International Journal of Clinical and Diagnostic Pathology

ISSN (P): 2617-7226
ISSN (E): 2617-7234
www.patholjournal.com
2024; 7(3): 173-175
Received: 08-05-2024
Accepted: 09-06-2024

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A comparative study of PSA and PSAD with histomorphological spectrum of prostatic lesions

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DOI: https://doi.org/10.33545/pathol.2024.v7.i3c.599

Abstract
Background: Prostate Specific Antigen Density (PSAD) calculation has been recommended as a more accurate and reliable method for differentiating benign and malignant lesions. The present study is undertaken to determine the PSA and PSAD levels in patients of BPH and carcinoma prostate, and to evaluate the diagnostic efficiency of PSAD in the diagnosis of carcinoma prostate and in differentiating from those of BPH and also to evaluate sensitivity and specificity of PSAD in diagnosis of carcinoma of prostrate.
Method: A study including 100 patients was undertaken in department of pathology, B J Medical College and Civil hospital, Ahmedabad. This study was conducted on 100 transurethral resection of prostate (TURP) and prostate needle core biopsy specimens obtained from patients presenting with complaints of enlargement of prostate in department of urosurgery and general surgery, B J Medical college and civil hospital, Ahmedabad. Prostatic volume was measured by transabdominal ultrasonography or MP-MRI prostate study.
Results: In the present study maximum incidence of BPH and CaP manifested in the age group of 61-70 (i.e., 35.18%) and Ca prostate were in age group of 71-80 (i.e., 50%). The maximum number of patients with BPH were having PSA values between 3-10 ng/ml and PSAD value<0.15 ng/ml/cc, where as in CaP the value of PSA varied between 10-20 ng/ml and PSAD value>0.15 ng/ml/cc. Accuracy of PSAD in diagnosing benign prostatic diseases: sensitivity: 93.15%, specificity: 85.18%, predictive value of positive test: 94.44%, predictive value of negative test: 82.14%, overall accuracy: 89.16%. Accuracy of PSAD in diagnosing malignant prostatic diseases: sensitivity: 85.18%, specificity: 93.15%, predictive value of positive test: 82.14%, predictive value of negative test: 94.44%, overall accuracy: 89.16%
Conclusion: PSAD offers a simple, readily acceptable, objective and economical approach to the detection and diagnosis of prostatic carcinoma and thereby mortality due to prostatic malignancy is reduced.

Keywords: PSA density, PSA, BPH, CaP, prostatic malignancy

Introduction
Prostate Specific Antigen (PSA) is a tumour marker of 1990's and it has replaced prostatic acid phosphatase as well as serum acid phosphatase as the prostatic tumour marker of choice. Because PSA is not prostate cancer specific and prostate cancer develops in man at an age when the prevalence of benign prostatic hyperplasia is high, several parameters have been developed and investigated to enhance the sensitivity and specificity of the PSA test.
PSA levels are elevated approximately 0.12 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 0.15 ng/ml/cc. PSA density (PSAD) has been described as, the PSA value divided by the prostate volume. Benign prostatic hyperplasia produces 0.3 ng/ml of PSA per gram of prostate tissue and prostate cancer produces 10 times of this amount. PSAD greater than 0.15 ng/ml/cc is associated with 25% incidence of cancer, and a PSAD less than 0.10 ng/ml/cc is associated with 5% incidence of cancer [1].
Histologically, Adenocarcinomas produce well-defined gland patterns. The glands are typically smaller than benign glands and are lined by a single layer of cuboidal or columnar epithelium. The outer basal cell layer typical of benign glands is absent.

The cytoplasm of the tumour cells ranges from pale-clear as seen in benign glands to a distinctive amphophilic appearance. Nuclei are large and often contain one or more large nucleoli. Mitotic figures are uncommon [2].
The cut off value for PSAD to differentiate benign and malignant prostatic disease is >0.15 ng/ml/cc [3-5].

Material and Method

A study including 100 patients was undertaken in department of pathology, B J Medical college and civil hospital, Ahmedabad. This study was conducted on 100 transurethral resection of prostate (TURP) and prostate needle core biopsy specimens obtained from patients presenting with complaints of enlargement of prostate in department of urosurgery and general surgery, B J Medical college and civil hospital, ahmedabad. Brief clinical data noted from the case records, which included the age, presenting symptom, serum PSA levels, USG or MP-MRI findings and clinical diagnosis and calculate PSAD.

Inclusion criteria

1. All age groups were included above 40 years patients presenting with lower urinary tract symptoms which would include.
2. Incomplete voiding, frequency, intermittency, urgency, weak stream, straining, nocturia.

Exclusion criteria

1. Patients with age below 40 years.
2. Poorly preserved specimen and inadequate tissue volume.
3. Patients with retention of urine due to other causes other than prostatic lesions like urethral stricture and calculi were excluded.

All the prostatic specimens which were received in 10% formalin, weighed and subjected to a careful detailed gross examination. For the first 12g of tissue, six cassettes were filled. If the specimen weighed more than 12g then one additional cassettes was filled for each subsequent 5gm. For needle core biopsy, tissue were filled in cassettes. Paraffin embedded tissue sections from these specimens were used for microscopic study. Approx 4-6µm thick sections were prepared and stained routinely with H & E stain using standard procedures. Prostate specific antigen density (PSAD) was calculated by dividing serum PSA values with prostate volume. In this Present study the cut off value for PSAD to differentiate benign and malignant prostatic disease is >0.15 ng/ml/cc [3-5].

Results and Observation

Distribution of range of the PSA in benign and malignant prostate diseases

BPH and CaP manifested clinically between the age group of 41-90, in which the Maximum incidence of BPH and CaP manifested in the age group of 61-70 (35.18%) & 71-80 (50%) respectively. The maximum number of patients with BPH is shown the PSA value between 3-10 ng/ml, where as in CaP the value varied between 10.1-20 ng/ml (see Table 1 and Graph 1).

Distribution of PSA density in benign and malignant prostatic diseases

BPH is more prevalent in patients with PSAD less than 0.15 ng/ml/cc and CaP is more prevalent in patients with PSAD more than 0.15 ng/ml/cc (see Table 2).

Accuracy of PSAD in diagnosing benign prostatic diseases.

Accuracy of PSAD in diagnosing benign prostatic diseases: sensitivity: 93.15%, specificity: 85.18%, predictive value of positive test: 94.44%, predictive value of negative test: 82.14%, overall accuracy: 89.16% (see Table 3).

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Accuracy of PSAD in diagnosing malignant prostatic diseases: sensitivity: 85.18%, specificity: 93.15%, predictive value of positive test: 82.14%, predictive value of negative test: 94.44%, overall accuracy: 89.16% (see Table 4).

Mean of PSA and PSAD in benign and malignant prostatic diseases (Table 5)

Mean of PSA and PSAD in benign and malignant prostatic diseases described in Table 5.
At a PSAD cut off 0.15 ng/ml/cc,7 the sensitivity and septicity were 85% and 93% respectively in present study; as compared to 70% and 74% respectively in study done by Hugo Alexandre Socrates de Castro, *et al*. [6].

Tables, Charts and Figures

Table 1: Distribution of range of the PSA in benign and malignant prostate diseases

PSA (ng/ml)	BPH	CaP	Total	BPH (%)	CaP (%)
3-10	64	10	74	86.48	13.51
10.1-20	7	12	19	36.84	63.15
20.1-30	0	4	4	0	100
30.1-40	0	3	3	0	100

Chart 1

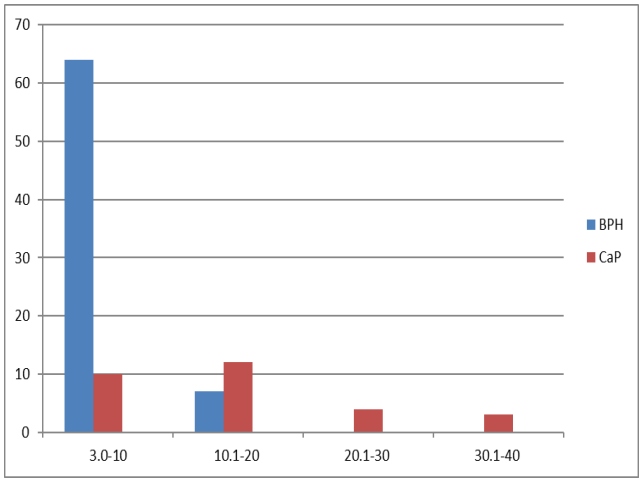

Table 2: Distribution of PSA density in benign and malignant prostatic diseases

PSAD ng/ml/cc	BPH	CaP	Total	BPH (%)	CaP (%)
<0.15	68	4	72	94.44	5.55
>0.15	5	23	28	17.85	82.14

Table 3: Accuracy of PSAD in diagnosing benign prostatic diseases

PSAD ng/ml/cc	BPH +Ve	BPH–Ve	Total
<0.15	68	4	72
>0.15	5	23	28

Table 4: Accuracy of PSAD in diagnosing malignant prostatic diseases

PSAD ng/ml/cc	CaP +Ve	CaP –Ve	Total
>0.15	23	5	28
<0.15	4	68	72

Table 5: Mean of PSA and PSAD in benign and malignant prostatic diseases

Mean	PSA	PSAD
BPH	6.36	0.107
CaP	14.78	0.245

Images

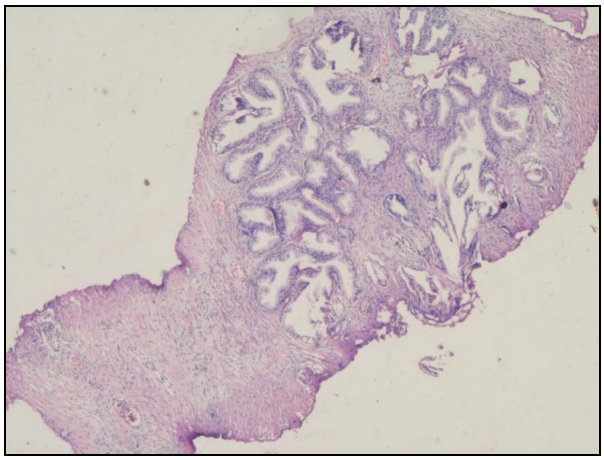

Fig 1: Benign prostatic hyperplasia, in this figure H&E stain (10x)

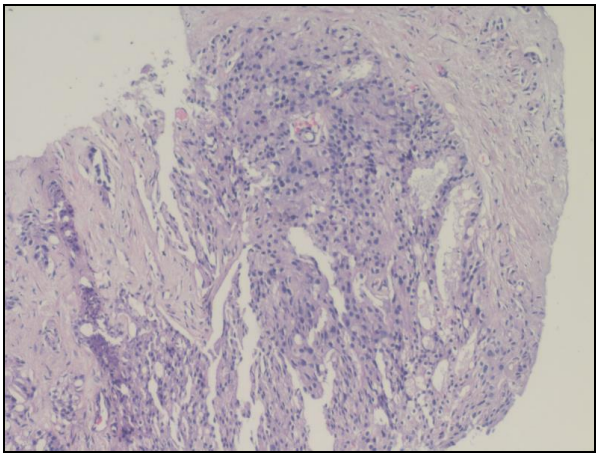

Fig 2: Prostatic adenocarcinoma, in this figure H&E stain (20x)

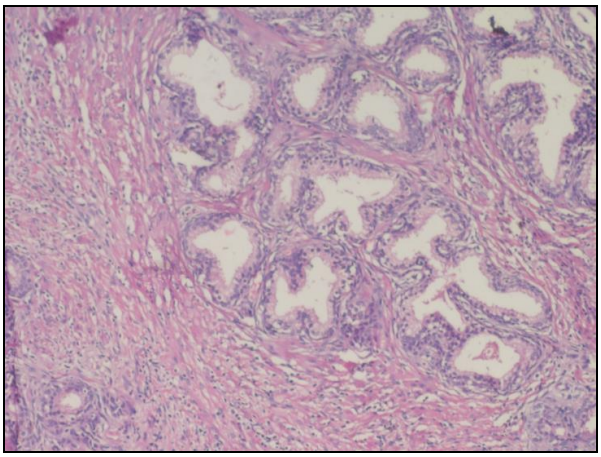

Fig 3: Prostatic adenocarcinoma, in this figure H&E stain (20x)

Conclusion

PSA estimation with PSAD is the initial test in men older than 50 years. PSAD offers a simple, readily acceptable, objective and economical approach to the detection of prostatic carcinoma. Further, immunohistochemistry and molecular genetic analysis are suggested. Screening protocols and awareness programs need to be instituted. A comprehensive histopathological study of prostatic biopsy specimens should be done to confirm the diagnosis of NH, PIN and prostatic carcinoma. Keeping in mind the cost-effectiveness and simple clinical application, PSAD is a popular PSA derivative even in the era of modern biomarkers.

Conflict of Interest

Not available

Financial Support

Not available

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How to Cite This Article

Nakrani MM, Goswami H, Parikh U. A comparative study of PSA and PSAD with histomorphological spectrum of prostatic lesions. International Journal of Clinical and Diagnostic Pathology. 2024;7(3):173-175.