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The effect on the sensitivities of PSA and PSA-age volume score of IPSS and nocturia in predicting positive prostate biopsy findings

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KEYWORDS
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Abstract
Objective: The PSA-age volume (PSA-AV) score was calculated by multiplying the age and prostate volume and then dividing the total by the prebiopsy PSA level. The aim of this study was to evaluate the effect on the sensitivities of PSA and PSA-AV score of International Prostate Symptom Score (I-PSS) and nocturia in predicting positive prostate biopsy findings.
Subjects and methods: A total of 1302 biopsies data were divided into two groups according to presence/absence of nocturia. Of these biopsies, 452 biopsies data with I-PSS were also divided into three groups according to severity of I-PSS. The sensitivities, specificities, positive and negative predictive values of the PSA-AV and PSA in all the groups were calculated separately.
Results: Although the sensitivities of PSA and PSA-AV were similar in the patients with nocturia (94.1% and 95.8%, respectively), the sensitivity of PSA-AV (99.2%) was higher than PSA (91.8%) in the patients without nocturia. The sensitivities of PSA in mild, moderate and severe I-PSS group were found to be 100%, 92.9% and 95%, respectively (the sensitivities of PSA-AV were 100%, 94.4% and 88.2%, respectively). While severity of I-PSS was decreasing, although sensitivity of PSA-AV increased regularly, sensitivity of PSA was variable.
Conclusions: All our data shows that if we remove most of the factors which effect PSA such as age, prostate volume, prostatitis and BPH, we may increase the sensitivity of PSA for predicting positive prostate biopsy. Further PSA formulas contain of result of some tests (I-PSS, uroflowmetry or postvoiding residue urine) as well as age and prostate volume should increase the sensitivity and specificity of PSA for detecting prostate cancer.

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Introduction

Prostate cancer (PCa) is the second most common cancer and the fifth most common cause of cancer death worldwide. The age-adjusted incidence rate of PCa was 104.2 per 100,000 persons in Australia/New Zealand, 94.1 in Western Europe, 85.6 in Northern America, however only 8.2 in Eastern Asia [1]. The incidence has more than doubled since 2000 when only 57 new cases per 100,000 men in Australia were registered in 2000 [2].

The digital rectal exam (DRE) and serum prostate specific antigen (PSA) are important for PCa screening and early detection programs, they are considered as standard component [3]. PSA is organ specific, but not disease specific, thus its use for PCa screening lacks adequate sensitivity [4]. Therefore, due to the false-positive results obtained by PSA during screening, some of patients are unfortunately candidate to an unnecessary transrectal ultrasound-guided prostatic biopsy (TRUSPB), that is an invasive procedure which can lead to significant morbidity, and even mortality such as sepsis [5,6]. Recently, various strategies were introduced to improve the sensitivity and specificity of the PSA. Patel et al. developed a novel formula named PSA-age volume (PSA-AV) that incorporates age, prostate volume and PSA level into a single score for prostate cancer detection [7]. Their aim was to reduce the effect of prostate volume and age on serum PSA level by using this formula. They suggested that this formula was useful for predicting positive biopsy findings. An increasing level of PSA can also been seen in benign prostatic hyperplasia (BPH) and prostatitis. These diseases can increase International Prostate Symptom Score (I-PSS) as well as age and prostate volume [8].

The purpose of the present retrospective study was to evaluate the effect on the sensitivities of PSA and PSA-age volume score of IPSS and nocturia in predicting positive prostate biopsy findings.

Subjects and methods

This retrospective study was based on the data of 1408 TRUSPB procedures performed at our institution between 2005 and 2013. The indications for performing a TRUSPB were elevated or increasing PSA levels, abnormal DRE findings or a previous abnormal TRUSPB. The database consisted of variables including age, prebiopsy PSA level, prostate volume, digital rectal examination, nocturia and IPSS score (only in 452 patients) information. TRUSPBs were performed using the LOGIQ machine by the urologists. The prostate volume was calculated using ultrasonography during the TRUSPB. The number of biopsy cores (6–12 cores) was determined by the urologists according to their preference. In patients with an abnormal DRE or ultrasound findings, additional biopsy cores were taken. We eliminated those biopsy records that did not have complete data, patients who were <40 years or >79 years old, and patients who had undergone repeat biopsies. A total of 1302 biopsy specimens were analyzed. The PSA-age volume (PSA-AV) score was calculated by multiplying the age and prostate volume and then dividing the total by the prebiopsy PSA level [7].

A total of 1302 biopsies data were divided into two groups according to presence/absence of nocturia. Of these biopsies, 452 biopsies data with I-PSS were also divided into three groups according to severity of I-PSS (mild: 1–7; moderate: 8–19; severe: 20–35). The sensitivities, specificities, positive and negative predictive values of the PSA-AV cutoff of 700 and PSA cutoff of 4 ng/mL in all the groups were calculated separately. Statistical analyses were carried out using SPSS 13.0 (SPSS Inc.). P values < 0.05 were considered significant.

Results

The mean age of the patients in our study was 64.92 ± 8.49 ($n = 1302$). The mean PSA level, PSA-AV score and mean prostate volume were 9.98 ± 24.91 ng/mL, 395.71 ± 357.21 and 48.77 ± 26.56 cm^3, respectively. Of the 1302 prostate biopsies, 358 biopsy specimens (27.5%) were positive for prostate cancer.

The mean of age, prostate volume, PSA and PSA-AV in the patients with and without nocturia were given Table 1. Although the sensitivities of PSA and PSA-AV were similar in the patients with nocturia (94.1% and 95.8%, respectively), the sensitivity of PSA-AV (99.2%) was higher than PSA (91.8%) in the patients without nocturia (Table 2).

Table 3 shows the mean of age, PSA, PSA-AV and prostate volume in the three groups that were divided according to I-PSS. The sensitivities of PSA 4 ng/mL in mild, moderate and severe I-PSS group were found to be 100%, 92.9% and 95%, respectively (Table 4). The sensitivities of PSA-AV cutoff of 700 in mild, moderate and severe I-PSS group were 100%, 94.4% and 88.2%, respectively. While severity of I-PSS was decreasing, although sensitivity of PSA-AV increased regularly, sensitivity of PSA was variable.

Discussion

The use of PSA as a serum marker has revolutionized the diagnosis of PCa [9]. Although PSA is a highly organ-specific marker, it is not a cancer-specific marker. Thus, serum levels may be elevated in the presence of BPH, prostatitis and other non-malignant conditions as well as age and prostate volume [10]. PSA-AV was developed by Patel et al. to correct the impact of prostate volume and age on PSA levels [7]. They noticed that a PSA-AV score of 700 was a useful formula for predicting positive biopsy findings in patients with small

Table 1 The mean of age, prostate volume, PSA and PSA-AV of patients with and without nocturia.

	Nocturia (+) ($n = 819$) Mean ± SD	Nocturia (−) ($n = 483$) Mean ± SD	P-value
Age	65.66 ± 8.46	64.18 ± 8.53	0.003*
Prostate volume	48.67 ± 26.90	48.87 ± 26.21	0.877
PSA (ng/mL)	10.16 ± 29.68	9.8 ± 20.12	0.683
PSA-AV	388.91 ± 327.75	402.49 ± 372.41	0.537

PSA-AV: PAS-age volume.
* $P < 0.05$ was considered statistically significant.

Table 2 The sensitivities, specificities, positive and negative predictive values of PSA 4 ng/mL and PSA-AV 700 for predicting positive prostate biopsy in the patients with and without nocturia.

	Nocturia (+)		Nocturia (−)	
	PSA 4 ng/mL	PSA-AV 700	PSA 4 ng/mL	PSA-AV 700
Sensitivity (%)	94.1	95.8	91.8	99.2
Specificity (%)	16.5	13.7	15.8	11.6
PPV (%)	31.3	31.0	26.9	27.5
NPV (%)	87.3	88.9	85.1	97.7

PSA-AV: PSA-age volume, PPV: positive predictive value, NPV: negative predictive value.

Table 3 The mean of age, PSA, PSA-AV and prostate volume in the three groups that were divided according to I-PSS.

	Mild ($n=88$) Mean ± SD	Moderate ($n=244$) Mean ± SD	Severe ($n=120$) Mean ± SD	*P*-value
Age	61.46 ± 8.55	63.79 ± 7.46	65.66 ± 8.08	0.009*
Prostate volume	40.95 ± 20.63	48.22 ± 25.00	47.84 ± 19.49	0.225
PSA (ng/mL)	9.40 ± 7.51	13.96 ± 20.36	14.04 ± 23.29	0.262
PSA-AV	396.57 ± 253.48	461.90 ± 340.20	477.61 ± 403.86	0.141

Mild: I-PSS = 1–7, moderate: I-PSS = 8–19, severe: I-PSS = 20–35, PSA-AV: PSA-age-volume.
* $P < 0.05$ was considered statistically significant.

Table 4 The sensitivities, specificities, positive and negative predictive values of PSA 4 ng/mL and PSA-AV 700 for predicting positive prostate biopsy in the patients with mild, moderate and severe I-PSS.

	Mild ($n=88$)		Moderate ($n=244$)		Severe ($n=120$)	
	PSA	PSA-AV	PSA	PSA-AV	PSA	PSA-AV
Sensitivity (%)	100	100	92.9	94.4	95.0	88.2
Specificity (%)	16.4	8.9	17.4	17.6	10.3	21.3
PPV (%)	21.5	19.0	20.4	19.0	17.9	16.9
NPV (%)	100	100	91.4	93.9	90.9	90.9

Mild: I-PSS = 1–7, moderate: I-PSS = 8–19, severe: I-PSS = 20–35, PSA-AV: PSA-age-volume.
PPV: positive predictive value, NPV: negative predictive value.

prostates. Currently, most clinicians recommend a biopsy once a patient's serum PSA rises above 4.0 ng/mL. Catalona et al. reported this PSA level or higher was appropriate as the PSA cutoff value for the screening of PCa. Since then, this value has been the most commonly used clinically [11]. We investigated the sensitivities of PSA and PSA-AV in patients with and without lower urinary tract symptoms (LUTS). We found that although the sensitivities of PSA and PSA-AV for predicting positive prostate biopsy in the patients with nocturia were similar (94.1% and 95.8%, respectively), the sensitivity of PSA-AV (99.2%) in the patients without nocturia was higher than the sensitivity of PSA (91.8%). The mean age in the patients with nocturia were significantly higher than the patients without nocturia ($P = 0.003$). Similarly, Patel et al. reported that PSA-AV was a useful formula for predicting positive biopsy findings in younger patients with small prostates [7].

We also analyzed the sensitivities of PSA and PSA-AV in three groups that divided according to I-PSS. Our data showed that while I-PSS was decreasing, sensitivity of PSA-AV was rising (Table 4). However we did not find any relationship between sensitivity of PSA and I-PSS (Table 4). While I-PSS was decreasing, sensitivity of PSA was variable. This may be the effect of prostate volume and age on PSA. Because when we minimized this effect by using PSA-AV formula, we found a negative correlation between I-PSS severity and sensitivity of PSA-AV. We suggest that PSA-AV score may contribute to predicting positive prostate biopsy of PSA especially in the patients with low I-PSS score and PSA 2.5 to 4.0 ng/mL.

All our data shows that if we remove most of the factors which effect PSA such as age, prostate volume, prostatitis and BPH, we may increase the sensitivity of PSA for predicting positive prostate biopsy. PSA-AV removes only the impact of age and prostate volume on PSA. The other factors (BPH and prostatitis) are evaluated I-PSS, uroflowmetry or postvoiding residue urine. We think that further PSA formulas consist of other factors which may increase in PSA as well as age and prostate volume may increase the sensitivity and specificity of PSA for detecting prostate cancer.

Conflict of interest

None declared.

Source of Funding

None.

Ethical Committee Approval

The study protocol was approved by the ethics committee of our institution.

Authors' contributions

A – research concept and design; OÜ, B – collection and/or assembly of data; İÇ, C – data analysis and interpretation; OÜ, GT, TM, D – writing the article; OÜ, E – critical revision of the article; OÜ, TM, F – final approval of article; TM, GT.

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