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Research Article

Prostate-Specific Antigen versus Digital Rectal Examination in the Diagnosis of Prostate Cancer

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Abstract: Prostate cancer is the most commonly diagnosed non-cutaneous cancer and the third most common cause of death from cancer in males in the US. An increasing life expectancy in male population and increasing use of prostate-specific antigen (PSA) for early detection of the disease are probably the two main factors accounting for higher detection rate. The DRE is still the basis in the suspicion of Carcinoma prostate in males with normal or minimally high PSA levels. The aim of the study is to evaluate the effectiveness of PSA versus DRE in detecting cases of Carcinoma prostate among men presenting with symptoms of bladder outflow obstruction. This study was conducted over a period of 2 years. The patients included in this study were those presented with LUTS, All study subjects were clinically assessed and thoroughly examined. A total of 400 men aged 50 years and over with lower urinary tract symptoms (LUTS) were selected. The ability of PSA to identify Carcinoma prostate can be improved by selecting out groups of patients and by adjusting the cut-off level of PSA to the patients under study, the normal range of this test should be adjusted according to the population under study. DRE and serum PSA provides a good discrimination between patients with and without Carcinoma prostate.
Keywords: CA PROSTRATE, PSA, DRE

INTRODUCTION:

Prostate cancer is the most commonly diagnosed non cutaneous cancer and the third most common cause of death from cancer in males in the US [1]. The number of men diagnosed with carcinoma prostate is increasing in many areas in the world. An increasing life expectancy in male population [2] and increasing use of prostate-specific antigen (PSA) for early detection of the disease [3] are probably the two main factors accounting for higher detection rate. Most cases of carcinoma prostate diagnosed nowadays are non-metastatic disease [4, 5] and thus, many patients being suitable for potentially curative therapy. PSA is serine-like protease produced by epithelial cells of the prostate gland, releasing from prostatic epithelium, and appears in the blood. PSA is considered the most useful tumor marker currently available for diagnosis and management of the carcinoma prostate [6]. However; it is not specific for carcinoma prostate. Several non-malignant conditions of the prostate are associated with elevated PSA levels e.g. prostatic intraepithelial neoplasia, acute prostatitis, prostatic ischemia, and nodular prostatic hyperplasia [6, 7, 8]. Furthermore, not all carcinoma prostate cause an elevated PSA concentration [9]. Nodular prostatic hyperplasia is still the most common cause of elevated serum PSA in non-malignant causes [10]. The DRE is still the basis in the suspicion of Carcinoma prostate in males with normal or minimally high PSA levels. When palpable, Carcinoma prostate is usually represented by induration of the prostate on DRE [11, 12].

AIM OF STUDY:

The aim of the study is to evaluate the effectiveness of PSA versus DRE in detecting cases of Carcinoma prostate among men presenting with symptoms of bladder outflow obstruction.

METHODS:

This study was conducted on the patient attending the surgical outpatient department or admitted to the surgical ward of Subharti Medical College,

Subhartipuram, and Meerut over a period of 2 years between June 2011 – May 2013 with symptoms of prostatism. The patients included in this study were those presented with LUTS, All study subjects were clinically assessed and thoroughly examined. A total of 400 men aged 50 years and over with lower urinary tract symptoms (LUTS) were selected. The exclusion criteria were patients with previously diagnosed Carcinoma prostate and patients with lower urinary tract symptoms owing to causes other than bladder outflow obstruction. All patients included were first examined by DRE and then sent for PSA measurement. Any asymmetry, nodularity or indurations were considered abnormal. Blood sample was sending for PSA measurement at Subharti Hospital lab. PSA level was determined by the enzyme-linked immunosorbant assay (ELISA). A PSA value of ≥ 4 ng/ml is considered abnormal. Any patient with suspicious DRE or PSA level ≥ 4ng/ml submitted to Tru-cut biopsy of the prostate using a spring- driven biopsy gun under local anesthesia & antibiotic cover. Three specimens were obtained from each side and an additional biopsy from the suspicious area.

RESULTS:

The mean age of the patients was 69.6 ± 8.3 years and ranged from 50 – 99 years. Out of the 400 symptomatic patients included in the study, 213 (53.2%) underwent histopathological examination (Tru-cut biopsy of the prostate, open prostatectomy or TURP).

Table 1 shows the clinical distribution of men who underwent histopathological examination.

Table 2 shows that 55% of cases of Carcinoma prostate had PSA ≥ 40 ng/ml, compared to only 0.6% in other diseases of the prostate. 80.7% of patients with prostate disease other than Carcinoma prostate (80.7%) had PSA level < 10 ng/ml compared to only 12.5% in cases with Carcinoma prostate.

Table 1. Distribution of the study population underwent biopsy by DRE results

DRE	Biopsy (N= 213)			Total No. (%)
	NPH No. (%)	CA Prostate No. (%)	Non-specific Granulomatous Prostate No. (%)	
Positive	5 (3.0)	35 (85.4)	1 (33.3)	41 (19.2)
Negative	164 (97.0)	6 (14.6)	2 (66.3)	172 (80.8)
Total	169 (100.0)	41 (100.0)	3 (100.0)	213 (100.0)

DRE = digital rectal examination, NPH = nodular prostatic hyperplasia

Table 2 Distribution of study population by PSA level

PSA	Biopsy CA prostate No. (%)	Biopsy Other Prostatic diseases No. (%)	Total No. (%)
4-<10	5 (12.5)	138 (80.7)	143 (67.8)
10-<20	6 (15.0)	26 (15.2)	32 (15.2)
20-<40	7 (17.5)	6 (3.5)	13 (6.2)
40+ 22	(55.0)	1 (0.6)	23 (10.9)
Total	40(100.0)	171 (100.0)	211 (100.0)

Other Prostatic disease includes NPH and Non-specific granulomatous prostatitis.

Table 3 shows that all cases of Carcinoma prostate documented by biopsy and with positive DRE had PSA ≥ 4 ng/ml, but 83.3% of Carcinoma prostate cases with negative DRE had PSA ≥ 4 ng/ml.

The sensitivity (TPR), specificity (TNR), false positive rate (FPR), false negative rate (FNR), positive predictive value (PPV), negative predictive value (NPV), positive likelihood ratio (+ve LR) and negative likelihood ratio (-ve LR) for cut-off levels of PSA were summarized. PSA is sensitive marker for the presence of Carcinoma prostate with a sensitivity of 87.8% at 10 ng/ml in men presenting with symptoms suggestive of bladder outflow obstruction, but its specificity is high (91%) at 10 ng/ml. The sensitivity of the test is diminished at a level 40ng/ml to only 52.1.

Table 3 Distribution of men who underwent biopsy by DRE and PSA results

DRE	PSA (ng/ml)	Biopsy			Total No. (%)
		NPH No. (%)	CA Prostate No. (%)	Non-specific Granulomatous Prostate No. (%)	
POSITIVE (N= 41)	≥4	5 (100.0%)	35 (100.0%)	1 (100.0%)	41 (100.0%)
NEGATIVE (N= 172)	≥4	163 (99.4%)	5 (83.3%)	2 (100.0%)	170 (98.8%)
	<4	1 (0.6%)	1 (16.7%)	0	2 (1.2%)
	Total	164(100.0%)	6 (100.0%)	2 (100.0%)	172(100.0%)

DRE digital rectal examination, PSA prostatic specific antigen, NPH nodular prostatic hyperplasia

Table 4 Sensitivity, Specificity, FPR, FNR, PPV, NPV, + ve LR and – ve LR of PSA test

Positive if PSA ≥	**Sensitivity TPR %**	**Specificity TNR %**	**FPR** %	**FNR** %	**PPV** %	**NPV** %	**Positive LR**	**Negative LR**
4	100	51.5	48.5	0	19	100	2.06	0
10	87.8	91	9	12.2	52.9	98.5	9.74	0.13
20	70.7	98	2	29.3	80.5	96.7	35.35	0.3
40	51.2	99.4	0.6	48.8	91.3	94.7	85.33	0.5
60	41.5	99.4	0.6	58.5	89.5	93.7	69.2	0.6
80	26.8	99.7	0.3	73.2	91.7	92.3	89.33	0.7
100	22	99.7	0.3	78	90	91.8	73.3	0.8

DISCUSSION

PSA is produced by prostatic epithelial tissue and is detected in the epithelial cells of prostate, NPH tissue, primary and metastatic Carcinoma prostate cells [13]. There is evidence that the rate of increase in the serum PSA is proportional to the cancer burden [14, 15, 16]. This study confirms that the sensitivity of PSA is a useful marker for detection of Carcinoma prostate, but shows that its specificity is poor at low cut-off levels [17]. Eighty one percent of patients with NPH had PSA level between 4-10ng/ml, elevated PSA level (PSA > 4 ng/ml) was found in 53.8% of Patients with symptomatic NPH which could be due to either urinary retention or indwelling Foley catheter [18]. In this study PSA demonstrates the specificity problems. As Oesterling had said [19], the serum PSA concentration itself lacks sufficient sensitivity and specificity for diagnosing Carcinoma prostate in an ocean of NPH. Some patients with Carcinoma prostate have serum PSA within normal range [14, 20], our results showed that about 2.44% of patient with Carcinoma prostate have normal PSA. This limits the usefulness of PSA as a guide to the need for prostatic biopsy. In patients presenting with symptoms of bladder outflow obstruction, with a marginally elevated PSA level between 4 and 10 ng/ml and in whom non- surgical treatment is proposed one is faced with a diagnostic dilemma.Many men would undergo unnecessary prostatic biopsy if PSA was used as the sole criterion for biopsy. In an attempt to improve the discriminating ability of PSA in patients with normal DRE and PSA level between 4 and 10 ng/ml, (the level at which PSA is least specific), the concept of PSA density (the PSA concentration divided by volume of the prostate) has been introduced [21, 22]. However, Brawer et al.; [23] was unable to confirm the advantage of PSA alone in identifying Carcinoma prostate. The concept of PSA velocity (the rate of change of PSA with time) has been advocated as a more useful test for detecting Carcinoma prostate than a single measurement of PSA. Carter et al.; [24] found that a PSA velocity of 0.75 ng/ml per year had 90% specificity for Carcinoma prostate compared with a cut-off value for serum PSA of ≥ 4 ng/ml. Many men with NPH have high PSA levels because of large volumes of hyperplastic tissue [16] and this will tend to cause an overlap in PSA levels between patients with Carcinoma prostate and those with NPH. However, serum PSA provides good discrimination between patients with or without Carcinoma prostate. The specificity and sensitivity of PSA can be improved by excluding men with symptomatic NPH [17]. DRE has been used in diagnosis and screening for Carcinoma prostate for many decades and its importance is well established [25]. The sensitivity of DRE in the diagnosis of Carcinoma prostate was found to be 39-45% in clinical trials [26, 27]. The high percentage rate of positive DRE in the present study arises because most of the patients with Carcinoma prostate had abnormal DRE and thus represent a selected population in which 35 out of 41patients had carcinoma prostate proved by biopsy. The high incidence of the Carcinoma prostate in the study population can be explained by late presentation combined with patients' selection, which was about 55% in patients with PSA ≥40ng/mL. Granulomatous inflammation of the prostate has been report in some patients receiving Bacillus Calmette-Guerin (BCG) therapy for bladder cancer, after TURP and in patients with systemic granulomatous disease,

both infectious and non-infectious [28]. Most cases, however, are non-specific and resolve spontaneously with no therapy. In this study 1.23% had non-specific granulomatous prostatitis.

CONCLUSIONS AND RECOMMENDATIONS:

In conclusion, the ability of PSA to identify Carcinoma prostate can be improved by selecting out groups of patients and by adjusting the cut-off level of PSA to the patients under study, the normal range of this test should be adjusted according to the population under study. DRE and serum PSA provides a good discrimination between patients with and without Carcinoma prostate. The sensitivity and specificity of PSA can be improved by excluding men with symptomatic NPH and patients with serum PSA level between 4-10 ng/ml. The specificity of PSA as a diagnostic test for Carcinoma prostate is reduced in men with symptoms of bladder outflow obstruction. No method alone reached a satisfactory diagnostic value for Carcinoma prostate. Only when these methods were combined (DRE & PSA level) an accuracy rate of 96.6% was achieved. This study also emphasizes that there is no single normal level for PSA. However, to determine which method is superior to predict Carcinoma prostate, further study needs to be done. The most effective method is to admit TRUS in addition to PSA and DRE in men with normal DRE and PSA between 4-10 ng/ml to diagnose Carcinoma prostate.

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