

## Original Research Article

# PSA density as a parameter in prostate biopsy decision of patients with prostate sized 80 mL or larger

Caner Ediz<sup>1\*</sup>, Serhan Cimen<sup>2</sup>, Serkan Akan<sup>1</sup>, Muhammed Cihan Temel<sup>1</sup>,  
Omer Yilmaz<sup>1</sup>, Ozlem Koksall<sup>3</sup>

<sup>1</sup>Department of Urology, Sultan Abdulhamid Han Education and Research Hospital, Istanbul, Turkey

<sup>2</sup>Department of Urology, Malatya Education and Research Hospital, Istanbul, Turkey

<sup>3</sup>Department of Biostatistics, Sultan Abdulhamid Han Education and Research Hospital, Istanbul, Turkey

**Received:** 07 January 2019

**Accepted:** 07 February 2019

### \*Correspondence:

Dr. Caner Ediz,

E-mail: [drcanerediz@gmail.com](mailto:drcanerediz@gmail.com)

**Copyright:** © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

## ABSTRACT

**Background:** Patients with high prostate volume (>80 ml) and high PSA levels make it difficult to decide on prostate biopsy. In this study, author aimed to detect of predictive factors to distinguish malignant or benign prostatic lesions in patients with prostate size over 80 ml.

**Methods:** A total of 299 patients underwent TRUSBP at the clinics between 2012-2017. Cases with prostate volume over 80 ml were divided into groups according to the pathology by benign (group 1) or malign (group 2). Author evaluated the predictive factors in two groups. Patient's age, grading and findings of digital rectal examination, prostate volume, number of received cores, total (tPSA) and free PSA (fPSA) before biopsy, rate of percentage of free to total prostate specific antigen (f/tPSA) and PSA density was compared in both groups.

**Results:** Benign prostate hyperplasia was detected in 217 patients (72.58%) and prostate adenocarcinoma was detected in 82 patients (27.42%). The patient's age, tPSA, fPSA and PSA density were 63.81 years, 9.71 ng/ml, 1.78 ng/ml and 0.10 g/ml<sup>2</sup> in group 1 and 69.10 years, 38.32 ng/ml, 5.86 ng/ml and 0.42 ng/ml<sup>2</sup> respectively. Patient's age, tPSA, fPSA and PSA density was statistically significant between in two groups (p<0,05). Number of received cores and rate of f/tPSA were 14.02-13.84% and 19.06-17.62% in group 1 and 2, respectively and was not statistically significant. In group 2, prostate adenocarcinoma was most common detected with Gleason score 4+3 in 21 of 82 patients (25.6%).

**Conclusions:** High prostate volume (>80 ml) has a significant influence in PSA values and results of the biopsy, PSA density is extremely important in performing prostate biopsy decisions.

**Keywords:** High prostate volume, Prostate biopsy, PSA density

## INTRODUCTION

Description of sextant biopsy by Hodge et al, was opened a new era in 1989, Transrectal ultrasound-guided biopsy of the prostate (TRUSBP) has a vital place in the determination of prostate tumor (PCa).<sup>1</sup> Prostate volume (PV) is still an actual headline in the studies for PCa. Especially, patientst with high PV (>80 ml) and high PSA

levels make it difficult to decide on prostate biopsy. Uzzo et al, and Karakiewicz et al, was found that PCA detection rate drops in high-volume prostates.<sup>2,3</sup> Smaller PV and high grade prostate carcinoma has the inverse relationship. In addition that Kulkarni et al, has found a larger prostate results in fewer high grade cancers diagnosed at biopsy.<sup>4</sup> Author aimed to assess the relationship between high PV (>80 ml) and PCA in

patients with benign and suspicious digital rectal examination (DRE) and determine the most important factor (tPSA, fPSA, f/tPSA, PSA density) for decision of biopsy in the prostate biopsy cohort.

## METHODS

### Study population

Patients in the clinics between 2012-2017 were enrolled in a retrospectively. Age, grading and findings of digital rectal examination, total and free serum PSA in all patients was assessed before biopsy. TRUSBP was then performed in 299 men during the study period. For men with multiple biopsy sessions only the initial session was included in analysis.

The criteria for inclusion in the study were as follows: DRE results suggestive or non-suggestive of neoplasia, elevated PSA (>2.5 ng/mL in men), a prostate volume >80 ml. Disease of coagulopathies, patients with urinary tract infections, individuals who have had surgery in the past year, total number of cores less than 12, and patients who had previous anti-androgen, 5- $\alpha$  reductase inhibitory treatment or prostatic radiation therapy were also excluded from the study. The patient's medical records were reviewed, patients with inadequate data were not included the study. Individuals age, grading and findings of digital rectal examination, TRUS calculated PVs with the ellipse method (length X depth X width X  $\pi/6$ ), number of received cores, total (tPSA) and free PSA (fPSA) before biopsy, rate of percentage of free to total prostate specific antigen (f/tPSA) and PSA density were noted PSA density was calculated as total PSA (ng/ml) divided by prostate volume (ml).

One day before the procedure, oral administration of 500 mg levofloxacin and 400-mg etodolac was started and it was continued until the end. The day of biopsy a rectal enema (250 mL) was performed before the biopsy. The procedure was performed while the patient was in the left lateral position with the thighs flexed. The procedure was performed under the guidance of ultrasound device with a 7.5 MHz biplanar probe.

The biopsy was performed on an outpatient basis in a room equipped with all material necessary for emergency intervention. Sedation and anesthesia were not achieved. 10 minutes before the procedure, periprostatic nerve blockade was performed in addition to perianal intrarectal lidocain gel. Injections were delivered at the angle between the seminal vesicle and prostate on each side using 5 cc of 2% lidocain. The 12-24 quadrant prostate biopsies were performed by multiple experienced urologists.

Pathological specimens were reviewed by a single genitourinary pathologist based on the 2005 International Society of Urological Pathology Consensus Conference on Gleason Grading of Prostatic Carcinoma.<sup>5</sup> Cases with

prostate volume over 80 ml were divided into groups according to the pathology by benign (group 1) or malign (group 2). Patients with high grade prostatic intraepithelial neoplasia (HGPIN) and atypical small acinary proliferations (ASAP) were excluded for the sake of clarity of the results. The detection of clinically significant or clinically insignificant disease by targeted over 12-24 core biopsy was separated with Gleason score.

### Statistical analysis

All data was analysed with SPSS 16 Windows package (SPSS Inc. Chicago, II, USA) and Microsoft excel computer programs. In the analysis of the data, the normality hypothesis was first investigated using the Kolmogorov-Smirnov test, followed by Mann-Whitney U test, Chi-Square as the statistical method.  $P < 0.05$  was accepted as statistically significant.

## RESULTS

Benign prostate hyperplasia was detected in 217 patients (72.58%) and prostate adenocarcinoma was detected in 82 patients (27.42%). The mean ages were statistically significant between two groups:  $63.81 \pm 7.32$  for group 1 and  $69.10 \pm 7.94$  for group 2. The tPSA, fPSA and PSA density were statistically significant between two groups  $9.71$  ng/ml,  $1.78$  ng/ml and  $0.10$  ng/ml<sup>2</sup> in group 1 and  $38.32$  ng/ml,  $5.86$  ng/ml and  $0.42$  ng/ml<sup>2</sup> in group 2, respectively ( $p < 0.05$ ). Number of received cores and rate of f/tPSA were similar  $14.02$ - $13.84$  and  $19.06$ - $17.62\%$  in group 1 and 2, respectively and was not statistically significant (Table 1).

**Table 1: Descriptive characteristics and results of patient groups.**

	Group 1	Group 2	p
Patients (n)	217	82	
Age (years)	63.81	69.10	0.01*
PV (ml)	92.99	94.84	0.227
tPSA (ng/mL)	9.71	38.32	0.01*
fPSA (ng/mL)	1.78	5.86	0.01*
f/tPSA (%)	19.06	17.62	0.274
PSA Density (ng/ml <sup>2</sup> )	0.10	0.42	0.01*
Mean Core (n)	14.02	13.84	0.887

\* $p < 0,05$

In group 2, prostate adenocarcinoma was most common detected with Gleason score 4+3 in 21 of 82 patients (25.6%) (Table 2).

About 81.1% of patients with benign pathology results were not detected a normal digital rectal examination finding, but 50% of patients (n=41) with malign pathology results were had the digital rectal examination findings such as prostatic asymmetry, nodule and hard prostate (8.5%, 14.6% and 26.8%, respectively).

**Table 2: Distribution of prostate cancer results according to Gleason score.**

Gleason Score (Group 2)	n (Overall)	%
3+3	17	20.7
3+4	1	1.2
4+3	21	25.6
4+4	14	17.1
4+5	1	1.2
5+3	1	1.2
5+4	12	14.6
5+5	15	18.3

## DISCUSSION

The beginning of serum tPSA screening for prostate cancer (PCa) was a major innovation in the early diagnosis of the disease, Prostate biopsy for high level tPSA values is extremely important for the early diagnosis of PCa. TRUSBP has been the classical procedure for diagnosing PCa. At the present time, there are a lot of information which cause scientific chaos about the biopsy decision. Threshold values for tPSA and number of received cores are still not fully defined. At this point the high prostate volume have a bad influence on the selection of the patients in whom biopsy is to be performed.

tPSA is the most frequently used parameter in current practice. In the recent years, studies on PSA threshold value have not clearly established with common consensus. The current threshold value for tPSA is assumed to be 2.5ng/mL and varies with age. TPSA thresholds are available in different age groups from 2.5 to 6.5ng/mL.<sup>6</sup> In present study, in only 1 patient under 70 years of age (n=44), PCa was detected below these reference values. Despite that, it was found in 3 patients over 70 years (n=38). It was detected that these reference values had a margin of error about 5% in these results. Author thought that the values of tPSA by age are extremely useful in this sense.

The amount of serum tPSA is a parameter that can be influenced by the prostate volume. tPSA and prostate volume associations were first reported by Veneziano, et al in 1991.<sup>7</sup> Threshold of greater than 0.15 PSA density for benign lesions and less than 0.15 for malign lesions are still being used nowadays. In the outcomes, author determined a correlation of 14.74% for benign lesions and 46.34% for malignant lesions based on these thresholds. There are numerous studies on biopsy failure due to these unexplained contradictions between tPSA and PV. In a study on the reduction of biopsy yield by Demura et al were found that PV is associated with a decrease in size and detectability of cancer lesions resulting in a decrease in biopsy yield.<sup>8</sup> For this reason, different PSA forms are utilized for biopsy prediction. In this sense, fPSA cannot be used because of close relationship with prostate volume. Coban et al was found fPSA is much more related with PV than tPSA.<sup>9</sup> In use of

fPSA is extremely difficult for differentiation of benign or malignant lesion. So, its use alone can be as misleading as tPSA. The absence of significant difference f/tPSA results between of benign and malignant lesions supports that. In 1996, as defined by Rubens et al, use of only excess PSA (serum PSA level minus predicted PSA level [prostate volume x 0.12]) of  $> \text{ or } = 0$  ng/mL to initiate prostate biopsy results in the best combination of sensitivity and specificity compared with the other standard parameters.<sup>10</sup> In the results accuracy rate of excess PSA was found  $> \text{ or } = 0$  ng/mL in 37 of 82 (45.12%) patients with malign and 57 of 217 (26.26%) (false-negative) patients with benign pathology. Even though PV affects the biopsy results, the combination of low PV with high tPSA is still a reliable parameter. Although tPSA, fPSA and PSA density can be used safely, additional parameters are needed. The most reliable parameter for the decision of prostate biopsy that is least affected by volume is PSA density.

Another difficulty in making a biopsy decision in patients with a large prostate volume is the weakness of the analgesic efficiency on the during the biopsy. Luan et al were compared with local anesthesia and periprostatic nerve block and found that the analgesic effect is inefficient. In these patients, personal observation was consistent with the literature.<sup>11</sup> In contrast to what's supposed to be the 12-core biopsy was an efficient method in men with a prostate volume of  $\geq 40$  mL.<sup>12</sup> Therefore, author believed that the number of cores should be 12. Another point was contrary to the information in the literature, the mean prostate volume was higher in the malignant group than in the benign group. Another thing that should be emphasized is clinically significant prostate cancer rates are determined in pathology in the prostate biopsy. 65 of 82 (79.3%) patients had clinically significant prostate cancer. Aganovic et al were found higher PSA density is related to a higher Gleason score and it supports the results.<sup>13</sup>

## CONCLUSION

Many factors influence prostate biopsy decision. A large prostate volume is one of these factors. tPSA levels associated with prostate volume do not always predict correct outcome in this patient group. Another problem that needs to be solved is that tPSA, fPSA, f/tPSA rates and PSA density cutoffs are not sufficient for a proper diagnosis of prostate cancer. Author think that the most effective parameter is PSA density in this matter. However, it should not be forgotten that PSA values by age are also extremely effective and reliable. Especially in patients over 65 years of age with a large prostate volume, a possible prostate adenocancer should be remembered before deciding on curative treatment.

*Funding: No funding sources*

*Conflict of interest: None declared*

*Ethical approval: Not required*

## REFERENCES

1. Hodge KK, McNeal JE, Terris MK, Stamey TA. Random systematic versus directed ultrasound guided transrectal core biopsies of the prostate. *J Urol.* 1989;142(1):71-4.
2. Uzzo RG, Wei JT, Waldbaum RS, Perlmutter AP, Byrne JC, Vaughan D. The influence of prostate size on cancer detection. *Urol.* 1995;46(6):831-6.
3. Karakiewicz PI, Bazinet M, Aprikian AG, Trudel C, Aronson S, Nachabé M, et al. Outcome of sextant biopsy according to gland volume. *Urol.* 1997;49(1):55-9.
4. Kulkarni GS, Al-Azab R, Lockwood G, Toi A, Evans A, Trachtenberg J, et al. Evidence for a biopsy derived grade artifact among larger prostate glands. *J Urol.* 2006;175(2):505-9.
5. Epstein JI, Allsbrook Jr WC, Amin MB, Egevad LL, ISUP Grading Committee. The 2005 International Society of Urological Pathology (ISUP) Consensus Conference on Gleason Grading of Prostatic Carcinoma. *Am J Surg Pathol.* 2005;29(9):1228-42.
6. DeAntoni EP. Age-specific reference ranges for PSA in the detection of prostate cancer. *Oncology (Williston Park).* 1997;11(4):475-82.
7. Veneziano S, Pavlica P, Querzè R, Viglietta G, Trenta A. Importance of specific prostatic antigen to prostatic volume ratio in the selection of patients for ultrasonography-guided biopsy of the prostate. *Radiol Med.* 1991;81(6):857-60.
8. Demura T, Takada T, Shimoda N, Hioka T, Iwaguchi Y, Ichihara S, et al. Mechanism underlying the negative effect of prostate volume on the outcome of extensive transperineal ultrasound-guided template prostate biopsy. *Cancer Med.* 2018;7(2):336-43.
9. Coban S, Doluoglu OG, Keles I, Demirci H, Turkoglu AR, Guzelsoy M, et al. Age and total and free prostate-specific antigen levels for predicting prostate volume in patients with benign prostatic hyperplasia. *Aging Male.* 2016;19(2):124-7.
10. Rubens DJ, Gottlieb RH, Maldonado Jr CE, Frank IN. Clinical evaluation of prostate biopsy parameters: gland volume and elevated prostate-specific antigen level. *Radiol.* 1996;199(1):159-63.
11. Luan Y, Huang TB, Gu X, Zhou GC, Lu SM, Tao HZ, et al. Effect of prostate volume on the peripheral nerve block anesthesia in the prostate biopsy: A strobe-compliant study. *Medicine (Baltimore).* 2016;95(28):e4184.
12. Yoon BI, Shin TS, Cho HJ, Hong SH, Lee JY, Hwang TK, et al. Is it effective to perform two more prostate biopsies according to prostate-specific antigen level and prostate volume in detecting prostate cancer? Prospective study of 10-core and 12-core prostate biopsy. *Urol J.* 2012;9(2):491-7.
13. Aganovic D, Prcic A, Kulovac B, Hadziosmanovic O. Influence of the prostate volume, prostate specific antigen density and number of biopsy samples on prostate cancer detection. *Med Archives.* 2012 Jan 1;66(1):41.

**Cite this article as:** Ediz C, Cimen S, Akan S, Temel MC, Yilmaz O, Koksall O. PSA density as a parameter in prostate biopsy decision of patients with prostate sized 80mL or larger. *Int J Res Med Sci* 2019;7:914-7.