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Predictive Effect of EPS Results on Prostate Cancer Detection in Patients with High PSA Values

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Abstract

Objective: The aim of this study was to evaluate prostate cancer detection rates with the expressed prostatic secretion test to avoid unnecessary prostate biopsy procedures and increase prostate-specific antigen reliability in patients with high prostate-specific antigen values.

Methods: Ninety-three expressed prostatic secretion-positive and 97 expressed prostatic secretion-negative patients with serum prostate-specific antigen levels of 2.5 ng/mL were included in this retrospective study. The diagnostic evaluation included a detailed history and physical examination, digital rectal examination, urinalysis, urine culture, and the expressed prostatic secretion test. Transrectal ultrasonography was used both to measure the prostate volume and obtain 12-core prostate biopsies.

Results: In our study, the mean age of the 190 patients was 62.59 ± 8.47 years. The mean prostate-specific antigen value of the patients was 5.25 ± 1.7 ng/mL, the mean International Prostatism Symptom Score was 11.8 ± 7, and the mean prostatic volume was 47.5 ± 20 mL. Prostate cancer was detected in 10 patients in the expressed prostatic secretion-positive group and 20 patients in the expressed prostatic secretion-negative group (P = .034).

Conclusion: In the expressed prostatic secretion-negative group, the rate of prostate cancer detection was statistically significantly higher.

Keywords: EPS, PSA, prostate cancer

Introduction

Prostate-specific antigen (PSA), first described by Wang et al[1] in 1979, is secreted from the ductal epithelial cells of the prostate. The rate of prostate cancer detection has increased with the use of PSA in prostate cancer screening.[1] However, an increase in the PSA level is seen not only in prostate cancer but also in conditions other than cancer, such as benign prostatic hyperplasia (BPH), chronic prostatitis, ejaculation, and non-malignant conditions.[2,3] Chronic prostatitis is an important known cause of lower urinary tract symptoms and chronic pelvic pain in men, and the prevalence of symptomatic chronic prostatitis has been reported to vary between 4% and 11%.[4] Some studies have shown the presence of a relationship between chronic prostatitis and increased serum PSA levels and determined that chronic prostatitis may be an important cause of increased serum PSA and it decreased to normal limits after treatment in some of these cases.[5,6]

In 1995, the National Institute of Health (NIH) divided prostatitis into 4 categories in 1995. The NIH defined category IV as asymptomatic chronic prostatitis with a diagnosis of expressed prostatic secretion (EPS) or the presence of inflammatory cells during the histopathological examination of prostate biopsies obtained from asymptomatic men.[7] However, since chronic prostatitis can also cause increased serum PSA levels, this can potentially result in unnecessary biopsy procedures, overdiagnosis, and overtreatment, increasing medical costs.[2] Prostate cancer can be detected in only 38% of all biopsies performed on the basis of elevated PSA.[8] The empirical use of antibiotics to lower PSA in asymptomatic patients is common in current clinical practices, but previous studies examining this issue have yielded conflicting results. While some studies indicate that serum PSA can be reduced with a range of antibiotics,[9] others suggest that antibiotic treatment does not have an effect on serum PSA levels.[10] In addition, there are problems related to unnecessary antibiotic use, treatment-related bacterial resistance, drug toxicity, and treatment cost.

The aim of this study was to compare the detection rate of prostate cancer in EPS-positive and -negative patients and to predict chronic prostatitis that may cause unnecessary biopsies.

Methods

This study included 190 patients with PSA values ranging from 2.63 ng/mL to 9.90 ng/mL. The EPS test was performed on the patients, and all had normal digital rectal examination findings. Then, patients who underwent a prostate evaluation with transrectal ultrasonography followed by a biopsy under ultrasonography guidance were included in the study. The exclusion criteria were as follows: (1) pyuria (more than 5 leukocytes), (2) history of urinary tract infection, (3) history of urethral disorder or intervention, (4) history of 5-alpha reductase therapy, (5) antibiotic or anti-inflammatory therapy within the last 2 months, (6) neurological disorders that could have an effect on lower urinary tract function, (7) previous prostate biopsies or genitourinary surgery, (8) presence of acute urinary retention, and (9) previous history of prostatitis. After the patients emptied their bladder, periurethral cleansing was performed with an alcohol sponge. EPS samples were obtained from all the patients after a prostate massage. Liquid samples were counted on microscope slides at 40× magnification and were considered positive for prostate inflammation if the leukocyte count

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was ≥10.[11] After a detailed physical examination, urinalysis, urine culture analysis, and antibiogram were undertaken on all the participants. The patients' serum PSA levels, IPSS (international prostatism symptom score), prostate volumes, and EPS results were recorded. Prostate volumes were measured using the formula 0.52 (L × W × H) (L: length from top to bottom, W: horizontal length, and H: anterior–posterior length). An ultrasound-guided 12-core prostate biopsy was performed using an automatic prostate biopsy gun with an 18-G 30-cm needle. According to the pathology results, the cases were evaluated as BPH, prostatitis, and prostate cancer.

Health Sciences University Gazi Yaşargil Training and Research Hospital Ethics Committee approval was obtained with the number Date: March 26, 2022, approval no: 742.

Statistical Analysis

Statistical data analysis was performed using Statistical Package for the Social Sciences software version 20.0 (IBM SPSS Corp., Armonk, NY, USA) software package (descriptive statistical analysis, Pearson's chi-square, and correlation test). $P < .05$ was considered statistically significant.

Results

The mean age of the 190 patients included in this study was 62.59 ± 8.47 years. The mean PSA value was 5.25 ± 1.7 ng/mL, the mean IPSS was 11.8 ± 7, and the mean prostate volume was 47.5 ± 20 mL. There was no statistically significant difference between the EPS-positive and EPS-negative groups in terms of the mean PSA, free PSA, IPSS, and prostate volume ($P > 0.05$); however, a statistically significant difference in age ($P = .001$) (Table 1).

When the pathology results of the EPS-positive and EPS-negative groups were evaluated according to the presence of BPH, prostatitis, and prostate cancer, no significant difference was found in terms of the rates of BPH ($P > .05$). As a result of the biopsies performed, prostatitis was detected in 35.8% (30/190) of the patients, 43% (40/93) in the EPS-positive group, and 28.9% (28/97) in the EPS-negative group. The difference between the 2 groups was statistically significant ($P = .042$). Prostate cancer was detected in 15.8% (30/190) of the patients. This rate was 10.8% (10/93) in the EPS-positive group and 20.9% (20/97) in the EPS-negative group, indicating a statistically significant difference ($P = .034$) (Table 2).

Table 1. Basic Patient Characteristics

	EPS Positive	EPS Negative	Total	*P*
Age	62.1	66.1	62.59 ± 8.4	**.001**
PSA	5.17	5.24	5.25 ± 1.7	.969
fPSA	1.11	1.21	1.14 ± 0.68	.222
IPSS	12.6	11.12	11.8 ± 7.0	.250
Prostate volume	47.7	46.38	47.50 ± 20	.656

EPS, expressed prostatic secretion; PSA, prostate-specific antigen; fPSA, free PSA; IPSS, International Prostatism Symptom Score.

Table 2. Distribution of Prostate Cancer and Prostatitis Between the Study Groups

	EPS Positive (n = 93)	EPS Negative (n = 97)	*P*
Prostate cancer (%)	10.75	20.6	**.034**
Prostatitis (%)	43	28.86	**.04**

EPS, expressed prostatic secretion.

Discussion

With the widespread use of serum PSA, the early detection of prostate cancer has significantly increased. However, the diagnostic utility of PSA is limited by its lack of specificity, particularly in men with serum PSA levels between 4.0 and 10.0 ng/mL. Since serum PSA levels also increase in BPH and acute or chronic prostatitis, unnecessary prostate biopsies can be performed in men after aggressive prostate manipulation or prostate needle biopsies.[12] Although prostate cancer does not result in more free PSA than normal prostate epithelium, a larger fraction of PSA produced by prostate cancer appears to escape proteolysis (activation or degradation).[13] Despite PSA being the best diagnostic serum marker for prostate cancer, its sensitivity and specificity are limited. The detection rate of prostate biopsy cancer varies between 19% and 45% in 6-10 core biopsies.[14,15] Nadler et al[5] reported that clinically detectable prostate cancer accounted for only 34% of elevated serum PSA levels.[5] Therefore, there must be other factors as possible causes of elevated serum PSA values, such as prostate volume, prostate stone, and acute-chronic inflammation. The incidence of prostate cancer diagnosed in the early stage has increased due to the widespread use of PSA testing. In another study, the clinical detection rate of prostate cancer at high serum PSA levels was reported to vary between 17.5% and 38%.[9] In the current study, prostate cancer was detected in 30 patients as a result of prostate biopsies performed on 190 patients, and the incidence of prostate cancer was 15.8%. This rate was 10.8% in the EPS-positive group and 20.6% in the EPS-negative group. Thus, prostate cancer was seen at a lower rate in the chronic prostatitis group despite high PSA levels.

In the detection of any prostate cancer, the estimated sensitivity of PSA at a cut-off value of 4.0 ng/mL is 21% and its specificity is 91%.[16] However, a wide range (10%-80%) of false-positive results are reported.[17,18] Studies have shown that the prevalence of symptomatic chronic prostatitis ranges from 4% to 16%.[19,20] Hasui et al[21] reported that the degree of acute and chronic inflammation present in transurethral prostatectomy specimens was associated with increased serum PSA levels.[21] In a study by Potts[6], 42% of patients presenting with a high PSA value had laboratory signs of prostatitis. In studies involving a needle biopsy analysis, the incidence of prostatitis has been reported on a wide scale, ranging from 17.2% to 42%.[22,23] In a study conducted to evaluate the population participating in a prostate cancer awareness screening program, the incidence of NIH category IV prostatitis was found to be 32.2%.[24] Morote et al[25] examined 284 patients without evidence of cancer on sextant ultrasound-guided biopsies and found benign tissues without signs of inflammation in 23.2% of these cases. The authors stated that chronic prostatitis was detected in 68.3% of the patients and acute prostatitis in 8.4%. In the current study, prostatitis was detected in 35.8% (68/190) of the patients, of whom, 43% (40/93) were in the EPS-positive group and 28.9% (28/97) in the EPS-negative group. The difference between the 2 groups was statistically significant, which is consistent with the literature.

Minardi et al[26], examining free and total PSA ratios, showed that prostate inflammation associated with benign hypertrophy could lead to false-positive tPSA(total PSA) and f/tPSA (free/total

PSA) levels considering that the f/tPSA ratio was below 16% in 60% of these patients. Okada et al.[26] reviewed negative prostate needle biopsies in 93 patients and observed that the degree of inflammation was correlated with serum PSA levels at different ages and prostate volumes. The presence of histological inflammation was found to be significantly correlated with serum PSA. In a study by Bozeman et al[28], the use of antibiotics and anti-inflammatory drugs for 4 weeks reduced the tPSA level below 4 ng/mL in 36.4% of the patients, and the tPSA level remained at this level for another 11.4 months during the follow-up of approximately half of these cases.[28]

In our study, according to the pathology results of the prostate biopsies, there was a statistically significant difference between the EPS-positive and EPS-negative groups in terms of the rate of patients diagnosed with prostate cancer and prostatitis. Although there was no significant difference in the PSA levels of the 2 groups, the presence of more prostate cancer diagnoses in the EPS-negative group supports the literature. Furthermore, it was determined that chronic prostatitis caused an increase in PSA levels and led to unnecessary prostate biopsies. However, we did not evaluate the current multi-parametric magnetic resonance imaging findings of the patients, which can be considered as a limitation of the study.

A lower rate of prostate cancer was detected in the EPS-positive patients compared to the EPS-negative patients. The diagnosis of prostatitis should be considered in patients with high PSA levels, and the EPS evaluation may protect some patients from unnecessary biopsies. There is a need for prospective studies on this subject with a larger series.

Ethics Committee Approval: Ethical committee approval was received from the Ethics Committee of Health Sciences University Gazi Yaşargil Training and Research Hospital (Date: March 26, 2022, approval no: 742).

Informed Consent: Written informed consent was obtained from all participants who participated in this study.

Peer-review: Externally peer-reviewed.

Declaration of Interests: The author declare that they have no competing interest.

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