

PSA DENSITY IS BETTER INDICATOR FOR PREDICTING PROSTATE CARCINOMA THAN TOTAL PSA VALUE IN GRAY ZONE PSA LEVELS

Pathology

Dr. Vaishali Pipaliya

MBBS, 3rd year pathology resident, Department of Pathology, B.J. Medical Collage and Civil hospital, Asarwa, Ahmedabad- 380016, Gujarat, India.

Dr. Hansa Goswami*

MBBS, MD Pathology, Professor & Head of the Department, Department of Pathology, B.J Medical Collage and Civil hospital, Asarwa, Ahmedabad- 380016, Gujarat, India.
*Corresponding Author

Dr. Urvi Parikh

MBBS, MD Pathology, Assistant Professor, Department of Pathology, B.J Medical Collage and Civil hospital, Asarwa, Ahmedabad- 380016, Gujarat, India.

ABSTRACT

Objective: To study the profile of patients with PSA level between 4.1 and 10.0 ng/ml and submitted to prostate biopsy, determining possible patterns that might lead to a reduction of unnecessary procedures.

Materials and Methods: In the period from January 1st, 2019 and December 31st, 2019, a study was developed with 76 patients with PSA levels between 4.1 and 10.0 ng/ml, and submitted to prostate biopsy.

Results: Cancer prevalence was 32%. On average, the patients with positive biopsies were older, with higher PSA levels and density, and smaller prostate volume as compared with the patients with negative biopsies. In the analysis of PSA density, the cancer patients averaged 0.19 ng/ml/cc, while patients with negative results averaged 0.11 ng/ml/cc. Utilizing a cutoff value of 0.15 ng/ml/cc for PSA density as a cancer positiveness criterion, the sensitivity and specificity obtained was 79% and 84% respectively.

Conclusion: The systematic use of PSA density as an indicator to proceed with the investigation of a patient with biopsy could substantially reduce the amount of unnecessary procedures.

KEYWORDS

Prostate; Prostate biopsy; Prostate cancer; PSA density.

INTRODUCTION:

According to the World Health Organization, prostate cancer is the second most common cancer in men, being the fifth most frequent cause of deaths among the male population worldwide.^{1,2}

Prostate cancer affects mostly patients above 50 years of age and preferably occurs in the prostate peripheral zone. Mortality rate is relatively low, particularly in early diagnosed cases.¹

Digital rectal examination and serum prostate-specific antigen (PSA) test are the most utilized methods of prostate cancer screening. The digital rectal examination presents limitations in case of nonpalpable prostatic lesion (early stages), and whenever a change is detected, the differentiation between malignant and benign lesions is difficult.³

Serum PSA testing is the most frequently utilized tumor marker for the screening of prostate cancer. It plays an important role in the early diagnosis of such cancer, with a considerable impact on the reduction of the disease morbidity and mortality.³

The epithelial cells in the transition zone are accountable for PSA serum levels and the increase in prostatic volume is directly related to the increased level of such antigen. A number of factors may affect the PSA levels, and should therefore be considered in the interpretation of tests results. The most common causes for the increase in PSA levels are prostatitis, benign prostatic hyperplasia and prostate cancer.⁴

The screening by means of PSA testing is aimed at detecting the highest possible number of cases. In spite of its high sensitivity, this test has a low specificity for prostate cancer, which means that in order to achieve acceptable diagnosis rates, many patients are submitted to unnecessary biopsies. There is a doubtful/gray zone traditionally considered as the PSA range between 4.1 and 10.0 ng/ml within which all patients are considered to be under suspicion of prostate cancer. Within this doubtful zone, PSA testing has a low specificity.^{5,6}

For an improved screening of candidates' PSA density (PSAD), which is the ratio between the PSA value and the prostate volume is in use, might increase the specificity of the PSA test.⁵

AIM AND OBJECTIVES:

To study PSAD in gray zone PSA levels for prediction of prostate carcinoma.

MATERIALS AND METHODS:

The present study was carried out on 76 patients admitted in urology department in between January 1st, 2019 and December 31st, 2019 with complain of urinary retention. Total PSA and prostate volume were measured and biopsies of suspected cases were sent for histopathological examination. Those patients with PSA value in between 4.1 and 10 ng/ml were selected for study.

The biopsies were received at histopathology section of Department of Pathology. After 24 hours of tissue fixation in 10% neutral buffered formalin, routine tissue processing was done. Examination of haematoxylin and eosin stained slides was done and diagnosis was established.

RESULTS:

Among the 76 patients with PSA level between 4.1 to 10 ng/ml submitted to prostate biopsy, the prevalence of cancer was 32 %. The remaining 68 % presented negative results for prostate cancer.

The patients group whose biopsies did not confirm prostate cancer had a mean age of 66 years, while the group with prostate cancer had a mean age of 67 years (Table).

As the prostate volume was evaluated, the patients with positive results for prostate cancer presented a mean prostate volume of 36.7 cm³, while for those with negative results the mean prostate volume was 60.3 cm³ (Table).

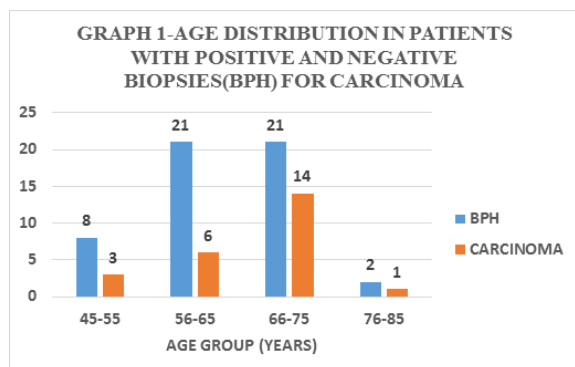
In the analysis of PSA levels, the patients with positive results for prostate cancer presented a mean value of 7.37 ng/ml, while those with negative results presented a mean value of 6.78 ng/ml. Mean PSA values for both groups were within the range of 4.1 to 10.0 ng/ml, which corresponded to the evaluated doubtful zone.

As the PSAD was evaluated, it was observed that the patients with prostate cancer presented a mean value of 0.20 ng/ml/cc, while those with negative results presented a mean value of 0.11 ng/ml/cc (Table).

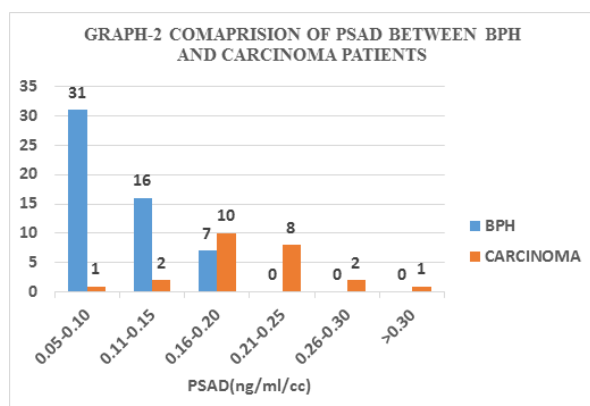
By utilizing the PSAD cutoff point of 0.15 ng/ml/cc as a cancer positivity criterion, as suggested by the literature,⁷ a sensitivity and specificity of PSAD was 79% and 84% respectively in this study.

Table- Comparison of various parameters in biopsies positive and negative for prostate cancer

PARAMETERS	POSITIVE FOR PROSTATE CANCER	NEGATIVE FOR PROSTATE CANCER
AGE (year)	66(49-76)	64(45-82)
PSA VALUE (ng/ml)	7.37(5.3-10)	6.78(4.2-10)
PROSTATE VOLUME (cc)	36.72(22-60)	60.35(36-115)
PSAD (ng/ml/cc)	0.20(0.1-0.32)	0.11(0.05-0.2)
TOTAL NO.	24/76 (32%)	52/76 (68%)



Graph 1 shows age distribution in patients with positive and negative biopsies for carcinoma. There is no significant difference in age between both groups.



Graph 2 shows difference in PSAD between patients with positive and negative biopsies (BPH) for prostatic carcinoma. It suggests that PSAD is higher in patients with positive biopsies for prostatic carcinoma, though the PSA value is between 4.1 to 10 ng/ml in both the groups.

DISCUSSION:

The present study evaluating the profile of patients submitted to prostate biopsies highlights the importance of PSAD and its impact on the reduction of the number of unnecessary prostate biopsies, with their consequential complications and costs.

There is a widespread consensus that the PSA level testing is the best available method for prostate cancer screening. Its utilization increases the detection of prostate cancer in up to 81% as compared with digital rectal examination alone.^{3,4,8} In cases of increased PSA, it is difficult to differentiate cancer from benign prostatic hyperplasia, particularly in patients with intermediate levels between 4.1 and 10.0 ng/ml. In order to optimize the PSA effectiveness as a diagnostic test within that PSA range, several options were proposed with a view on increasing the specificity of the test and avoiding unnecessary biopsies, which occurs approximately 75% of the cases.

One observed that the prevalence of cancer proportionally increased with age. More than 65% of all prostate cancers will be diagnosed in men above 65 years of age,¹² as observed in the present study, in which 72% of the patients with cancer were 65 years old or older.

Patients with PSA levels below 4.0 ng/ml are considered as at low risk

for prostate adenocarcinoma. The values between 4.1 and 10 ng/ml are considered as gray zone, as some benign and non-neoplastic conditions may also give rise to PSA level. So additional tests are required to avoid unnecessary biopsies of that patients. In those cases, PSAD is used as a method to increase the PSA testing specificity, by dividing the total PSA value by the total prostate volume.

As prostate volume was analysed, one could observe that in patients with cancer, the average prostate volumes were 36.72 cm³, on average smaller than in those patients with negative results for cancer (60.35 cm³). By using PSAD in such gray zone PSA, one would lead to a more significant correlation with benign and malignant processes, consequently reducing the number of unnecessary biopsies, without compromising the cancer detection.

At a PSAD cut off 0.15 ng/ml/cc,⁷ the sensitivity and specificity were 79% and 82% respectively in present study; as compared to 70% and 74% respectively in study done by Hugo Alexandre Socrates de Castro et al.⁹

CONCLUSION:

In the present study, it was observed that the patients with prostate cancer were on average older, with higher PSA and PSAD values, and had a smaller prostate volume. The present data indicate a good PSAD accuracy in the prediction of prostate cancer, with the potential of substantially reducing the number of unnecessary biopsies.

Source of funding: Self

Conflict of Interest: Nil

REFERENCES:

- Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin.* 2018;68(6):394-424. doi: 10.3322/caac.21492.
- Ferlay JEM, Lam F, Colombet M, Mery L, Pineres M, Znaor A, Soerjomataram I, et al. Global cancer observatory: cancer today. Lyon, France: International Agency for Research on Cancer. Available from: <https://gco.iarc.fr/today>, Accessed 02 February 2019.
- Tawfik A. Prostate specific Antigen(PSA)- Based Population Screening for Prostate Cancer: An Economic Analysis. *Ont Health Technol Assess Ser.* 2015; 15(11): 1-37
- Nickel JC. Inflammation and benign prostatic hyperplasia. *Urol Clin North Am.* 2008;35:109-15.
- Catalona WJ, Smith DS, Ornstein DK. Prostate cancer detection in men with serum PSA concentrations of 2.6 to 4.0 ng/mL and benign prostate examination. Enhancement of specificity with free PSA measurements. *JAMA.* 1997;277:1452-5
- Catalona WJ, Southwick PC, Slawin KM, et al. Comparison of percent free PSA, PSA density, and age-specific PSA cutoffs for prostate cancer detection and staging. *Urology.* 2000;56:255-60.
- Benson MC, Whang IS, Pantuck A, et al. Prostate specific antigen density: a means of distinguishing benign prostatic hypertrophy and prostate cancer. *J Urol.* 1992;147(3 Pt 2):815-6.
- Catalona WJ, Richie JP, Ahmann FR, et al. Comparison of digital rectal examination and serum prostate specific antigen in the early detection of prostate cancer: results of a multicenter clinical trial of 6,630 men. *J Urol.* 1994;151:1283-90.
- Hugo Alexandre Socrates de Castro et al. Contribution of PSA density in the prediction of prostate cancer in patients with PSA values between 2.6 and 10.0 ng/ml. *Radiol Bras.* 2011 Jul/Ago;44(4):205-209.