

PROSTATE – SPECIFIC ANTIGEN (PSA) AS A SCREENING TOOL FOR BENIGN PROSTATE HYPERPLASIA (BPH) AND PROSTATE CANCER (PCa) IN SULAIMANI PROVINCE

Sirwan Mustafa Muhammad¹ And Intissar Numman Waheed²

¹Dept. of Biology, College of Science, University of Sulaimania, Kurdistan – Region, Iraq.

² Dept. of Biology, Faculty of Sciences, University of Zakho, Kurdistan – Region, Iraq.

(Accepted for publication: June 9, 2013)

ABSTRACT

The current study was applied to evaluate the significance of serum Prostate- Specific Antigen (PSA) as a screening tool for the PCa and the role of percent free - to- total PSA ratio in the discriminating between BPH and PCa. Prostatic biopsies and blood were collected from (62) patients aged between (50-89) years. Eleven healthy men with negative digital rectal examination, (median age, 60.6yr) were enrolled in this study as a control group. The common diseases encountered were BPH (59.7%), BPH with prostatitis (19%), adenocarcinoma (17.7%), and transitional cell carcinoma (3.2%). 54% of BPH cases had tPSA level < 4 ng/ml as well 13.5% of them having tPSA>10, while 15.3% of malignant cases had tPSA level < 4 ng/ml and 84.7% of them having tPSA>10. The statistical analysis showed a significant difference between (BPH and PCa); (PCa and control cases) and (prostatitis and control) in regard to tPSA. Regarding to % cPSA the entire case of PCa showed levels >60% aligned with only 75%, 27%, 16% in prostatitis, control and BPH groups successively. The mean comparison showed statistically significant differences between the PCa patients and control cases and between prostatitis and control cases, while no significant differences between BPH and control group. Regarding to % fPSA, 53.8 % of PCa cases showed ≤15, along with 16.6 % of prostatitis showed ≤15, while no cases of both BPH and control revealed fPSA ≤15. Comparison of the means showed a statistically large difference between the (PCa and BPH), (PCa and control) and (prostatitis and control) cases. While no significant differences between (BPH and control) cases. In conclusion, combinational use of tPSA with other molecular forms of PSA especially proportion of fPSA provide higher diagnostic and differentiative accuracy than the tPSA alone.

KEYWORDS: Prostatic specific antigen, Free PSA, Prostate cancer, BPH, Prostatitis, cPSA, tPSA.

INTRODUCTION

Benign prostatic hyperplasia (BPH) and Prostate cancer (PCa) are common in elderly men. Although they may coexist within the prostate, they appear to share risk profiles, making it difficult to elucidate the independent role, if any, of BPH in PCa etiology ((Jemal *et al.*, 2005; Hsing and Chokkalingam, 2006). In 1986, prostate specific antigen (PSA) testing was approved by food and drug administration (FDA) as a tool for monitoring PCa treatment and, in 1993 approval was extended for its use in detecting PCa in men aged over 50 years. Prostate specific antigen is a glycoprotein (a serine protease) produced solely by the prostate. Its function is to liquefy semen, small amounts leak into the bloodstream, where it can be measured. PSA is the most important biomarker for diagnosing and monitoring of PCa (Magklara *et al.*, 1999, Mitchell *et al.*, 2008, Brett, 2011). Baseline PSA measurements at a young age are significant predictors of later PCa diagnosis and disease-specific outcomes. Thus baseline PSA testing may be used for risk stratification and to

guide screening protocols (Stacy.*et al.*, 2012). PSA is present in serum in several different molecular forms, all of which are enzymatically inactive. These forms can be classified into two general categories: complexed PSA (i.e. bound to serum protease inhibitors) and free PSA (i.e. unbound, inactive PSA) (Lilja *et al.*, 2000). A major portion of PSA exists in circulation as a complex with α_1 -antichymotrypsin (PSA-ACT) and α_2 -macroglobulin (PSA-A2M). Trace amounts of α_1 -antitrypsin can also be found. Any remaining PSA is in the free form (fPSA) (Christensson *et al.*, 1993; Jung *et al.*, 2000).

Benign enlargement remains the most common cause overall for raised PSA higher levels. Surgery such as transurethral resection of prostate (TuRP) and less invasive laser treatments can reduce and complicate the interpretation of PSA and PSA kinetics (Modi *et al.*, 2010).

Levels of 4.0 ng/ml or higher are strong indicators of the possibility of PCa (Catalona *et al.*, 1993). However, elevated serum PSA levels have also been attributed to BPH and prostatitis, leading to a large percentage of false positive

screening results (Catalona *et al.*, 1991). A potential solution to this problem involves the determination of FPSA levels (Bangma *et al.*, 1995). Preliminary studies have suggested that the percentage FPSA is lower in patients with PCa than those with BPH (Lilja *et al.*, 1991). The proportion of PSA-ACT is increased in PCa (Jung *et al.*, 2000). Thus, the measurement of free serum PSA in conjunction with total PSA (tPSA), can improve specificity of PCa screening in selected men with elevated serum tPSA levels, which would subsequently reduce unnecessary prostate biopsies with minimal effects on cancer detection rates (Etzioni *et al.*, 2004). This study was designed to 1) measure and evaluate the serum total, free and complexed PSA in a group of men with BPH, PCa and prostatitis and comparison of their means in different prostatic disorders, 2) assess the prevalence of PCa in the studied sample.

PATIENTS AND METHODS

This study was carried out during the period from January 2007 to October 2007. The total number of patients and healthy men enrolled was (73). Sixty two men, aged 50-89 yr (median age.68.8 yr) with BPH, PCa and prostatitis were studied as a patient group. Eleven healthy men (who were not complaining from any of prostatic disorders and having negative digital rectal examination (DRE)) aged 46 -75 (median age, 60.6yr) were enrolled in this study as a control group. All cases were collected from both Toomalek Private Hospital and Department of Urology at the Sulaimani Teaching Hospital. The present study includes the estimations of free and total serum PSA in both patients and control groups.

Blood samples and serum preparation

The majority of blood samples and prostatic biopsies were collected from the patients at the hospital prior to treatment, whereas blood samples from control cases were collected at the time of interview. From each cases of 62 patients and 11 control, about 5ml of venous blood was collected in non - anticoagulated tube and allowed to clot for 20-30 minutes at 37C° then centrifuged at 2500-3000 rpm for 10 minutes, the sera were frozen at (-30 to -35C°).

Estimation of serum prostate specific antigen level

Frozen sera were thawed once for the analysis of TPSA and FPSA. The concentrations of TPSA and FPSA was measured by an immunofluorometric assay procedure using VIDAS ® systems from (bioMerieux Vittek, Inc.Italia, S.P.A model 12; serial no. V12I1360) and by using VIDAS (TPSA) kit (REF No 30 428) and VIDAS (FPSA) kit (REF No.30 440) both kits are intended for use with a VIDAS instrument as an automated enzyme-linked fluorescent immunoassay (ELFA) for the quantitative measurement of PSA in human serum according to the instructions of the manufacturers. The % FPSA were calculated using the formula below (as described in the assay kit):

$$\% \text{ FPSA} = \text{FPSA conc.} / \text{TPSA conc.} \times 100$$

Also the percentage cPSA to tPSA was calculated using the formula:

$$\% \text{ c PSA} = \text{c PSA conc.} / \text{TPSA conc.} \times 100.$$

The following working operational definitions were used to calculate sensitivity, specificity and PPV (kumar, 2004)

$$\text{Sensitivity} = \text{TP} / \text{TP} + \text{FN} \quad \text{Specificity} = \text{TN} / \text{FP} + \text{TN} \quad \text{PPV} = \text{TP} / \text{TP} + \text{FP}$$

As: True Positive (TP) = Histologically malignant with serum PSA level >4, >10 and >50 ng/ml respectively.

True Negative (TN) = Histologically not malignant, with serum PSA level <4, <10 and < 50 ng/ml respectively.

False Positive (FP) = Histologically not malignant but serum PSA level >4, >10 and >50 ng/ml respectively.

False Negative (FN) = Histologically malignant but serum PSA level <4, <10 and <50 ng/ml respectively. (bioMerieux, 2007).

* Cut point values which are age-adjusted reference intervals for tPSA and are established to improve the ability of tPSA testing to detect early PCa according to (Oesterling *et al.*, 1993). Three tPSA cut points were used (≤ 4 , 4-10 and ≥ 10 ng/ml). * Cut off levels for % FPSA: The values that are optimized to differentiate PCa from other benign prostate cases, thus reducing the number of unnecessary biopsies, it was also depended on three cut off levels (which included $\leq 15\%$, 15-20 and >20) according to (Oesterling, 1995). * For better representation of the results and in order to study the clinical usefulness of tPSA in the present study three levels of tPSA were used for comparison which are (>4 as suggestive, >10 as indicative and >50 as

diagnostic of malignancy respectively and are expressed in percentages (Kumar,2004).

Histopathological studies

The clinical tissue specimens (biopsies) in this study were obtained from patients who underwent prostatectomy or by transurethral resection of prostate (TURP), each tissue specimen was fixed in 10% formalin, embedded and 3-5 microns, thick sections were cut and stained with Hematoxylin and Eosin (H&E) stain, for histopathological diagnosis. (Kumar, 2004). The slides were examined and diagnosed by three expert pathologists and the Gleason's grade for each carcinoma case was established.

Statistical analysis

The obtained data were statistically analyzed using the available software (STATIGRAPHIC version.4) to compare the means of serum parameters measured in both patients and the control group by using the t-test.

RESULTS

Out of the 62 patients studied, 37 (59.7%) had BPH, 13 (20.9%) of them had PCa and 12 (19.3%) had prostatitis. Among the malignant cases 11 of them (17.7%) were found to be adenocarcinomas, with average Gleason grade 4, and 2 of them (3.2%) were found to be primary transitional cell carcinoma. The relationship between age groups and frequency of prostatic disorders were shown in the table (1).

Table (1): Relation between age groups & frequency of the prostatic disorder

Age Class	No. of cases (%)	No.of PCa(%)	No.of BPH (%)	No. of BPH +Prostatitis (%)
50-59	4(6.4)	0	1(2.7)	3(25)
60-69	27(43.6)	4(30.7)	18(48.6)	5(41.7)
70-79	28(45.2)	7(53.9)	17(45.9)	4(33.3)
80-89	3(4.8)	2(15.4)	1(2.7)	0
Total No.	62(100)	13(100)	37(100)	12(100)

Histopathological studies

The histopathological studies of the prostatic tissue in BPH cases demonstrated the hyperplasia of both prostatic glandular (epithelial) and stromal elements. They consisted of nodules of hyperplastic glandular tissue and the acini were tortuous and papiliform growth of epithelium into the lumen occurred in some of them as well as the stroma was composed of varying amounts of collagen and smooth muscle fibers (Fig.1A)

The histopathological studies of PCa cases demonstrated variation in the disruption of the glands normal architecture with different degrees

of differentiation of the glands, which ranged from well differentiated, moderately differentiated and poorly differentiated adenocarcenoma glands; with the absence of the basal cell layer (Fig 1.B). The cytological characteristics consisted of hyperchromatic, enlarged nuclei with prominent nucleoli and often variation in the nuclear-to-cytoplasmic ratios as well as the ctoplasm was often slightly blue-tinged or basophilic. A 5 basic Gleason grade patterns was used to generate histologic scores and the average Gleason grade was established as 4 among the adenocarcenoma cases.

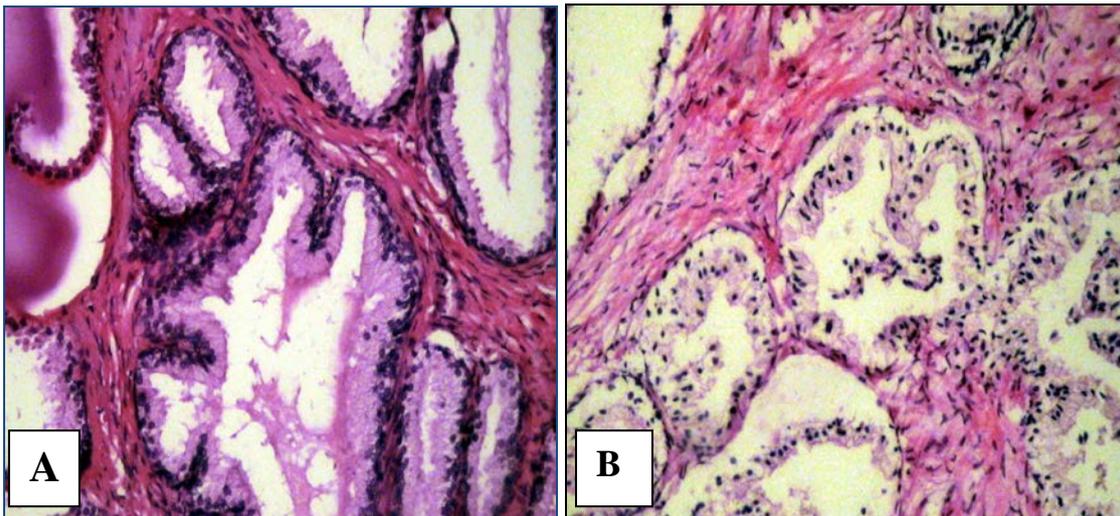


Figure 1: (A) Photomicrographs of BPH stained with H&E (X200). The hyperplasia of both prostatic glandular (epithelial) and stromal elements. (B) Photomicrographs of poorly differentiated PCa, stained with H&E (X200). The disruption of the glands normal architecture with poorly differentiated adenocarcinoma glands; with the absence of the basal cell layer.

Serum tPSA and the correlation with PCa, BPH and prostatitis

The results of the t PSA level in benign and malignant prostatic cases are presented in table (2). The statistical analysis showed a highly significant differences between (PCa and BPH) cases and between (PCa and control) cases at levels of (P=0.00000006), (P=0.000075)

respectively. At the same time, a significant difference was noted between: control and BPH cases at the 95.0% confidence level, between Prostatitis and control, BPH, and PCa cases (P=0.04917), (P-value =0.00013), (P=0.011401) and (P=0.00083) respectively at the 95.0% confidences level.

Table (2): Shows the serum t PSA level in benign and malignant prostatic cases.

t PSA ng/ml	Total (%)	PCa No. (%)	BPH No. (%)	Prostatitis No. (%)	Control No. (%)
≤ 4	22(35.5)	2(15.4)	20(54)	0	1(100)
4-10	17(27.4)	0	12(32.4)	5(41.70)	0
≥10	23(37)	11(84.7)	5(13.5)	7(58.3)	0
Total No (%)	62(100)	13(100)	37(100)	12(100)	11(100)
t-test comparison of means	P-values	0.000075**	0.04917*	0.00013**	95.0% confidence level

Percent FPSA in correlation with benign and malignant cases

Table No. 3 demonstrate that the majority of PCa cases (53.8%) showed serum % FPSA values ≤15, while (100%) of the (control and BPH), and (83.3%) of prostatitis showed serum %FPSA values >20. Comparison of the means in regard to % FPSA showed statistically

significant differences between the PCa cases and (BPH, Prostatitis, and control cases), (P=0.00) at the level 95.0%, (P= 0.00012) and (P= 0.00) respectively and between BPH+.Prostatitis and control cases (P=0.01640). While the comparison of the means of both BPH and control showed no statistically significant differences (P = 0.952) at the level of 95.0% .

Table (3): Shows the distribution of serum %FPSA cutoffs in different studied cases

%FPSA cutoff	PCa	BPH	BPH+ Prostatitis	Control	Total
≤ 15%	7(53.8%)	0	2(16.65%)	0	9(12.3%)
15-20%	2(15.4%)	0	0	0	2(2.7%)
>20	4(30.7%)	37(100%)	10(83.3%)	11(100%)	62(85%)
Total	13	37	12	11	73(100%)
Means	15.7	48.6	36.04	49.1	
P-values	0.00	0.952	0.01640		

Complexed PSA (cPSA) in malignant and benign cases

According to the results of the current study, the %cPSA levels were classified into four categories (30-40; 40-50; 50-60; and >60) as in table (4). This table shows the distribution of serum %c PSA levels in different studied groups.

The statistical analysis showed significant differences between all the PCa and control cases ($P=0.00$); BPH+Prostatitis and control cases ($P= 0.016$) and between BPH+Prostatitis and PCa cases ($P=0.00017$), whereas the comparison between BPH and control cases showed no statistically significant differences at the 95.0% confidence level with ($P= 0.965$).

Table (4): Distribution of serum %c PSA levels in different studied groups

%cPSA categories	PCa %	BPH%	BPH+ Prostatitis%	Control%	Total
30-40	0	3(8)	0	3(27.2)	6(8.2)
40-50	0	14(37.8)	2(16.6)	2(18.2)	18(24.6)
50-60	0	14(37.8)	1(8.3)	3(27.2)	18(24.6)
>60	13(100%)	6(16.2)	9(75)	3(27.2)	31(42.5)
Total	13(100%)	37(100%)	12(100%)	11(100%)	73(100%)
P-values	0.00	0.9648	0.016460		

Clinical usefulness of tPSA (suggestive, indicative and diagnostic of malignancy)

1- tPSA > 4 ng/ml as suggestive of malignancy was shown in table (5). 84.7% of malignant cases had serum tPSA level > 4, which is suggestive of malignancy. While, 61% of benign cases showed values > 4 ng/ml .

Table (5)- Suggestive of malignancy in regard to t PSA (> 4ng/ml)

tPSA level (ng/ml)	Biopsy results		Total
	Malignant	Benign	
> 4	11 (84.7%)	30(61%)	41 (66%)
≤4	2 (15.3%)	19(39%)	21 (34%)
Total	13(100%)	49 (100%)	62(100%)

2- tPSA > 10 ng/ml as indicative of malignancy:

84.7% of PCa cases had tPSA level >10 ng/ml which is indicative of malignancy, while only 24% cases of benign diseases had serum tPSA level > 10 ng/ml (Table 6).

Table (6)- Indicative of Malignancy (>10ng/ml).

tPSA Level(ng/ml)	Biopsy results		Total
	Malignant	Benign	
>10	11 (84.7%)	12 (24%)	23(37%)
≤10	2 (15%)	37(76%)	39(63%)
Total	13 (100%)	49 (100%)	62 (100%)

3- tPSA >50 ng/ml as diagnostic of malignancy

The serum tPSA level of >50 ng/ml, was demonstrated in 53.8% of the PCa cases and non in benign cases (Table 7).

Table (7) - Diagnostic of malignancies (> 50 ng/ml).

tPSA level (ng/ml)	Biopsy results	Total
	Malignant	
>50	7(53.8%)	13 (100.0%)
≤50	6 (46.2%)	

Calculation of sensitivity and specificity and positive predictive values of tPSA values in PCa

The sensitivity, specificity and positive predictive values (PPV) of tPSA value were illustrated in table No. (8).

Table 8- Calculation of sensitivity, specificity &PPV of t PSA values in PCa

Serum tPSA level ng/ml	Sensitivity	Specificity	Positive predictive value
0-4	50%	41%	6.2%
10-20	67%	85%	29%
20-50	75%	41.7%	22.2%
>50	88%	100%	100%

Percent FPSA in correlation with benign and malignant cases

The majority of PCa cases (53.8%) showed serum % FPSA values ≤15, whereas 16.6 % of prostatitis showed % FPSA ≤15 while no cases of BPH and control revealed % FPSA ≤15. Furthermore in cut off of >20, the result indicated that 30.7 % of PCa cases had cutoff >20%. While 83.3%, 100% and 100% of prostatitis, BPH and control had cut off >20% (Table 9). Comparison of the means in regard to

% FPSA showed statistically significant differences between the PCa cases and BPH cases (P=0.00) at the level 95.0%, also between PCa and control cases (P=0.00), prostatitis and control cases (P= 0.0164) and between PCa and prostatitis cases (P= 0.00012) .While the comparison of the means of both BPH and control group showed no statistically significant difference (P = 0.952) at the level of 95.0% (Table 9).

Table (9)-Distribution of serum %FPSA cutoffs in different studied groups.

%FPSA	PCa	Prostatitis	BPH	Control	Total
≤15%	7(53.8 %)	2(16.6 %)	0	0	9(12.3%)
15-20%	2(15.4%)	0	0	0	2(2.7%)
>20	4 (30.7 %)	10(83.3 %)	37(100%)	11(100%)	62(85%)
Total	12	37	11	73	110%
Means	15.7	36.04	48.6	49.1	
p-values	0.01640	0.01640	0.0]0	0.952156	

Complexed PSA (cPSA) in malignant and benign cases

According to the results of the current study, %cPSA levels were classified into four categories as shown in table (10). Therefore this table showed the distribution of serum % cPSA levels in different studied groups using t-test to compare the means of % cPSA which showed statistically significant differences between all the PCa patients and control cases (P=0.00);

there was also a statistically significant difference between the means of Prostatitis and control cases (P= 0.016) and between Prostatitis and PCa cases (P=0.00017), whereas the comparison of the means of both BPH and control group showed no statistically significant differences at the 95.0% confidence level with (P= 0.965).

Table (10)- Distribution of serum %c PSA levels in different studied groups.

% c PSA level	Types of studied groups				Total n (%)
	PCa %	Prostatitis %	BPH %	Control %	
30-40	0	0	3(8)	3(27,2)	6(8.2)
40-50	0	2(16.6)	14(37.8)	2(18.2)	18 (24.6)
>60	13(100)	9(75)	6(16.2)	3(27.2)	31(42.5)
Total	13 (100%)	12(100%)	37(100%)	11(100%)	73(100%)
p-values	0.00	0.016460	0.964891		

DISCUSSION

The concept of measuring PSA in serum is based on the fact that under normal conditions each epithelial cell of prostate gland synthesizes a certain amount of PSA, which maintains the serum concentration (Oesterling, 1995). Elevated levels of PSA can occur in men with BPH, prostatitis, urinary tract infection or prostatic infarction. Elevation also may occur after prostate biopsy, aggressive DRE, ejaculation, bicycle riding, physical exercise and bicycle riding or postejaculation (Modi *et al.*, 2010, Brett, 2011).

There is no doubt that PCa screening with PSA will lead to detection and treatment of some PCa that would not otherwise have been diagnosed during the patient's life time. The data of the present study indicates a considerable difference in the average of tPSA in different prostatic disorders and 84.7% of PCa had elevated serum tPSA level more than 10ng/ml, while only 53.8% of them had elevated tPSA value >50 ng/ml with sensitivity of 88% and specificity 100% and 100% positive predictive value. A study performed in Ohio, USA by Gerstenbluth *et al.*, (2000) demonstrated that serum tPSA > 50 ng/ml was 98.5% accurate in predicting the presence of prostatic carcinoma in tissue biopsy which supports the findings of the present study. Prostatitis is a broad term used to describe inflammation of the prostate and include a heterogenous group of infectious and noninfectious disorders, most of which are not sufficiently evaluated with regard to the determination of their causes. It is important to realize that inflammation and infection of the prostate can significantly elevate serum PSA and yield a low %FPSA ratio (unlike the high ratio found more commonly in PBH), this elevation of PSA may be caused by inflammatory changes within the prostate architecture, leading to false-positive readings and potentially unnecessary biopsies (Potts and Payne, 2007). The data from

the present project indicated a significant increase in the level of tPSA and remarkable lowering of %FPSA in patients diagnosed as having BPH and prostatitis, also the results highlighted that all cases of BPH with prostatitis have tPSA values >4 ng/ml and 58% of them have values ≥ 10 . Theoretically, the occurrence of the various PSA molecular forms in serum allows for better differentiation between PCa and BPH. The tPSA serum test has contributed to earlier detection, however, the majority of moderately elevated tPSA levels are attributed to BPH, often resulting in unnecessary biopsies (Oesterling, 1995). Free PSA normally comprise 10–35% of the total PSA in serum, and it is not bound to serum proteins (Jung *et al.*, 2000). Percent FPSA may be related to biologic activity of the tumor. The ratio of free- to- total PSA or %FPSA in serum have been reported to be significantly higher in individuals with BPH than in PCa patients, even at PSA concentrations 10 ng/ml, where the measurement of tPSA fails to discriminate efficiently between the two clinical conditions (Magklara *et al.*, 1999).

In the present study the percent of FPSA was expressively lowered in patients with PCa compared to the BPH patients and the cut-off of 15-20% could play a useful discriminative role. The value of the % FPSA cut point depends on factors such as the incidence PCa in the population, the prostate biopsy technique, the patient's age, PSA level, prostate volume, the biochemical method used for determination of both free PSA and total PSA, and even the patient's race (Catalona *et al.*, 1997).

Complex PSA can be found by subtracting free from total (Zhang *et al.*, 1997; Jung *et al.*, 2000). Several studies have addressed whether cPSA or %FPSA (ratio of free to total) are more sensitive and specific than tPSA. In this study, all cases of PCa showed % c PSA levels >60 compared to the control and showed statistically significant differences, while there was no statistically significant difference between the means of

cPSA in both BPH and control at the 95.0% confidence level. In conclusion combinational use of tPSA with other molecular forms of PSA especially proportion of fPSA provides a higher diagnostic and differentiative accuracy than the tPSA alone.

REFERENCERS

- Bangma, C.H., Kranse, R., and Blijenberg, B. (1995). The value of screening tests in the detection of prostate cancer. Part II: Retrospective analysis of free- total prostate-specific antigen, age-specific reference ranges, and PSA density. *Urol*: 46:779-785.
- Brett, T. (2011). Prostate specific Antigen. *Australian Family Physician*. 40 (7):497-500.
- bioMerieux. (2007). Prostate Specific Antigen (VIDAS PSA assay kit; the information booklet), bioMerieux Incorporation, France: 2-3.
- Catalona, W.J., Beiser, J.A., and Smith, D.S. (1997). Serum free prostate specific antigen and prostate specific antigen density measurements for predicting cancer in men with prior negative prostatic biopsies. *J Urol*. 158:2162-2167.
- Catalona, W.J., Smith, D.S., Ratliff, T.L., Dodds, K.M., Coplen, D.E., and Yuan, J.J. (1991). Measurement of prostate-specific antigen in serum as a screening test for prostate cancer. *N Engl J Med*. 325:1324.
- Catalona, W.J., Smith, D.S., Ratliff, T.L., and Basler, J.W. (1993). Detection of organ confined prostate cancer is increased through prostate-specific antigen based screening. *JAMA*. 270: 948-954.
- Christensson, A., Bjork, T., and Nilsson, O. (1993). Serum prostate specific antigen complexed to α 1-antichymotrypsin as an indicator of prostate cancer. *J Urol*. 150:100- 105.
- Etzioni, R., Seth, F., Peter, H.G., Charles, L.K., David, F.P., and Meir, J.S. (2004). Prostate-specific antigen and free prostate-specific antigen in the early detection of prostate cancer: do combination tests improve detection?. *Cancer Epidemiol Biomarkers Prev*. 13(10): 1640-1645.
- Gerstenbluth, R.E., Seftel, A.D., Hampel, N.O., Oefelein, M.G., and Resnick, M. (2000). The accuracy of the increased prostate specific antigen levels (greater than an equal to 20 ng/ml) in predicting prostate cancer; is biopsy always required? *J Urol*. 168:
- Hsing, A.W., and Chokkalingam, P.A. (2006). Prostate cancer epidemiology. *Frontiers in Bioscience*. 11:1388-1413.
- Jemal, A., Murray, T., Ward, E., Samuels, A., Tiwari, R.C., Ghafoor, A., Feuer, J. and Thun, M. J.(2005). Cancer statistics 2005CA Cancer. *J. Clin*. 55: 10-30.
- Jung, K., Ulrike, E., Michael, L., Brigitte, B., Pranav, S., Birgit, R., Steffen, H., Dietmar, S., and Stefan, A.L. (2000). Ratio of free or complexed prostate specific antigen (PSA) to total PSA: Which ratio improves differentiation between benign prostatic hyperplasia and prostate cancer? *Clinical Chemistry* 46:1:55-62.
- Kumar, P. (2004) Role of Prostate Specific Antigen in Differentiating Various Prostatic Pathology, Ph.D. thesis, Tribhuvan University, Nepal .:15-49.
- Lilja, H., Christensson, A., and Dahlen, U. (1991). Prostate-specific antigen in serum occurs predominantly in complex with α 1- antichymotrypsin. *Clin Chem*. 7:1618-1625.
- Lilja, H., Piironen, T.P., and Rittenhouse, H.G. (2000). Prostate-specific antigen. In Vogelzang NJ, Shipley WU, Scardino PT, Coffey DS eds, *Comprehensive Textbook of Genitourinary Oncology* . Philadelphia: Lippincott, Williams and Wilkins Publishers: 638-650
- Magklara, A., Andreas, S., William, J.C., and Eleftherios, P.D. (1999). The combination of human glandular kallikrein and free prostate-specific antigen (PSA) enhances discrimination between prostate cancer and benign prostatic hyperplasia in patients with moderately increased total PSA. *Clinical Chemistry*. 45(11): 1960-1966.
- Mitchell, D.M., Swindell, R., Elliott, T., Wylie, J.P., Taylor, C.M., and logue, J.P. (2008). Analysis of prostate-specific bounce after i(125) permanent seed implant for localized prostate cancer. *Radiother Oncol*. 88:102-107.
- Modi, P., Helfand, B.T., and McVary, K.T. (2010). Modifications and surgical interventions for benign prostatic hyperplasia are potential confounders of prostate-specific antigen. *Curr Urol Rep*. 11:224-227.
- Oesterling, J.E. (1995). Prostate specific antigen: its role in the diagnosis and staging of prostate cancer. *Cancer*. 75:1795-1804.
- Oesterling, J.E., Jacobsen, S.J., and Chute, C.G. (1993). Serum prostate-specific antigen in a community-based population of healthy men: Establishment of age-specific reference ranges. *JAMA*; 270:860-864.
- Potts, J., and Payne, R.E. (2007). Prostatitis: Infection, neuromuscular disorder, or pain syndrome? Proper patient classification is key. *Cleveland Clinic Journal of Medicine*; 74:64-66.
- Stacy, Loeb, A.H., Ballentine Carter, B., William, J., Catalona, C., Judd, W., Moul, D., Fritz, H., and Schroder, E. (2012). Baseline Prostate-Specific Antigen Testing at a Young Age. *European Urology*. 61: 1-7.
- Zhang, W.M., Leinonen, J., Kalkkinen, N., and Stenman, U.H. (1997). Prostate specific antigen forms a complex with and cleaves α 1-protease inhibitor *in vitro*. *Prostate*. 33: 87-96.

استخدام المستضد الخاص بالبروستات كوسيلة للفحص المبكر لتضخم البروستات الحميد وسرطان البروستات في مدينة السليمانية

الخلاصة

صممت الدراسة الحالية لتقدير أهمية المستضد الخاص بالبروستات كعدة للمسح والتشخيص لسرطان البروستات وكذلك دور FPSA% الى tPAS% في التمييز بين تضخم البروستات الحميد وسرطان البروستات. تم جمع عينات الدم و خزعات البروستات من (62) مريض بمعدل عمري (50-89) سنة. وكذلك شملت الدراسة (11) رجل سليم صحيا (كمجموعة سيطرة) وبمعدل عمري (60 سنة) وذلك بعد ان اظهروا استجابة سالبة لفحص المستقيم الرقمي. كان تضخم غدة البروستات الحميد هي الحالة النسجية الأكثر شيوعا حيث بلغت (59.7%)، يليها تضخم غدة البروستات الحميد مع التهاب غدة البروستات (19%)، ومن ثم سرطان البروستات من نوع adenocarcinoma (17.7%) والسرطان من نوع Transitional cell carcinoma (3.2%). 54% من حالات تضخم غدة البروستات الحميد كان عندها مستوى tPSA% اقل من 4 نانوكرام/ ملليتر و 13.5% منهم أظهرت نسبة مئوية tPSA أكبر من 10 نانوكرام / ملليتر. بينما 15.3% من الحالات الخبيثة كان عنده مستوى tPSA% اقل من 4 نانوكرام/ ملليتر و 84.7% منهم كان عنده مستوى أكبر من 10. بينت نتائج التحليل الإحصائي وجود اختلاف معنوي بين كل من (تضخم البروستات الحميد وسرطان البروستات) ، (سرطان البروستات و مجموعة السيطرة) ، و (التهاب البروستات و مجموعة السيطرة). إما فيما يتعلق بالنسبة المئوية ل cPSA فقد أظهرت جميع حالات السرطان مستويات أكبر من 60% مع فقط 75%، 27%، و 16% في مجاميع التهاب

البروستات ، مجموعة السيطرة و مجموعة تضخم البروستات الحميد على التوالي. كما و أظهرت مقارنة المتوسطات اختلافات معنوية بين مرضى (سرطان البروستات و مجموعة السيطرة)، وبين (حالات التهاب البروستات و مجموعة السيطرة)، بينما لم يسجل وجود اختلاف معنوي بين (تضخم البروستات الحميد و مجموعة السيطرة). أما فيما يخص FPSA% ، 53.8% من حالات السرطان أظهرت قيم اقل من 15%، سوية مع 16.6% من حالات التهاب البروستات أظهرت نسبة اقل من 15%، بينما لم يظهر اي من حالات تضخم البروستات الحميد و مجموعة السيطرة قيم ل FPSA% اقل من 15%. مقارنة المتوسطات أظهرت اختلافات كبيرة بين حالات السرطان و تضخم البروستات الحميد، وبين سرطان البروستات و مجموعة السيطرة وبين حالات التهاب البروستات و مجموعة السيطرة وكذلك بين (سرطان البروستات و مجموعة السيطرة)، وبين (التهاب البروستات و مجموعة السيطرة)، بينما لم يلاحظ وجود أي اختلاف معنوي بين حالات (تضخم البروستات الحميد و مجموعة السيطرة). من خلال هذه النتائج نستنتج بان استعمال tPSA مع الإشكال الجزئية الأخرى للمستضد الخاص بالبروستات وبصورة خاصة FPSA يعطي دقة عالية في التشخيص عما لو اعتمد tPSA لوحده.

پوخته

ئهنجامدانی ئهم توێژینهوه یه به مه بهستی لیکولینهوهی توانایی و کاریگهاری ئنتیجینی تابهت به پروستات PSA پشکینکی کرا بو به دوا دا گهران و هه رچی زورتر ناسینهوهی شیره نهجهی رژینی پروستات وه جیا کرده نهوهی له گه وهه بوونی بیوهی رژینی پروستات به پیوانه کردنی رژیهی سه دی (PSA) ی سه ره به ست (freePSA) بو کۆی گشتی (total PSA). وه ده رکهوت که یه که به دوا ی یه که بهم شیوهیه بوون : گه وهه بوونی (59.7%) ،

گهوره بوونی بیوهی له گهل ههوکردنی پرۆستات (19.3%) ، شیرپهنجهی جۆری adenocarcinoma (17.7%) وه شیرپهنجهی جوری خانهی گهروک transitional cell carcinoma (3.2%) بو. وه دهرکهوت که زۆریه زۆری لوه پیسهکان لهو نهخۆشانهدا بوو که تهمنیان له نیوان 70-79 سالدا بوو ، له کاتیکیدا زۆریه زۆری لوه بیوه یهکان (پاکهکان) توشی ئهوه نهخۆشانه بوو بوون که تهمنیان له نیوان 60-69 سالدا بوو . ههروهها دواتر 24 ئهونهی بریدراوه له شانهی پرۆستات (پاکه 20 = ژ ؛ 4 =) که خرابونه سهر سلایدی بارگای کراوی پۆزیتیف وه بهرهنگی تایبتهت و به به کارهینانی رینگای کیمیای و بهرگری شانیهی IHC به مهبهستی دهرخستنی ئهنتیجینی تایبتهت به پرۆستات PSA له شانهدا . وه تۆمارکردنی چرپی رهنگ بوونه که به به کارهینانی چوار پله که بریتی بوون له (3,2,1,0) ، دهرکهوت 27% ی شانهمانی گهوره بوونی بیوهی پلهی رهنگ بوونی به هینزی ژماره (3) یان دهرخستوه وه 47% یان پلهی ژماره (1) یان دهرخست ، له کاتیکیدا 50% ی شانهمانی شیرپهنجه پلهی رهنگ بوونی ژماره (1) یان دهرخست بهلام هیچ کام له شانهمانی شیرپهنجه و BPH +Prostatitis پلهی رهنگ بوونی به هینزی ژماره (3) یان دهرخست . 54% ی نهخۆشیهکانی گهوره بوونی بیوهی پرۆستات ریتزهی tPSA ی خوینیان کهمتر بوو له نانوگرام / ملیلتر ، له کاتیکیدا تهنها 24% یان ریتزهی tPSA ی خوینیان زیاتر بوو له 10 نانوگرام / ملیلتر . ئهمه له کاتیکیدا که 15.3% ی نهخۆشیه پیسهکان ریتزهی tPSA ی خوینیان کهمتر بوو له 4 نانوگرام / ملیلتر ههروهها 84% یان ریتزهی tPSA ی خوینیان زیاتر بوو له 10 نانوگرام / ملیلتر . وه شیکاری ئاماری دهری خست که جیاوویهکی گهوره هیه له نیوان ریتزهی tPSA له حالتهی گهوره بوونی بیوهی له گهل ریتزهکی له حالتهی شیرپهنجهی پرۆستات . سهبارتهت به ریتزهی سهدی بهشی پهیههستی ئهنتیجینی تایبتهت به پرۆستات c PSA % له ههموو حالتهکانی شیرپهنجهی پرۆستاتدا ریتزهکی زیاتر بوو له 60% ، ئهمه له کاتیکیدا که ریتزهکی یهک به دوا یهک 75% ، 27% ، 16% بوو له ههر یهک له گهوره بوونی بیوهی +ههوکرنی پرۆستات ، گهوره بوونی بیوهی وه کۆنترۆل . بهراوردکردنی ناوهندهکانیان دهری خست که جیاوویهکی گهوره بوونی بیوهی +ههوکرنی پرۆستات به بهراورد له گهل کۆنترۆل ئهمه له کاتیکیدا که ریتزهکی هیچ جیاوویهکی ئهوه تۆی نهبوو له ههر یهک له گهوره بوونی بیوهی پرۆستات و کۆنترۆل . سهبارتهت به ریتزهی سهدی بهشی سهربهستی ئهنتیجینی تایبتهت به پرۆستات FPSA % دهرکهوت که له 53.8% حالتهکانی شیرپهنجهی پرۆستاتدا ریتزهی سهدیان کهمتر بوو له 15 وه له 16.6% ی حالتهکانی گهوره بوونی بیوهی + ههوکرنی پرۆستات ریتزهی سهدیان یان کهمتر بوو له 15 ئهمه له کاتیکیدا که هیچ کام له حالتهکانی گهوره بوونی بیوهی پرۆستات و کۆنترۆل ریتزهی % FPSA کهمتر له 15 یان پيشان نهدا . بهراوردکردنی ناوهندهکانیان دهری خست که جیاوویهکی گهوره هیه له نیوان ریتزهکی له شیرپهنجهی پرۆستات به بهراورد له گهل گهوره بوونی بیوهی پرۆستات وه له گهوره بوونی بیوهی + ههوکرنی پرۆستات به بهراورد له گهل کۆنترۆل ، بهلام بهراوردکردنی ریتزهی FPSA % هیچ جیاوویهکی ئهوه تۆی دهرنه خست له نیوان گهوره بوونی بیوهی پرۆستات وه کۆنترۆل .