PPV was 71.43%. When DRE and serum PSA >10ng/ml was combined the sensitivity and specificity was raised to 90% and 70% respectively. The PPV was 60%. This was almost comparable with the combination of DRE, serum PSA >10ng/ml and TRUS which has got 90% sensitivity and 85% specificity. The PPV was 75%. None of the single screening tools has got that much efficacy in differentiating carcinoma of prostate from benign hypertrophy of prostate in patients with LUTS. Combining PSA, DRE and TRUS increases sensitivity, specificity and PPV of PC detection.*

Keywords: LUTS, Prostate Specific Antigen, Digital Rectal Examination, Trans rectal ultrasound, Prostate Cancer

1. Introduction

The term prostatomegaly encompasses both Benign Hyperplasia of prostate [BPH] and Carcinoma of Prostate. Men with LUTS are screened for prostate cancer with PSA testing and a digital rectal examination [DRE] as a part of routine prostate assessment. [4] There is general agreement among clinicians that the PSA test has the highest predictive value for prostate cancer as compared to DRE or Trans-rectal ultrasound [TRUS] alone [5,6]. In clinical practice, biopsies are generally performed only when the results of a PSA test or DRE is abnormal. This leads to misdiagnosis of most of the small PCs present in many older men. Patients with LUTS who have PSA levels higher than 4ng/ml are primarily advised to undergo prostate biopsy to rule out cancer. [7] But PSA is organ specific but not cancer-specific, so the presence of other prostate diseases such as benign prostatic hyperplasia [BPH], and prostatitis may influence its effectiveness for cancer detection. [8] Hence, the PSA-based prostate cancer detection is fraught with high false-positive rate.

As an early detection of the cause of LUTS is necessary to offer selective treatment to the concerned subjects and also selecting patients for Radical prostatectomy in organ confined disease, the present study is an attempt to have a comparative analysis among the sensitivity, specificity and positive predictive value of DRE, Serum PSA and TRUS. This study may enable us to find out an ideal diagnostic tool for the early diagnosis of the cause of LUTS, so that specific treatment can be instituted at an early stage.

2. Methods and Material

This prospective descriptive study was carried out in I.P.G.M.E.R and S.S.K.M Hospital, Kolkata, West Bengal, India, in the period of March 2011 to March 2012. The patients were selected from the outdoor of Department of Urology. Institutional ethical committee clearance and informed consent of all patients were obtained. Sixty men at or above fifty years of age presenting with LUTS specifically attributed to prostate problems and with IPSS score not less than 7 were included in the study. Men with calcified or fibrotic prostate, with skeletal or distant metastasis or LUTS caused by any urological malignancy

other than prostate and who had previous prostatic surgery or pelvic radiotherapy or complications of urinary obstruction, were excluded from the study.

The sampling technique is as follows: considering the 15 percent prevalence of LUTS patients in this region, out of the 4000 patients at urology outdoor/year, 600 patients with LUTS were expected to present in one year. Taking into account the feasibility and available resources, around ten percent of this subset, i.e. sixty patients were proposed for the study. Random sampling was done for case selection.

The findings of systemic digital rectal examination [DRE] performed by urologist was noted for all patients as subjective examination according to the following true findings: hard swelling of the prostate, firm swelling, nodular swelling, irregular surface, obligation of middle sulcus attachment to the mucosal of the rectum. As a routine practice, DRE examination was scheduled after collection of blood sample to avoid an increase in serum PSA that may follow digital manipulation of the gland.

Blood samples were collected in 5 ml sterile container containing ethylene diamine tetra acetic acid [EDTA]. The samples were centrifuged within 20 minutes after collection at 500 x g for 10 min, and sera were stored at -20 degree C until assay. The total prostate specific antigen was assessed using ELISA.

PSA levels less than 4 ng/ml were considered as normal, those between 4-10 ng/ml as diagnostic gray zone and above 10ng/ml as indicative of cancer. [9, 10]

All the patients were subjected to TRUS examination and followed by TRUS guided biopsy. TRUS was performed using a real time Biplanar 7.0 or 7.5 MHz ultrasound probe. Whole of the prostate gland was carefully evaluated for any hypo-echoic, An-echoic, Hyper-echoic or Iso-echoic zone. The classical description of prostate cancer on TRUS is a hypo-echoic SOL. [11] Bulging or irregularity of the prostate capsule, extension of hypo-echoic areas on from the central zone into the seminal vesicles, or any area corresponding to an abnormality on DRE, are carefully evaluated.

TRUS guided biopsy was performed in all patients at the time of TRUS examination through peri-anal route. Biopsies were done under antibiotic cover. Systematic sector [Sextant] biopsies were taken with "Autovac" biopsy gun from the base, mid gland and apex of the right and left side and also from any suspicious area. Each of the samples was submitted for pathological examination. The post-intervention patients were kept for observation overnight and discharged next morning with the advice to continue antibiotic for 48 hours and to attend OPD or emergency room in case any problem like haematuria, fever, dysuria or hemo-spermia arises.

Data were analyzed using the Statistical Package for Social Sciences software version 17 for Windows. Sensitivity, specificity, and positive predictive values [PPV] were calculated.

3. Result and Analysis

A total of 60 male patients presenting with lower urinary tract symptoms [LUTS] were included in this study. Their mean age was 66 years [range 50-82]. The patients were selected according to IPSS scores which was not less than 7. Among 60 patients 22 had IPSS 7-10, 32 had IPSS between 11 to 14 and 6 patients had IPSS>14.

Out of 60 men presented with LUTS, 66.66% [40 men] were diagnosed with benign prostatic hypertrophy [BPH], and 33.33% [20 men] with Prostate Cancer [PC]. [Table 1]

The mean of total PSA was 12.09 ng/ml. Out of 40 men with BPH 52.5% [21 men] had total PSA below 4.0 ng/ml, 20% [8 men] had total PSA between 4.0-10.0 ng/ml and 27.5% [11 men] had total PSA >10 ng/ml. While in case of PC [20 men], 5% [1men] showed total serum PSA below 4.0 ng/ml, 10%[2] had total PSA between 4.0-10.0 ng/ml and 85% [17 men] showed total PSA >10.0 ng/ml. [Table 1] For serum PSA >10.0 ng/ml, sensitivity was 85%, specificity was 72.5% and PPV was 60.7% [Table 2].

The DRE result revealed 15 patients [25%] had abnormal DRE suggesting PC, while 45 patients [75%] had no suspicious PC. In the study group, DRE in the detection of PC has sensitivity of 60%, specificity of 92.5% while the PPV was 80% [Table2].

On TRUS, 21 patients showed one or more hypo-echoic areas and 15 among them had carcinoma on biopsy. 5 out of thirty patients with iso-echoic area also showed carcinoma on their biopsy. TRUS showed sensitivity of 75%, specificity of 85% and PPV was 71.43% [Table 2].

When DRE and PSA [>10ng/ml] both combined to detect PC, 18 [90%] out of 20 prostate cancer patient were correctly diagnosed to have PC. 28 [70%] out of 40 BPH patient were detected accurately by this method. The sensitivity, specificity and PPV of this method were 90%, 70% and 60% respectively [Table3].

When DRE, PSA [>10ng/ml] and TRUS were combined to detect PC, 18 [90%] out of 20 PC patient were correctly diagnosed to have prostate cancer. [Table 4] The sensitivity, specificity and PPV were 90%, 85% and 75% respectively.

Table 1: Distribution of patients according to serum PSA, DRE findings and Biopsy results

Serum-PSA value (ng/ml) (n=60)		DRE + (n=15)	DRE - (n=45)	Biopsy +/PC (n=20)	Biopsy -/BPH (n=40)
<4.0	n= 22(36.66%)	2(13.3%)	20(44.44%)	1(5%)	21(52.5%)
4.0-10.0	n= 10 (16.66%)	4(26.6%)	6(13.33%)	2(10.0%)	8(20.0%)
>10.0	n= 28(46.66%)	9(60%)	19(42.22%)	17(85%)	11(27.5%)

Table 2: Results of prostate specific antigen [PSA], digital rectal examination [DRE] and TRUS in detection of prostate cancer [PC]

Tests	Biopsy+/Prostate Cancer	Biopsy -	Total	Sensitivity and specificity
PSA, n				
<4.0 ng/ml	1	21	22	Sensitivity=95%, Specificity=46.66%, PPV=50%
4.0-10.0 ng/ml	2	8	10	Sensitivity=85%, Specificity=72.5% PPV=60.7%
>10 ng/ml	17	11	28	
DRE, n				
Non suspicious	8	37	45	Sensitivity=60%, Specificity=92.5% PPV=80%
Suspicious	12	3	15	
TRUS, n				
Hypo-echoic area	15	6	21	Sensitivity=75%, Specificity=85% PPV=71.43%
Iso-echoic area	5	25	30	
Hyper-echoic	0	6	6	
others	0	3	3	

Table 3: Distribution of patients according to DRE+ PSA [>10ng/ml] with biopsy results

Tests	Biopsy +/PC	Biopsy -	Total	Sensitivity, specificity & PPV
DRE + &/or PSA>10ng/ml	18	12	30	Sensitivity=90%, specificity=70% PPV=60%
DRE - &/or PSA<10ng/ml	2	28	30	

Table 4: Distribution of patients according to DRE+ PSA>10ng/ml +TRUS findings with biopsy results

Tests	Biopsy +/PC	Biopsy -	Total	Sensitivity, specificity & PPV
DRE + &/or PSA>10ng/ml &/or TRUS +	18	6	24	Sensitivity=90%, specificity=85% PPV=75%
DRE - &/or PSA<10ng/ml &/or TRUS-	2	34	36	

4. Discussion

In the present study 60 patients presented with LUTS and having IPSS not less than 7 were screened with serum PSA, DRE and TRUS followed by TRUS guided biopsy. The age distribution ranged from 51 years to 82 years [mean 66 years]. Among 60 patients 22 had IPSS 7-10, 32 had IPSS between 11 to 14 and 6 patients had IPSS>14.

Out of 60 men presented with LUTS, 66.66% [40 men] were diagnosed with benign prostatic hypertrophy [BPH], and 33.33% [20 men] with Prostate Cancer [PC].

In our study the sensitivity and specificity of PSA assay were found to be 85% and 72.5% respectively for the patients with serum total PSA level >10 ng/ml. The PPV was 60.7%. If 4 ng/ml is taken as lower cut off value for serum total PSA value, the sensitivity increases to 95% where specificity reduces to 46.66%.

All 60 patients were subjected to DRE for any findings suggestive of prostatic disorder. Among them 15 patients [25%] had positive DRE findings suggestive of carcinoma prostate. And rest of the 45 patients [75%] had negative DRE findings suggestive of BPH. This finding is comparable with that of Cooner et al [1990] and Catolina et al [1994] [12, 13] who showed DRE positivity ranges between 21%

and 53%. The low value of DRE positivity in our study among the patients with LUTS having IPSS more than 7 may be due to high incidence of BPH among the screened population as the value of DRE largely depends on the type of population screened. Irrespective of DRE findings all patients were subjected to TRUS examination followed by TRUS guided biopsy. 12 patients with positive DRE findings showed cancer on histology, whereas 3 patients with abnormal DRE showed BPH. On the other hand, eight patients with negative DRE showed cancer on histology. These findings suggests 60% sensitivity of DRE which is sufficiently low for diagnosis of carcinoma prostate, but have a high specificity [92.5%]. The PPV was 80%. Hence, the importance of DRE can never be denied in the detection of prostate cancer.

Although TRUS is not universally accepted as an initial screening test for prostatomegaly, all patients in our study were subjected to TRUS examination followed by TRUS guided biopsy for the purpose of comparative analysis with DRE and serum PSA in the early detection of prostate cancer among the patients with prostatomegaly. The classical description of prostate cancer on TRUS is a hypo-echoic SOL. In our study, 21 patients showed one or more hypo echoic areas and 15 among them had carcinoma prostate on biopsy. Whereas 5 among thirty patients who showed iso echoic texture, were also been detected to have carcinoma prostate on biopsy. Hyper echogenicity is an uncommon finding in prostate cancer and all six patients with these findings had BPH. Thus from our study it is seen that TRUS has got highest sensitivity [75%] among all three screening tools and also has highest specificity [85%]. But the PPV is 71.43%.

The patients with iso echoic SOL is most difficult to be correctly diagnosed by TRUS. Taking biopsy samples from such lesions is also difficult. In such cases multiple biopsy samples are taken from the peripheral Zone [PZ] of the prostate gland. In our study none of the patients showed abnormality of the prostatic capsule, ejaculatory ducts and seminal vesicles as well as surrounding organs. Only 4 patients had capsular breach. Areas of hemorrhages and necrosis were also not found in them but multiple areas of calcifications were found in 2 patients.

Hence in our study it was found that none of the single screening tools has got that much efficacy in differentiating carcinoma of prostate from benign hypertrophy of prostate in patients with LUTS. But when DRE and serum PSA >10ng/ml was combined the sensitivity and specificity was raised to 90% and 70% respectively. The PPV was 60%. This was almost comparable with the combination of DRE, serum PSA >10ng/ml and TRUS combination which has got 90% sensitivity and 85% specificity. The PPV was 75%. Conclusion: In the present study it was found that none of the single screening tool i.e serum total PSA, DRE or TRUS has got much efficacy in differentiating carcinoma prostate from benign hypertrophy in LUTS patients with IPSS not less than 7. Even the role of TRUS in detecting iso echoic SOL or organ confined diseases proved less effective. But the combination of DRE and serum total PSA or DRE, serum total PSA and TRUS showed higher sensitivity, specificity and positive predictive value.

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