The Impact of prostate – Specific Antigen Density In Predicting Prostate Cancer

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Abstract

The objective of this study is to evaluate the impact of prostate-specific antigen density (PSDA) when serum levels of prostate-specific antigen (PSA) are less than 10 ng\ml in predicting prostate cancer. We retrospectively analyzed 134 patients who underwent trans rectal ultrasound (TRUS)-guided prostate biopsies according to Cooner's algorithm. Histopathological examination revealed prostate cancer (PCa) in 22 (16%) and begin prostatic hypertrophy (BPH) in 112 (84%) patients.

Five patients (23%) with PCa had PSAD<0.15 of whom 3 had PSA<4 ng\ml and 2 had PSA between 4 and 10 ng\ml. In the BPH group, 60 patients (54%) had PSAD below 0.15 whereas 52 patients (46%) had PSAD over 0.15 . with 0.15 as the cutoff level of PSAD, the sensitivity and specificity of PSAD was found as 77 and 54%, respectively. In this patient population, PSA with the cutoff level of 4 ng\ml has sensitivity and specificity level of 77 and 33% respectively. According to these result, a statistically significant difference was found between PSA and PSAD only in terms of diagnostic specificity (chi-square, P<0.05) . There were 29 patients with negative digital rectal examination (DRE) and TRUS and PSA 4-10 ng\ml who underwent biopsy because of PSAD>0.15 . no cancer was detected in this group of patients, suggesting that biopsy in this subgroup may be unnecessary.

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Introduction

Prostate-specific antigen density (PSAD) with was introduced by [1] is defined as serum PSA\prostate volume. Initial studies have claimed an enhancement in the ability of predicting prostate cancer (PCa) when serum PSA levels were between 4 and 10 ng\ml by using PSAD [1,2]. However, initial enthusiasm was not supported by the following studies, which suggested that PSAD did not enhance the ability of serum PSA in predicting PCa [3,4]. In this retrospective analysis we examined 134 patients with PSA levels less than 10 ng\ml, who were evaluated by PSA, digital rectal examination (DRE) and transrectal ultrasound (TRUS). Indication for TRUS-guided biopsies were positive TRUS and\or DRE finding or a PSAD value greater than 0.15 (2).

Materials And Methods

In the years 1999-2002, 134 patients over age of 50 (mean age = 64 years) underwent TRUS-guided prostate biopsies after

evaluation with DRE, PSA and TRUS in urology services\medical city\Baghdad.

Serum PSA determinations by enzymatic immunoassay (Tandem-Hybritech) were performed prior to any rectal manipulation such as DRE, TRUS TRUS-guided biopsies. The indications for biopsy were suspicious rectal examination and\or hypo echoic nodule on TRUS or a PSAD value greater than 0.15 when PSA was between 4 and 10 ng\ml. PSAD was calculated by divided the PSA value\volume of prostate [4].

Ultrasound units with 7.0-Mhz Multiplan endosonic transducer were used in ultrasound evaluation and biopsy duidance in all cases. All biopsies were done by trans rectal route and tissue samples were obtained by an 18-gauge needle with the bard Biopsy gun. In the absence of hypoechoic lesions on TRUS, ultrasound-guided random biopsies were performed (3-4 cores from each lobe).

In the presence of hypoechoic lesions on TRUS, in addition to lesion-directed biopsies, random biopsies were also obtained. When DRE and TRUS finding were normal we performed an additional 2 cores of biopsy from the transitional zone. The histological diagnosis was made by the examination of the specimens obtained by TRUS-guided biopsies. For statistical analysis, analysis of difference between PSA and PSAD by Chi-Square, and calculation the percentage of accuracy, specificity, sensitivity, positive predictive value, and negative predictive value, to evaluation the PSA and PSAD in predicting prostate cancer have been done.

Results

According to the histological examination of the specimens, 22 (16%) patients were found to have PCa where as the remaining 112 (84%) patients were diagnosed as begin prostatic hypertrophy (BPH). In the BPH group, 75 patients (67%) had PSA levels between 4 and 10 ng\ml. Forty-six percent (52 patients) of BPH patients had PSAD levels greater than 0.15 . in the PCa group, 5 patients (23%) had PSA levels less than 4 ng\ml and 17 patients (77%) between 4 and 10 ng\ml. Twenty-three percent (5 patients) of PCa patients were found to have PSAD values less than 0.15 (Table 1).

In this group of patients, 2 had PSA values between 4 and 10 ng\ml, where PSAD is said to have its predictive value. The indiction for biopsy in these 2 patients was hypo echoic nodules on TRUS. Forty-Tow patients with PSA<4 ng\ml underwent TRUS-guided biopsies because of suspicious DRE and 5 (12%) were found to have PCa of whom 3 had PSAD<0.15 (Table 1).

There were 29 patients with normal DRE, normal TRUS and PSA 4-10 ng\ml who underwent TRUS-guided random biopsies because of PSAD exceeding the level of 0.15 . No patients were found to have PCa in this subgroup.

Table 1: Distribution of PSA and PSAD according to histopathological results.

Disease and PSA levels	PSAD		
	<0.15	>0.15	Total
BPH PSA<4 ng\ml	30	7	37
PSA 4-10 ng\ml	30	45	75
PCa PSA<4 ng\ml	3	2	5
PSA 4-10 ng\ml	2	15	17
Total	65	69	134

PSA with a cutoff of 4 ng\ml had an accuracy, sensitivity, specificity and positive redictive value of 40, 77, 33 and 18%, respectively. These rates were 57, 77, 54 and 25% for PSAD (cutoff level 0.15), respectively (Table 2).

Table 2: Predictive characteristics of PSA (cutoff level 4 ng\ml) and PSAD (cutoff level 0.15)

Predictive characteristics	PSA	PSAD
Accuracy %	40	57
Sensitivity %	77	77
Specificity %	33	54
Positive Predictive value %	18	25
Negative Predictive value %	88	92

Discussion

There are still many questions about the natural history of PCa and in spite of the new and improved diagnostic methods and treatments modalities, mortality rate of the disease remains uncharged [5]. PSAD has been proposed to enhance the diagnostic accuracy when PSA levels are between 4 and 10 ng\ml and DRE and TRUS findings are normal [2].

This study reveals that PSAD with a cutoff level of 0.15 increases the specificity from 33 to 54% without any decrease in sensitivity (77 versus 77%). However, it is not suitable to compare these rates of PSA and PSAD in our study population since no data in available on patients with normal DRE, normal TRUS, PSA 4-10 ng\ml and PSAD<0.15 . To overcome this problem, it is obvious that one should biopsy all of the cases with PSA>4 ng\ml. This will enable us to diagnose more cases of PCa but also bring the disadvantage of increasing the number of negative biopsies. Diagnosis of significant cancers more frequently is considered as another drawback [6,7]. The patient subgroup with DRE, normal TRUS and PSA 4-10 ng\ml were evaluated by [8]. Using systematic biopsies, they detected 23 (16%) PCa in 142 patients. With the application of PSAD (cutoff level 0.15) they would save 77 patients (54%) from the biopsy by missing only 2 cases (9%) of PCa.

In other words, the possibility of having PCa was only 1% (2\142) when DRE and TRUS were normal, and PSAD was less than 0.15 within the 4 to 10 ng\lm range of PSA. The authors concluded that systematic biopsies could be safely limited to cases with

PSAD>0.15 when PSA was between 4 and 10 ng\ml, and DRE and TRUS were normal.

Many authors reported their results of systematic prostate biopsies in 100 men with DRE and various PSA levels [7].

In contrast to the former study, all biopsies below a PSA level of 10ng\ml revealed BPH.

Results of the current study also suggest that prostate biopsies may be unnecessary in patients with normal DRE, normal TRUS and PSA<10 ng\ml.

However, other works biopsies 127 patient with the PSA levels between 4 and 10 ng\ml who did not have a suspicious rectal examination and found PCa in 23 (18%) of them [9]. Similar to the letter study, found that the cancer in 7 of 19 patients (37%) with normal DRE and a PSA between 4 and 10 ng\ml [10].

And others biopsies 121 patients with normal DRE, normal TRUS and a PSA between 4 and 10 ng\ml and diagnosed cancer in 23 (19%) patients (11). By using the polyclonal PSA assay, found cancer in 51 (25%) of 199 patients with normal DRE and PSA<30 ng\ml, which corresponds a PSA value of <20 ng\ml with monoclonal assay[12].

In a prospective previous study, followed 68 patients presenting with intermediate PSA levels (4-10 ng\ml), negative DRE and PSAD below 0.15, ten patients out of 68 should undergo biopsy secondary to a rising PSA, PCa was found in 3 patients (4.4%), whereas the remaining 65 patients continued on surveillance [13].

Contrary to the latter study, found cancer in 33 (20%) of 161 patients with normal DRE, normal TRUS and a PSA between 4 and 10 ng\ml of whom 16 had a PSAD less than 0.15 [14]. The authors suggested that the use of a PSAD cutoff above 0.15 for biopsy resulted in half of the tumors being missed and recommended that all men with DRE and TRUS but with a PSA more than 4 ng\ml should undergo biopsy.

In consideration of the whole study group, our data indicates that PSAD increases the diagnostic accuracy of PSA by increasing the specificity.

However, when combined with DRE and TRUS as in the clinical practice, PSAD did not bring any additional advantage in the diagnosis of PCa, since all the patients with PCa had DRE and\or TRUS findings, which were irrespective of PSA and PSAD values.

Although all of the cases with (2 cores), we failed to diagnose any transitional zone cancers in this subgroup of patients.

The reason for these contradictory findings may be the racial and geographical difference in the PSA levels and prevalence of PCa.

Methodological differences in determining the prostate volume may also result in different PSAD values.

Our study provided contradictory results compared to some of the reports in the recent literature [8,9,10,11,12,13 and 14].

According to our results, it seems unnecessary to biopsy patients with negative DRE, negative TRUS and PSA less than 10 ng\ml. Also, it seems that there is no place for PSAD in the diagnosis of PCa because it did not provide any additional information to DRE and PSA. It is surely possible to detect more cancer by performing biopsy on every patient with PSA greater than 4 ng\ml as proposed by [14]. However, this policy may increase the number of negative biopsies and insignificant cancers.

References

[1] Benson M. C.; Whang I. S.; Pantuck A.; et al. Prostate-specific antigen density. A means of distinguishing benign prostate hypertrophy and prostate cancer. J. Urol. 1992; 147:815-816.

[2] Cooner W. H. Rectal examination and ultrasonography in the diagnosis of prostate cancer. Prostate, 1992; 4(1):3-10.

[3] Brawer M. K.; Aramburu E. A. G.; Chen G. L.; et al. The inability of prostate specific antigen index to enhance the predictive value of prostate specific antigen in the diagnosis of prostate carcinoma. J. Urol. 1993; 150:369-373.
[4] Akdas A.; Dillioglugil O.; Cevik I.; et al. Impact of prostate specific antigen density in benign prostatic hyperplasia and prostate carcinoma. Eur. Urol. 1994; 25:299-303.
[5] Boring C. C.; Squire T. S.; Tong T. Cancer statistics C. A. 1992; 42:19.
[6] Partin A. W.; Oesterling J. E. The clinical usefulness of prostate specific antigen. J. UROL. 1994; 152: 1358-1368.
[7] Vallancien G.; Praootnich D.; Veillon B.; et al. Systematic biopsies in 100 men with no suspicious of cancer no digital rectal examination. J. Urol. 1991; 146:1308-1312.
[8] Banzinet M.; Meshref A. w.; Trudel C.; et al. Prospective evaluation of prostate-specific antigen density and systematic biopsies for early detection of prostate carcinoma. Urology; 1994; 43: 44-52.
[9] Benson M. C.; Whang I. S.; Olsson C. A.; et al. The use of prostate specify antigen density to enhance the predictive value of intermediate levels of serum prostate specific antigen. J. Urol. 1992; 147:817-821.
[10] Bare R.; Hart L.; McCullough D. L.; et al. Correlation of prostate-specific antigen and prostate-specific antigen density with outcome of prostate biopsy. Urology; 1994; 43:191-196.
[11] Rommel F. C.; Agusta F. E.; Breslin J. A.; et al. The use of prostate specific antigen and prostate specific antigen density in the diagnosis of prostate cancer in community based urology practice. J. Urol. 1993; 151:88-93.
[12] Rammon J.; Boccon-Gibod L.; Billebaud T.; et al. Prostate specific antigen density. A means to enhance detection of prostate cancer. Eur. Urol. 1994; 25:288-294.
[13] Benson M. C.; Olsson C. A. Prostate specific antigen and prostate specific antigen density. Cancer. 1994; 74:1667-1673.
[14] Catalona W. J.; Richie H. P.; Dekernion J. B.; et al. Comparison of prostate specific antigen concentration versus prostate specific antigen density in the early detection of prostate cancer. Receiver operating characteristic curves. J. Urol. 1994; 152:2031-2036.