PSA Density and PSA Transition Zone Density in the Diagnosis of Prostate Cancer in PSA Gray Zone Cases

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Abstract. This study assessed the efficacy of prostate specific antigen density (PSAD) and PSA transition zone density (PSATZ) in predicting prostate cancer in men with PSA levels of 4.0-10.0 ng/ml. Between July 1996 and July 2000, PSAD and PSATZ were determined in 202 patients who underwent ultrasonography-guided systematic sextant biopsies plus 2 transitional zone biopsies. Of the 202 patients, 27 (13.4%) had prostate cancer and 175 (86.6%) had benign prostatic hyperplasia (BPH) on pathologic examination. Although there was no significant difference in mean PSA level between the prostate cancer and BPH patients (p = 0.28), the mean PSAD (p = 0.011) and PSATZ (p = 0.036) were significantly higher in prostate cancer than in BPH patients. In discriminating prostate cancer patients, the cut-off values of 0.35 ng/ml/cc for PSATZ, and 0.15 ng/ml/cc for PSAD yielded specificity levels of 69 and 56, and sensitivity levels of 63 and 81%, respectively. In conclusion, no substantial advantage of PSATZ over PSAD could be demonstrated. (received 3 January 2003, accepted 29 March 2003)

Keywords: prostate cancer, benign prostatic hyperplasia, prostate specific antigen

Introduction

Prostate carcinoma is the most common male malignancy in the United States and the second most common cause of cancer deaths [1]. Prostate specific antigen (PSA) has unequivocally proved its clinical usefulness as a serum marker for prostate cancer. However, the sensitivity and specificity of PSA are insufficient to make it an ideal screening test for prostate cancer, since elevated PSA (greater than 4.0 ng/ml) may also occur in patients with prostatitis and benign prostatic hyperplasia (BPH). Prostate volume and age (which is correlated with volume) have been reported as factors that contribute to PSA elevation in the absence of prostate cancer [2]. Therefore, one approach to enhance the specificity of serum PSA has consisted of adjusting the contribution of PSA by determining the PSA density (PSAD), which is the ratio of the serum PSA concentration to prostate volume. Another approach, PSA transition zone density (PSATZ) (ie, serum PSA concentration divided by prostate transition zone volume) has also been suggested to enhance the performance of PSA [3,4]. Most PSA leakage from the prostate into the serum comes from the transition zone. Therefore, this study assessed the efficacy of PSAD and PSATZ in predicting prostate cancer in men with serum PSA levels in the “gray zone” of 4-10 ng/ml.

Materials and Methods

From July 1996 to July 2000, 202 patients (52 to 100 years old) were enrolled in a prospective study at our Urology Department. All men with serum PSA concentrations from 4.0 to 10.0 ng/ml were included in the study. Serum PSA determination was done using the Immulite PSA assay (Immulite, Los Angeles, USA) before digital rectal examination. Transrectal ultrasonography was performed in the left lateral decubitus position with a 7.5 MHz probe using a Siemens Sano Line-1 ultrasound device. The prostate gland was imaged in the sagittal and transverse planes. The volumes of the prostate and...
transition zone were calculated using the ellipsoid formula (volume = 0.52 x length x width x height). PSAD and PSATZ were calculated as PSA divided by the total prostate volume or the transition zone volume, respectively.

The transrectal ultrasonography and transrectal biopsy were performed at our department by one urologist who is experienced in sonography. Then, all men underwent ultrasonography-guided systemic sextant biopsies plus 2 transitional zone biopsies. Biopsies were performed from the base, midgland, apex, and transition zone of both sides of the prostate using the automated biopsy gun with an 18 gauge needle (ASAP, Microvasive, USA).

If a hypoechoic lesion was seen within the sector, the needle was specifically guided to the hypoechoic region, and 2 additional biopsies were performed in this area. All specimens were submitted for histological examination. All samples that were interpreted as atypical glands or prostatic intraepithelial neoplasia without evidence of malignancy were considered benign.

Data were expressed as mean ± SD. The significance of differences between groups was determined by unpaired t-test. Sensitivity and specificity of the analyzed and calculated parameters were calculated. Sensitivity was defined as the number of true positive results divided by the sum of true positive plus false-negative results. Specificity was defined as the number of true negatives divided by the sum of the true negatives plus false-positives.

### Results

Table 1 shows the mean age, serum PSA, PSAD, PSATZ, prostate volume, and transition zone volume in patients with BPH and prostate cancer. Overall, 27 of 202 patients (13.4 %) had histologically confirmed prostate cancer on biopsy. In 175 patients with BPH, the total and transition zone volumes were larger than in patients with prostate cancer (p = 0.008 and 0.011, respectively).

PSAD was significantly greater in patients with prostate cancer than in those with BPH (p = 0.015). Of 202 patients, 99 (49 %) had a PSAD of 0.15 ng/ml/cc, including 77 of 175 (44 %) with a negative biopsy and 22 of 27 (81.5 %) with a positive biopsy. A PSAD cutoff of 0.15 ng/ml/cc yielded a sensitivity of 81 % and a specificity of 56 %.

Mean PSATZ was 0.30 ± 0.20 and 0.39 ± 0.18 ng/ml/cc in the subjects with BPH and prostate cancer, respectively (p = 0.036). At a PSATZ cutoff value of 0.35 ng/ml/cc, sensitivity and specificity were calculated as 63 and 69 %, respectively.

### Discussion

Although PSA is the most important tumor marker in the detection of prostate cancer [5,6], patients with PSA concentrations from 4 to 10 ng/ml are in a “gray zone” where biopsy may be unnecessary. To decrease unnecessary biopsies, PSA indexes such as PSAD and PSATZ have been proposed. Several investigators have emphasized the importance of...
PSAD in improving the sensitivity of PSA for detecting prostate cancer [7,8]. Benson et al [7] introduced PSAD as an adjuvant tool to discriminate between benign and malignant prostatic disease, particularly in patients with moderately elevated PSA (4-10 ng/ml) and normal digital rectal examination and transrectal ultrasound findings. However, for these patients, recommendations about whether to perform biopsy remain controversial. Gustafsson et al [9] and Mettlin et al [10] found no superiority of PSAD over PSA. Cookson et al [11] did not find PSAD to be an accurate discriminator between benign and malignant disease in patients with a normal digital rectal examination and a PSA level of 4 to 10 ng/ml. They found the PSAD cutoff value of 0.15 to be unreliable in their patient population, with a sensitivity of 12.5% and a specificity of 61.1%. In a study by Men et al [12], neither PSA nor PSAD discriminated the patients with or without cancer in the gray zone cases.

PSATZ has been hypothesized to enhance the performance of PSA. In benign glands, the transition zone accounts for most of the PSA leakage into the serum and the volume of the transition zone is the best predictor of serum PSA [13]. Several authors reported that use of PSATZ significantly enhanced the prediction of prostate cancer in men with gray zone PSA [14-16]. However, there are controversial results regarding PSATZ. Lepor et al [17] speculated that PSATZ would not be significantly better than PSAD. Lin et al [18] compared the specificity of PSAD and PSATZ in patients with a PSA level from 4 to 10 ng/ml, and concluded that no significant difference was present between the parameters. Egawa et al [19] found no improvement in prostate cancer prediction with PSATZ compared to PSAD.

Ultrasonography has revealed major differences in the proportion of the transition zone volume compared to total prostate volume in men with or without BPH, implying significant differences between total prostate and transition zone PSA density. It has been noted that calculation of prostate gland volume is difficult [4]. Accuracy of transition zone volume measurement is ultrasonographer dependent. This influences the reproducibility of PSATZ. Transition zone limits may also be less distinct in prostate glands with diffuse calcifications.

We found that the mean PSAD and PSATZ values were both significantly higher in the prostate cancer group compared to the BPH group. Using a 0.15 ng/ml/cc PSAD cutoff in patients with a PSA of 4-10 ng/ml would have resulted in missing 18.5% of cancers while performing 44% unnecessary biopsies. Similarly, using a PSATZ cutoff value of 0.35 ng/ml/cc would have resulted in missing 37% of cancers. This value is too high from a clinical standpoint. In conclusion, in the present study no substantial diagnostic superiority of PSATZ over PSAD was evident in patients with serum PSA concentrations from 4 to 10 ng/ml.

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References


