PSAD: A Better Diagnostic Tool to Detect Early Carcinoma Prostate

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Abstract: BACKGROUND Carcinoma of prostate gland is the most common malignancy above 65 yrs of age in men. Most patients with early-stage Ca prostate are asymptomatic. It is important to detect Ca prostate at an early stage so that mortality due to this malignancy can be minimized. The use of PSA to screen patients who are at the highest risk has been controversial. PSAD (prostate specific antigen density)(PSA/Vol) can be used as a better diagnostic tool in early detection of Ca Prostate. AIMS AND OBJECTIVE 1)To evaluate the diagnostic value of PSA Density in pre-operative differentiation of benign and malignant prostatic diseases. 2)To evaluate the correlation of PSA density with histopathological examination reports in Prostatic carcinoma and benign prostatic hyperplasia patients. METHODOLGY In the present study110 patients from Surgery Department KVG Hospital with urinary obstructive and /or irritative symptoms were screened for prostatic diseases by DRE, blood PSA (ng/ml) estimation, prostatic volume by Transabdominal ultrasonography and Prostatic biopsy by FNAC or Trucut Biopsy. PSAD was correlated with HPE. Sensitivity, specificity, accuracy of PSAD for diagnosing malignant prostatic diseases is analysed. CONCLUSION DRE can be used as screening method which can be aided by PSAD as a diagnostic tool for early detection of ca prostate, especially in patients with PSA in range of 3-10ng/ml.

Keywords: PSA, PSAD, Prostate

1. Introduction

Prostate specific antigen (PSA) is a serine protease, elaborated almost exclusively by epithelial cells lining the acini and ducts of prostate. Once produced, it is secreted into the prostatic ductal system and is present in high concentrations in seminal plasma where it serves the purpose of liquefying the seminal coagulum. It gains access to general circulation by seeping through the disrupted physiological barrier in diseases affecting the prostate gland.

PSA is organ-specific but not cancer-specific, resulting in limitation of its ability to differentiate carcinoma of the prostate from a number of benign abnormalities that can produce elevated PSA. Additionally, PSA is not increased in all patients with carcinoma of the prostate. Thus, though PSA can play an important role in early detection and screening of carcinoma of the prostate, its usefulness is limited by false-positive and false-negative results.

To improve the ability of PSA to detect organ-confined carcinoma of the prostate, and reliably differentiate between carcinoma of the prostate and BPH, several new concepts have emerged in recent years, including PSA density, PSA velocity, age-specific PSA and free PSA.

The concept of PSA density (PSAD) has been described as, the PSA value divided by the prostate volume. This concept emerged from the information that benign prostatic hyperplasia produces 0.3 ng/ml of PSA per gram of prostate tissue and prostate cancer produces 10 folds of this amount. PSA levels are elevated approximately 0.3 ng/ml/g of BPH tissue. Thus, patients with enlarged glands due to BPH may have elevated PSA levels. The ratio of PSA to gland volume is termed the PSA density. Some investigators advocate prostate biopsy only if the PSA density exceeds 0.1 or 0.15, while others have not found PSA density to be useful. Problems with this approach include the facts that (a) epithelial- stromal ratios vary from gland to gland and only the epithelium produces PSA, and (b) errors in calculating prostatic volume may approach 25%.

2. Aims and Objective

- 1) To evaluate the diagnostic value of PSA Density in preoperative differentiation of benign and malignant prostatic diseases.
- 2) To evaluate the correlation of PSA density with histopathological examination reports in Prostatic carcinoma and benign prostatic hyperplasia patients.

3. Material and Methods

Study Design: Prospective study

Study Site: Department of Surgery, KVG Medical College Hospital, Sullia.

Sample Size: 110 cases satisfying the inclusion criteria

Consent: The qualifying patients were informed about the risks and benefits and were to sign a detailed informed consent in their native language

Patients were worked up with detailed history and clinical examination to rule out other causes of lower urinary tract symptoms (LUTS) and complications of benign prostatic hyperplasia (BPH).

Examination included DRE, serum PSA (ng/ml) estimation, prostatic volume by Transabdominal ultrasonography and Prostatic biopsy by Trucut Biopsy. PSAD was correlated with HPE. Sensitivity, specificity, accuracy of PSAD for diagnosing malignant prostatic diseases was analysed.Serum PSA was measured using IRMA count, PSA assay was done in all patients before biopsy or digital rectal examination (DRE)Volume of prostate was measured by 'Prostate ellipsoid formula' (Vol = 0.52 x L x W x H).

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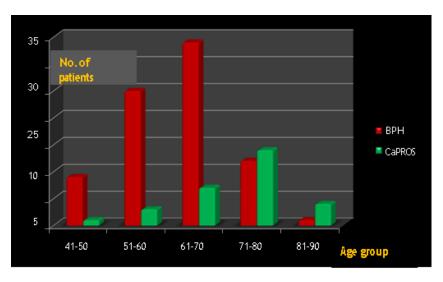
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PSAD was calculated by dividing serum PSA by volume of prostate. Collected data was analysed with descriptive statistics followed by Chi-square test and Pearson's Correlation was used to analyse the association and comparison between PSAD and Histopathological reports respectively. In this Present study the cut off value for PSAD to differentiate benign and malignant prostatic disease was taken as 0.15.Tests were used to analyse the sensitivity, specificity and overall accuracy of PSAD in diagnosing benign and malignant prostatic diseases.

4. Observation and Results

4.1 Age-wise distribution of cases



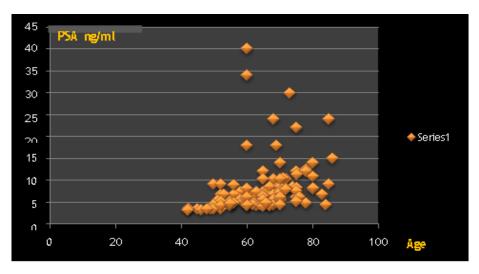
BPH and Ca Prostate typically manifested after the age of 40, with maximum incidence occurring in the age groups of 61-70(41.97%) & 71-80(48.27%) respectively.

Distribution of Range of PSA in Benign and Malignant Prostate diseases:

PSA (ng/ml) Range	BPH (n)	CaP (n)	Total	BPH (%)	CaP (%)
3 - 10	76	11	87	87.4	12.6
10.1 - 20	5	12	17	29.4	70.6
20.1 - 30	0	4	4	0	100
30.1 - 40	0	2	2	0	100

In maximum number of patients with BPH value of PSA ranged between 3-10ng/ml, where as in CaP the value varied between 10.1- 40ng/ml. Study population was distributed into 5 different age groups and corresponding values of PSA were studied. In maximum number of patients the range of PSA varied between 3-10ng/ml, in which majority (39.08%) of the patients were of 61 - 70 years of age group, followed by PSA range : 10.1- 20ng/ml in which, maximum number (52.94%) of the patients were in the age group of 71-80.

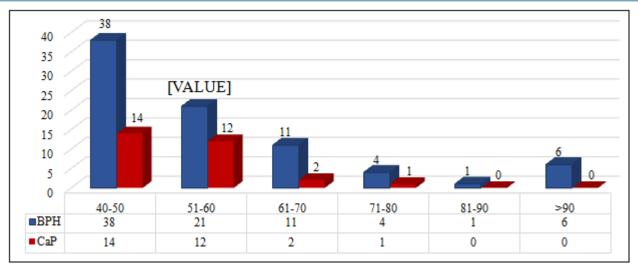
4.2 Correlation of Age and value of serum PSA



In the present study The Age of the patient when correlated with serum PSA value it was observed that there was significant rise in the PSA value with advancing age. **Pearson correlation=0.353, P < 0.01.

Distribution of Prostatic volume in Benign and Malignant Prostatic diseases

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In maximum number of patients with BPH and CaP the Trans Abdominal Ultrasonogram (TAUS) volume ranged between 40-50cc, of which majority (48.27%) were CaP patients, followed by BPH (46.91%).

Distribution of PSA density in Benign & Malignant Prostatic diseases

PSAD	BPH	CaP	Total	BPH (%)	CaP (%)
< 0.15	75	2	77	97.4	2.6
>0.15	6	27	33	18.2	81.8

Chi-square statistical test was applied to evaluate the association of PSA density in BPH &CaP and derived value X^2 =99.26 was statistically significant at the level of 0.05 X^2 =99.26, *P*<0.05hence proving strong association of PSA density with BPH and CaP which is highly significant (*p*<0.05).

Mean and SE of PSA, USGV and PSAD in Benign & Malignant Prostatic diseases

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	PSA	USGV	PSAD		
BPH	5.98±0.23	58.49±1.79	0.1199 ± 0.01		
CaP	15.68±1.89	53.58±1.79	0.2852 ± 0.03		

Tests to analyse the sensitivity, specificity, accuracy of PSAD in diagnosing Benign Prostatic diseases

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PSAD	+Ve (BPH)	-Ve	Total	
<= 0.15	75	2	77	
> 0.15	6	27	33	

Sensitivity: 92.59%,

Specificity: 93.1%

Predictive value of positive test: 97.4% Predictive value of negative test: 81.81% Percentage of false negative: 7.4% Percentage of false positive: 6.89% Overall accuracy: 92.72%

Tests to analyse the sensitivity, specificity, accuracy of PSAD in diagnosing Malignant Prostatic diseases

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	PSAD	+Ve(CaP)	-Ve	Total		
	>=0.15	27	6	33		
	< 0.15	2	75	77		
Sensitivity: 93.1%,						

Specificity: 92.59%

Predictive value of positive test: 81.81% Predictive value of negative test: 97.4% Percentage of false negative: 6.89% Percentage of false positive: 7.4% Overall accuracy: 92.72%

5. Discussion

BPH is the most common cause of prostatic enlargement, but carcinoma is the most feared one. Carcinoma of the prostate is the second most common cause of death from malignancy in males. Hence, a reliable method for early detection is required, a job which best taken care of by PSA, clearly the most tumor specific antigen known. The results are objective, quantitative and examiner-independent, and the procedure is quite acceptable to the patient, given its noninvasive nature. It has been unequivocally demonstrated that PSA is organ-specific but not disease-specific since its clinical introduction byWang et al. ^{1}

PSA, when used alone, cannot be used as an effective screening tool for carcinoma of the prostate due to its low sensitivity and specificity, especially in low and intermediate range. Large series have shown that 21-43% cancers will occur in patients with PSA in normal range^[2]. In the present study, 37.9% cancers had PSA between 4-10 .The normal PSA range used (0-4 ng/ml) does not take into account the rise of PSA production with age as the gland enlarges. Thus, age-specific ranges increase the sensitivity of PSA in the young and specificity in older males, eliminating the need for unnecessary TRUS and biopsy in many cases.

Oesterling et al,^[3] Richie et al^[4] and several others have demonstrated that PSA increases with age. In the present study the PSA range showed a statistically significant correlation with age (p<0.001).

The concept of PSAD developed by Benson et al ^[5,6] postulates that malignant cells produce more PSA per gram of tissue than normal or hyperplasic cells. In 1992, Benson et al released results of two studies applying PSAD. ^[5,6] A total of 61 patients, 41 with carcinoma and 20 with BPH were taken. Mean PSAD was 0.581 for carcinoma of the prostate group and 0.044 for BPH group, which were statistically significant. The use of PSAD further improved the diagnostic value of PSA. PSAD increased predictability

of detecting carcinoma and was found to be superior to PSA alone in detecting carcinoma in males with no palpable abnormality of prostate. However, the value of PSAD in early diagnosis of carcinoma of the prostate has been questioned by Thon et al.^[7]

In the present study, mean PSAD was 0.1199 for BPH group and 0.2852 for carcinoma of the prostate group, which were statistically significant.

In the present study when PSAD was calculated and compared with biopsy report positivity, it showed overall accuracy of 92.27% which is very much significant and helpful in predicting the prostatic diseases and prognosis. This study helps to have PSAD cut off value 0.15 which is diagnostic tool for early detection of Ca prostate, especially patients with PSA in range of 3- 10ng/ml. Patients with PSAD >0.15 should be advised for prostatic biopsy and regular follow up.

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