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THE DISCRIMINATIVE ABILITY OF PERCENT FREE PSA IN PATIENTS WITH PSA > 10 NG/ML

B.S. WADIE, E.S.A. ABDELFATAH, S.E. EMARA AND M.A. BAZEED
Department of Urology, Mansoura Urology & Nephrology Center, Mansoura, Egypt

Objective To study the discriminative role of % free PSA in patients with a total PSA > 10 ng/ml.

Patients and Methods Our patient cohort consisted of 90 males aged between 45 and 81 years (mean age: 67 ± 9 years). All patients had a biopsy-proven prostate pathology. Fifty-six patients had BPH (Group I) while 34 had prostate cancer (Group II). Blood samples were collected from all patients, and total PSA, free PSA and % free PSA were calculated in all specimens. Total PSA was measured using the IMx assay (Abbott, USA). The significance of the differences between the groups was assessed by the Mann-Whitney Wilcoxon rank sum test and Spearman's correlation coefficient for the correlation between % free PSA and the pathological diagnosis.

Results The difference in total PSA between the two groups was insignificant. The mean value in BPH patients was 11.7 ± 11.4 ng/ml, while in patients with prostate cancer it was 15.8 ± 19.2 (p = 0.8). The mean % free PSA was 18 ± 1% in patients with BPH and 16 ± 0.6% in patients with prostate cancer (p = 0.3). A strong correlation was evident between % free PSA 15% and the pathological diagnosis (p = 0.87). This was also true for the cutoff values of 20% and 25% (p=0.79 and 0.62, respectively).

Conclusion As a diagnostic test, % free PSA alone cannot be used for the differentiation between BPH and prostate cancer. In patients with a total PSA > 10 ng/ml, % free PSA has no value in the discrimination between benign and malignant pathology.

Key Words prostate specific antigen (PSA), BPH, prostate cancer

INTRODUCTION

Prostate specific antigen (PSA), the most well-known urological tumor marker, has revolutionized early detection of prostate cancer[1]. PSA is a glycoprotein which is produced primarily by the transition zone cells of the prostate. The reference range of total PSA in adults is 0 – 4 ng/ml[2]. According to this range, 25% of patients with benign prostatic hyperplasia (BPH) will have a high PSA value, i.e. more than 4 ng/ml. When using the widely accepted cutoff of 4 ng/ml for recommending prostate biopsy, up to four biopsies are needed to diagnose one case of prostate cancer (Pca)[3] . On the other hand, 38-48% of patients with organ-confined prostatic adenoma will fall within the normal range of 0 – 4 ng/ml[4]. In the serum, the PSA is complexed with plasma proteins (total PSA). The estimation of free PSA was introduced to increase the sensitivity of Pca detection in the total PSA range of 0 – 4 ng/ml[2].

This study was carried out to evaluate the usefulness of % free PSA in the detection of Pca in patients with a PSA > 10 ng/ml.

PATIENTS AND METHODS

This study comprised 100 consecutive patients aged between 45 and 81 years (mean age: 67 ± 9 years). The mean total PSA was 13.3 ng/ml. All patients had a biopsy-proven pathology revealed by sextant biopsy under transrectal ultrasound (TRUS) guidance using a 7.5 MHz probe (Panther®, B & K, Denmark). Indications for biopsy were: a PSA > 4 ng/ ml, a suspicious prostatic nodule on digital rectal examination (DRE) and a hypoechoic area on TRUS. Total and free PSA were assessed using the IMx Assay (Abbott, USA).

Ninety patients were valid for statistical evaluation.

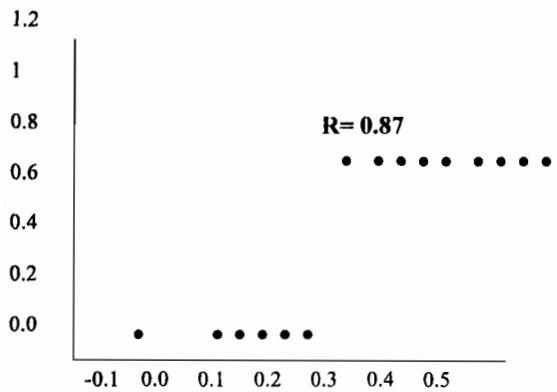

Fig. 1: Scatter diagram for the correlation between 15% cutoff and pathology

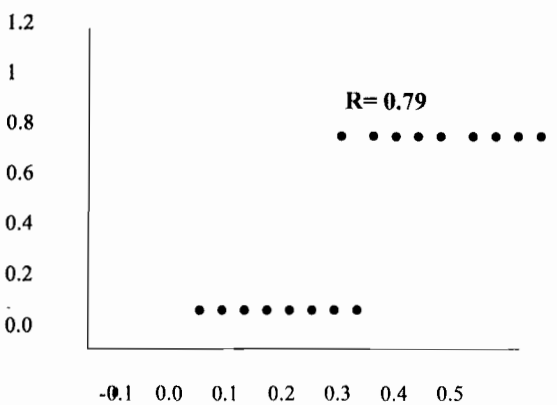

Fig. 2: Scatter diagram for the correlation between 20% cutoff and pathology

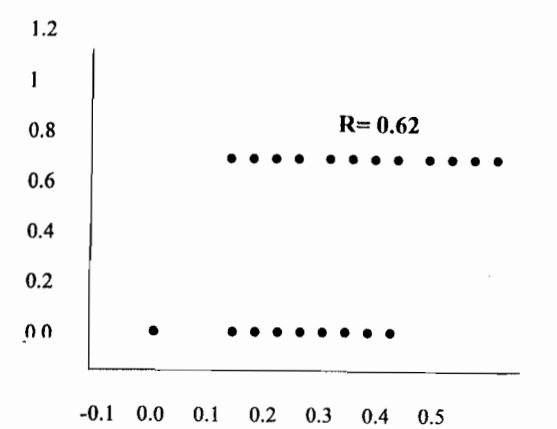

Fig. 3: Scatter diagram for the correlation between 25% cutoff and pathology

Table 1: Mean Total and % Free PSA of Patients with Benign and Malignant Pathologies

	BPH	Pca	p Value
No.	56	34	0.8
Mean PSA (ng/ml)	11.7 ± 11.4	15.8 ± 19.2	0.8
Mean % free PSA	18 ± 10%	16 ± 6%	0.2

The Mann-Whitney-Wilcoxon rank sum test was used for the assessment of significance, while Spearman's (ρ) correlation coefficient was used for the correlation of ordinal data (i.e. % free PSA and pathological diagnosis).

RESULTS

On biopsy, 56 patients were found to have BPH, while 34 were found to have Pca. The mean total PSA in the BPH patients was 11.7 ± 11.4 ng/ml, while it was 15.8 ± 19.2 ng/ml in the patients with Pca. The mean % free PSA in the BPH patients was 18 ± 10% compared to 16 ± 6% in the Pca patients. Table 1 illustrates the patients' total and % free PSA values. In our patient cohort (with a mean total PSA of > 10 ng/ml), total PSA had no significant relation to the pathology obtained on biopsy. The P-value was 0.8 using the Mann-Whitney-Wilcoxon test. The % free PSA was tested for a correlation with the pathological diagnosis using the Spearman's correlation coefficient. For a cutoff of 15%, Spearman's rho (ρ) was found to be 0.86, indicating a very good correlation. This degree of correlation decreased to a p value of 0.79 when testing for a cutoff value of 20%. A further decrease was noted at a cutoff value of 25% with a Spearman's ρ of 0.62. Figures 1, 2 and 3 show scatter diagrams of the correlations of the three cutoff values: 15%, 20% and 25%. Using the Mann-Whitney-Wilcoxon test, the % free PSA was of no use in the diagnosis of Pca. At a cutoff of 15%, the 2-tailed p-value was 0.1, at a cutoff of 20% it was found to be 0.29 and at a cutoff of 25% the p-value was 0.44. Obviously, none of these values was significant denoting that none of them can be used for the differentiation between benign and malignant pathology in a patient group like ours.

DISCUSSION

The % free PSA was introduced as early as 1995 as a PSA-related parameter that would increase the cancer detection rates[2]. In patients with a serum PSA of 4 – 10 ng/ml many methods were elucidated to decrease the rate of biopsy. One of these was the measurement of % free PSA that was found to be >23% in less than 10 cases of Pca[5]. The % free PSA was found to have a very good to excellent correlation to the pathological diagnosis in our patient cohort indicated by a Spearman's correlation coefficient ≥ ± 0.5[6]. A % free PSA cutoff of 15% showed the highest correlation with the pathological diagnosis. In a prospective study carried out by Recker et al. a PSA cutoff of 20% was selected to be the biopsy limit in a group of patients with a total PSA of 1-3 ng/ml. Patients with a % free PSA <20% were offered the choice of having TRUS and sextant biopsy[7]. Tornblom et al.[8] studied a cutoff of 18%, while Carter et al.[9] studied a cutoff of % free PSA of 14%. Using a cutoff of 15% there was no statistically significant difference between our group of patients with a benign pathology (n=56) and those with Pca (n=34) (p=0.1). The p values were even higher when cutoff points of 20% and 25% were studied (0.29 and 0.44, respectively). Masters et al. came to a similar conclusion regarding the free/total PSA ratio. They found that it did not offer any advantage in improving cancer detection rates, particularly in patients with a total PSA of 4 – 10 ng/ml[10].

In conclusion, this study confirms that in patients with a total PSA >10 ng/ml % free PSA has no value in the differentiation between benign and malignant pathology as diagnosed by sextant biopsy. However, a % free PSA of 15% yielded the highest correlation to the pathologic diagnosis.

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Editorial Comment:

In this interesting manuscript the authors show that when PSA is above 10 ng/ml, the percent-free PSA has no discriminative value between patients with a positive and a negative biopsy for prostate cancer. Although this is a finding that has been repeatedly published in the scientific literature, it is always worth to be repeated to avoid that urologists in practice ask for unnecessary costly tests which will have no impact on the clinical decision process.

Professor Laurent Boccon-Gibod
Paris, France

RESUME

Les Possibilités Discriminatives de la Fonction Libre de PSA chez les Patients dont le Taux de PSA est > 10mg/ml.

Objectifs : Etude du rôle discriminatif de la fraction libre de PSA pour les patients dont le taux de PSA est supérieur à 10 mg/ml. **Patients et Méthodes** : Il s'agit d'une cohorte de 90 patients de sexe masculin âgés de 45 à 81 ans avec une moyenne d'âge de 67 ± 9 ans. Tous les patients ont subi des biopsies prostatiques avec étude histopathologique : 56 patients présentent une HBP (Groupe I) et 34 patients un cancer de la prostate (Groupe II). Un prélèvement de sang a été réalisé chez tous les patients avec un dosage du PSA total et de la fraction libre de PSA. Le PSA total a été mesuré par un kit IMX (Abott, USA). L'étude statistique a été réalisée utilisant le Mann-Whitney Wilcoxon Rank test pour l'étude de la significativité de la différence entre les 2 groupes et le coefficient de corrélation de Spearman pour l'étude de la corrélation entre le rapport PSA libre/PSA totale et le diagnostic histologique. **Résultats** : La différence du PSA total entre les 2 groupes n'est pas significative. La moyenne des chiffres de PSA total dont l'anatomopathologie des biopsies a conclu à un cancer prostatique était de 11,7 ± 11,4 ng/ml alors que la moyenne chez le 2ème groupe présentant un cancer prostatique était de 15,8 ± 19,2 (P=0,8). La moyenne des rapports PSA libre/PSA total était de 18 ± 1% pour les patients présentant une HBP alors qu'elle était de 16 ± 0,6 % pour les patients présentant un cancer prostatique (P = 0,3). Une corrélation non significative a été remarquée entre un rapport PSA libre/PSA total de 15 % et le diagnostic histopathologique (P = 0,87). Ceci a été aussi vérifié pour une valeur charière de 20 % et 25 % (P=0,79 et 0,62 respectivement). **Conclusion** : Comme test diagnostic le rapport PSA libre / PSA total n'a pas de valeur discriminative entre une pathologie bénigne de la prostate et un cancer prostatique.

All correspondence to be sent to:

Bassem S. Wadie, M.D.
Mansoura Urology and Nephrology Center
Mansoura – Egypt
bwadie@netscape.net