Yeni Üroloji Dergisi - *The New Journal of Urology* **2020; 15-(3): 158-163, DOI: 10.33719/yud.616921**

Original Research / Özgün Araştırma

Role of Prostate Specific Antijen in Prostatic Adenocarcinoma Detection in Patients With Benign Prostate Hyperplasia and Were Placed Urethral Catheter After Acute Urinary Retention

Prostat Spesifik Antijenin Akut Üriner Retansiyon Sonrası Üretral Kateter Yerleştirilen ve Benign Prostat Hiperplazisi Olan Hastalarda Prostat Adenokarsinomu Saptamadaki Rolü

Ahmet Hacıislamoğlu [1], İsmail Evren [1], Abdullah Hızır Yavuzsan [2], İsmail Yiğitbaşı [1], Mithat Ekşi [1], Kamil Gökhan Şeker [1], Volkan Tuğcu [1]

1 Health Sciences University, Bakirkoy Dr. Sadi Konuk Training and Research Hospital, Department of Urology, Turkey

2 Health Sciences University, Sisli Hamidiye Etfal Training and Research Hospital, Department of Urology, Turkey

Geliş tarihi (Submitted): 2019-09-11

Kabul tarihi (Accepted): 2020-01-09

Yazışma / Correspondence
Abdullah Hizir Yavuzsan
Health Sciences University
Sisli Hamidiye Etfal Training and Research Hospital, Department of Urology, 34371, Istanbul / Turkey
E mail: hiziryavuzsan@gmail.com
Phone number: +90 544 843 02 50
Fax number: +90 212 414 64 99

ORCID

A.H.	0000-0002-6117-2098
I.E.	0000-0003-4008-8038
A.H.Y.	0000-0002-1561-895X
I.Y.	0000-0002-1674-6574
M.E.	0000-0003-1490-3756
K.G.S.	0000-0003-4449-9037
V.T.	0000-0002-4136-7584

Özet

Amaç: Akut idrar retansiyonu (AİR) benign prostat hiperplazisi (BPH) hastalarında en önemli komplikasyonlardan biridir ve tedavisi genellikle akut dönemde üretral kateterizasyondur. AİR ve üretral kateter yerleştirilmesinin serum PSA seviyelerinde bir artışa neden olabileceğini gösteren çalışmalar vardır. Bu çalışmada amacımız, AİR sonrası üretral kateter yerleştirilen hasta grubunda artmış PSA düzeyleri ile prostat kanseri (PCa) insidansı arasındaki ilişkiyi araştırmaktır.

Gereç ve Yöntemler: AUR nedeniyle kalıcı bir üretral kateteri olan 77 hastada, yüksek PSA seviyeleri nedeniyle yapılan prostat biyopsileri ve daha sonra klinik BPH için yapılan cerrahi tedaviler retrospektif olarak incelendi. Hastaların yaş, prostat hacimleri, biyopsi öncesi total serum PSA ve PSA dansiteleri kaydedildi. Biyopsi veya cerrahi örnek sonuçlarına göre total PSA oranları, PSA dansiteleri ve prostat hacimleri PCa'nın saptandığı (n = 6) ve saptanmadığı (n = 71) gruplar için karşılaştırıldı.

Bulgular: Hastaların yaş ortalaması 65.2 ± 3.9 idi. Ortalama prostat hacmi 64.1 ± 12.8 g, ortalama serum total PSA seviyesi 9.2 ± 4.2 ng / mL ve ortalama serum PSA dansitesi 0.15 ± 0.08 mg / mL / g olarak ölçülmüştür. Serum total PSA düzeyi ≤4.0, 4-10, 10-20 ve >20 olan PSA gruplarında PCa prevalansı sırasıyla % 0, % 4,3, % 13,4 ve % 20 olarak tespit edildi. Toplam PSA düzeyleri ve PSA dansiteleri, PCa tespit edilen grupta istatistiksel olarak daha yüksek bulundu.

Sonuç: AİR sonrası üretral kateter yerleştirilen hastalarda PCa insidansı düşüktür. Bu hastalar için prostat biyopsisi sadece seçilmiş vakalarda yapılmalıdır.

Anahtar Kelimeler: Akut üriner retansiyon, biyopsi, prostat kanseri

Abstract

Objective: Acute urinary retention (AUR) is one of the most important complications in benign prostate hyperplasia (BPH) patients and its treatment is generally urethral catheterization in acute period. Studies are showing that AUR and urethral catheter placement may cause an increase in serum PSA levels. Our objective in this study was to investigate the relationship between increased PSA levels and prostate cancer (PCa) incidence in the patient group after AUR and urethral catheter placement.

Material and Methods: Seventy-seven patients who had an indwelling urethral catheter due to AUR, performed prostate biopsy due to high PSA levels and then surgical treatment for clinic BPH were retrospectively examined. Age, prostate volumes, pre-biopsy total serum PSA and PSA densities were noted. Total serum PSA rates, PSA densities and prostate volumes were compared for the groups that PCa was detected (n=6) and not detected (n=71) according to biopsy or surgical specimen results.

Results: Mean age of the patients was 65.2±3.9 years. Mean prostate volume was measured as 64.1±12.8 g, mean serum total PSA level as 9.2±4.2 ng/mL and mean serum PSA density as 0.15±0.08 mg/mL/g. In PSA groups with a serum total PSA level of ≤4.0, 4-10, 10-20 and >20, PCa prevalence rates were detected 0%, 4.3%, 13.4% and 20%, respectively. Total PSA levels and PSA densities were found statistically higher in PCa detected group.

Conclusions: PCa incidence is low in patients who were placed urethral catheter after AUR. For these patients prostate biopsy should be performed only in chosen cases.

Keywords: acute urinary retention, biopsy, prostate cancer

INTRODUCTION

Benign prostate hyperplasia (BPH) is a progressive hyperplasia of both stromal and glandular parts of the prostate gland and is defined as a non-malign growth in prostate (1). Symptomatic presentations of BPH which is generally age-related effect males with a ratio of 20% in their 50s and 30-40% in their seventies (2). The relation between BPH and prostate cancer (PCa) is still a controversial topic. For example while a relation has been shown between BPH and PCa in some studies (3-4), no relation was shown in some others (5-6).

Acute urinary retention (AUR) is one of the most important complications of long-term BPH. Its prevalence was shown to be between 2% and 39% in BPH patients. The bladder is emptied through transurethral or suprapubic catheterization for treatment.

In literature, an increase was shown in prostate specific antigen (PSA) values due to causes such as bladder catheterization, chronic prostatitis and prostate volume increase (7-8). We still don't have any certain literature knowledge on whether reasons especially such as urethral catheter installation increase PSA or whether these reasons activate some factors to increase the PSA level. The number of studies on these subjects is not satisfactory and most of them were not made recently (7,9-10). The objective of our study is to evaluate the diagnostic value of high PSA in PCa in patients who had AUR due to BPH and a urethral catheter was placed and BPH operation was planned.

MATERIAL AND METHODS

4372 patients who had a transrectal ultrasound (TRUS) accompanied prostate biopsy in Bakırköy Dr. Sadi Konuk Training and Research Hospital between January 2006 and December 2016 were retrospectively scanned in this study. 156 of these patients were using a urethral catheter during the biopsy. Patients who had prostate cancer in history, prostate surgery, had urethral catheter due to neurogenic pathology, acute urinary infection symptoms, used 5α-reductase inhibitor and whose information couldn't be reached were not included in the study. Also, patients with abnormal digital rectal inspection were not included in the study to eliminate this confusing variable. As a result, 77 patients who had urethral catheter installation due to their first AUR and thus had TRUS biopsy were included in our study. In all the patients included in our study, urethral catheter was removed a week after its placement. But the patients were taken to the biopsy with the catheter due to unsuccessful urethral catheter removal.

Age, prostate volumes measured with transrectal ultrasound and digital rectal examination and pre-biopsy serum total PSA values and PSA densities were noted for all patients. The value taken a week after the occurrence of the first AUR was accepted as serum total PSA value. Patients were grouped as those with PSA levels of <4.0 ng/mL, 4-10 ng/mL, 10-20 ng/mL and >20 ng/mL.

As a clinical routine, especially in the early period of our study, we performed TRUS-Bx to all patients who had a higher level of PSA for >2.5 ng/mL. All biopsy procedures were made by urologists who passed the learning period and under local anesthesia minimum 10 core needle biopsies were taken under transrectal ultrasonographic guidance. Patients with benign pathology results after biopsy had transurethral resection of prostate (TUR-P) or retropubic prostatectomy operations and patients with malign results had radical prostatectomy operation. Radical prostatectomy operation was also applied for the patients in whom malignity was observed in TUR-P or retropubic prostatectomy pathology results. Patients who had malignity and benign pathology in transrectal biopsy or operation pathologies were compared.

Statistical Method

Mean, standard deviation, median minimum, maximum, frequency and ratio values were used in definitive data statistics. Kolmogorov Smirnov test was used to measure the distribution of the variables. Mann-Whitney U test was used for the analysis of quantative independent data. SPSS 22.0 program was used for the analyses.

RESULTS

All patients included in the study were Caucasians. Mean age of the patients was 65.2±3.9 years. Mean

prostate volume was measured as 64.1±12.8 g, mean serum total PSA level as 9.2±4.2 ng/mL and mean serum PSA density as 0.15±0.08 mg/mL/g.

While PCa was not observed in the group with PSA ≤4.0 ng/ml (n=3) according to PSA groups, PCa was detected in two patients with 4-10 ng/mL PSA (n=46) (4.3%). One of these cases was detected through biopsy (Gleason 3+3 for 3/12 cores) and the other was detected after retropubic prostatectomy (Gleason 3+3 with the <%5 involvement). PCa was detected through biopsy in three patients (Gleason 3+3 for two patients and 3+4 for one patient and 3/10, 5/12 and 1/12 cores showed positivity respectively) in the PSA = 10-20 ng/mL group (n=23) (13.4%) and in one patient (Gleason 3+4 for 2/12 cores) in PSA >20ng/mL group (n=5) (20%) (Table 1). All pathologic results are shown in Table 2.

When we compared the patients in benign and malign groups, serum total PSA level was found statistically significantly higher in the malign group (n=6) compared to the benign group (n=71) (14.6±5.9 vs. 9.2±4.2 ng/mL) (p=0.016). PSA density was also found statistically significantly higher in the malign group compared to the benign group (0.22±0.08 vs. 0.14±0.07 ng/mL/g) (p=0.015). No statistically significant difference was detected in age and prostate volumes among both groups (p>0.05). Parameter results among both groups and benign-malign rates according to PSA groups are given in Table 3.

Table 1. PCa incidence according to PSA groups

PSA (ng/ml)	n	PCa (%)
≤4.0	3	0 (0%)
4.1-10.0	46	2 (4.3%)
10.1-20.0	23	3 (13.4%)
>20	5	1 (20%)

PCa, Prostate cancer; PSA, Prostate specific antigen

Table 2. Pathologic results of 77 patients

Pathologic Results	**n-%**
Benign prostatic hyperplasia	43 (55.8%)
Chronic prostatitis	21 (27.2%)
Acute prostatitis	1 (1.2%)
Prostatic intraepithelial neoplasia	6 (7.7%)
Prostate cancer	6 (7.7%)

DISCUSSION

Prostate specific antigen (PSA) is a serine protease secreted from prostatic epithelial cells and has the function of liquifying the seminal fluid. Although less PSA is secreted from prostate cancer cells compared to normal cells, it is considered that PSA level increasing in cancer patients is due to the cancer-related destruction in cellular structure and intercellular PSA released to the blood due to this (11). But apart from prostate cancer, many factors such as prostatic manipulation,

Table 3. Examined parameters according to pathology results

		Benign				**Malign**				**P value***
		Mean±S.D. / n-%			**Median**	**Mean±S.D. / n-%**			**Median**	
Age (years)		65.2	±	3.9	65	64	±	2.8	62.5	0.985
Total PSA (ng/ml)		9.2	±	4.2	7.8	14.6	±	5.9	13.8	0.016
	2.5-4.0	3		4.2%		0		0.0%		
	4.1-10.0	44		62.0%		2		33.3%		
	10.1-20	20		28.2%		3		50.0%		
	> 20	4		5.6%		1		16.7%		
PSA density (ng/ml/g)		0.14	±	0.07	0.13	0.22	±	0.08	0.2	0.015
Prostate volume (g)		64.5	±	13.3	64	60.7	±	4.8	62	0.468

**Statistical analysis was performed with Mann-Whitney U test. PSA, prostate specific antigen*

ejaculation, benign prostate hyperplasia, infection and AUR which may cause an increase in serum PSA levels were stated in literature (12-13). It is considered that PSA increasing after AUR occurs due to prostatic tissue ischemia (14-15). The presence of urethral catheters is also among the causes of increasing serum PSA levels. In another study published by Batislam et al. (16), BPH patients with or without urethral catheter due to urinary retention were compared and it was shown that PSA was 2.6 times higher in patients with a urethral catheter. In our study, we only included BPH-related AUR patients with urethral catheter who had a prostate biopsy because of elevated PSA levels.

It was observed that prostate cancer incidence increased as PSA levels increased in our study. Prostate cancer prevalence was 4.3% with a PSA level of 4-10 ng/mL, 13.4% with PSA = 10-20 ng/mL 20% with PSA >20 ng/mL. These rates in our study were observed somewhat lower compared to the rates with biopsy due to high PSA in routine patient screenings. In a study including 1653 patients, prostate cancer detection rate was 22% with PSA = 4.0-9.9 ng/mL and it was 67% with PSA>10ng/mL (17). Again, in a study including 1249 patients, prostate cancer detection rate in groups with PSA levels of 4.1-10ng/mL and >10 ng/mL were reported as 26.5% and 50%, respectively (18). According to these results in the literature, low prostate cancer detection rates in our PSA groups support that high PSA may occur due to AUR and urethral catheter placement rather than prostate cancer.

There are different studies in the literature investigating the relationship between prostate volume and serum PSA level (19-21). In most of these studies made, a positive relation was shown between prostate volume and serum PSA level. In our study, while mean prostate volume was detected 60.7±4.8 cc in prostate cancer detected group, it was 64.5±13.3 cc in the group without prostate cancer. Prostate cancer was detected in 6 out of 74 patients with PSA level >4 ng/mL (8.1%) in our study. Based on this low prostate cancer rate, we think that rather than malignity, increased prostate volumes can be effective on elevated serum PSA level in our study.

There are studies showing that prostatic inflammation is also effective in serum PSA increase. In a prospective controlled study, the patient group with lower urinary system symptoms, normal DRE findings and PSA level>4ng/mL (n=160) and control group with normal DRE findings and normal PSA levels but without clinical BPH or any symptoms (n=50) were compared. IL-8 levels in the prostatic fluid were examined in order to detect serum total and free PSA levels and inflammation of the patients. It was shown that total PSA level and IL-8 level in prostatic fluid were statistically significantly higher in symptomatic patient group compared to the control group (22). In another study evaluating the relation between AUR and prostatic inflammation, 232 patients who had TURP due to BPH were included. In the study, groups with patients who had at least one or no AUR story before the operation were compared. While the occurrence rate of chronic prostatitis was 56% in the group with AUR story according to the histological evaluation, it was 37% in the group without AUR story. Also, it was shown that PSA level of the patients with prostatic inflammation in AUR group was statistically significantly higher those without prostatic inflammation (7.7 vs. 5.0 ng/mL respectively) (7). In a study investigating the relation between inflammation and pCa made on 293 patients who had prostate biopsy, it was shown that histological inflammation caused increase in serum PSA level but didn't have a significant relation with latter pCa (23).

Rates of acute and chronic prostatitis were only 1.2% and 27.2%, respectively, according to the histological evaluation made in this study. This shows that other factors may be effective on increased PSA levels in AUR patients apart from prostatic inflammation. If the pathological evaluation in our study was made only with biopsy, total prostatic inflammation rates of the patients could have been detected incompletely. However, in our study, all patients underwent surgical treatment for BPH after biopsy and the examination of surgical specimens strongly supported the fact that factors other than prostatic inflammation were effective on the elevated PSA level.

There are some limitations of our study. Since it was a retrospective study, PSA levels of the patients before

AUR are unknown. The comparison was not made with a control group that had not AUR but had a prostate biopsy after routine controls. Also, patient population which couldn't have spontaneous urination after AUR and had surgeries planned were included in the study. This may explain the large prostate volume which is among the factors which may cause an increase in PSA levels of the patients and constitutes one of the limitations of this study investigating only AUR and urethral catheter-related PSA increase.

CONCLUSION

According to the histological examinations made after biopsy and operation in these patients, it was observed that pCa rates were lower compared to pCa detection rate in routine patient screenings in literature. So application of standard biopsy shouldn't be recommended in every high PSA case observed after AUR and urethral catheter placement. If we consider the low pCa rates in our study, biopsy should only be applied in chosen cases especially in patients with PSA>10 ng/mL levels. Serum total PSA level and PSA density are regarded as auxiliary examinations for pCa detection in urethral catheter placed patients after AUR. But prospective randomized controlled studies with a wide patient population are still needed to support this study.

REFERENCES

1. Bushman W. Etiology, epidemiology, and natural history of benign prostatic hyperplasia. Urol Clin North Am 2009;36:403–15.
2. Bosch JL, Hop WC, Kirkels WJ, Schröder FH. The international prostate symptom score in a community-based sample of men between 55 and 74 years of age: prevalence and correlation of symptoms with age, prostate volume, flow rate, and residual urine volume. Br J Urol 1995;75:622–630.
3. Orsted DD, Bojesen SE, Nielsen SF, Nordestgaard BG. Association of clinical benign prostate hyperplasia with prostate cancer incidence and mortality revisited: a nationwide cohort study of 3,009,258 men. Eur Urol 2011;60:691-8.
4. Alcaraz A, Hammerer P, Tubaro A, Schröder FH, Castro R. Is there evidence of a relationship between benign prostatic hyperplasia and prostate cancer? Findings of a literature review. Eur Urol 2009;55:864–873 .
5. Schenk JM, Kristal AR, Arnold KB, et al. Association of symptomatic benign prostatic hyperplasia and prostate cancer: results from the prostate cancer prevention trial. Am J Epidemiol 2011;173:1419–1428.
6. Simons BD, Morrison AS, Young RH, Verhoek-Oftedahl W. The relation of surgery for prostatic hypertrophy to carcinoma of the prostate. Am J Epidemiol 1999;138:294–300.
7. Kefi A, Koseoglu H, Celebi I, Yorukoglu K, Esen A. Relation between acute urinary retention, chronic prostatic inflammation, and accompanying elevated prostate-specific antigen. Scand J Urol Nephrol 2006;40:155–60.
8. Shadi Al-Khalil, Christine Ibilibor, James Thomas Cammack, Werner de Riese. Association of prostate volume with incidence and aggressiveness of prostate cancer. Res Rep Urol 2016;8:201-205.
9. Kravchick S, Bunkin I, Peled R, et al. Patients with elevated serum PSA and indwelling catheter after acute urinary retention: prospective study of 63 patients with 7-year follow-up. J Endourol 2007;21:1203-6.
10. Antunes AA, Barbosa JA, Reis ST, et al. Prostate biopsy in patients with long-term use of indwelling bladder catheter: What is the rationale? Urol Oncol 2012;30:620-3.
11. Lilja H, Ulmert D, Vickers AJ. Prostate-specific antigen and prostate cancer: Prediction, detection, and monitoring. Nat Rev Cancer 2008;8:268–78.
12. Pienta KJ. Critical appraisal of prostate-specific antigen in prostate cancer screening: 20 years later. Urology 2009;73:11–20.
13. Parekh N, Lin Y, Marcella S, Kant AK, Lu-Yao G. Associations of lifestyle and physiologic factors with prostate-specific antigen concentrations: Evidence from the National Health and Nutrition Examination Survey (2001–2004). Cancer Epidemiol Biomarkers Prev 2008;17:2467–72.
14. McNeill SA, Hargreave TB. Efficacy of PSA in the detection of carcinoma of the prostate in patients presenting with acute urinary retention. R Coll Surg Edinb 2000;45:227–30.
15. Feero P, Nickel JC, Brawn P, Young I. Prostatic infarction associated with aortic and iliac aneurism repair. J Urol 1990;143:367–8.
16. Batislam E, Arik AI, Karakoc A, Uygur MC, Germiyanoglu RC, Erol D. Effect of transurethral indwelling catheter serum prostate- specific antigen level in benign prostatic hyperplasia. Urology 1997;49:50–4.

17. Catalona WJ, Smith DS, Ratliff TL, et al. Measurement of prostate specific antigen in serum as a screening test for prostate cancer. N Engl J Med 1991;324:1156–61.
18. Brawer MK, Chetner MP, Beatie J, Buchner DM, Vessella RL, Lange PH. Screening for prostatic carcinoma with prostate specific antigen. J Urol 1992;147:841-5.
19. Pinsky PF, Kramer BS, Crawford ED, et al. Prostate volume and prostate-specific antigen levels in men enrolled in a large screening trial. Urology 2006;68:352-6.
20. Mochtar CA, Kiemeney LA, van Riemsdijk MM, et al. Prostate-specific antigen as an estimator of prostate volume in the management of patients with symptomatic benign prostatic hyperplasia. Eur Urol 2003;44:695-700.
21. Putra IB, Hamid AR, Mochtar CA, Umbas R. Relationship of age, prostate-specific antigen,and prostate volume in Indonesian men with benign prostatic hyperplasia. Prostate Int 2016;4:43-8.
22. Agnihotri S, Mittal RD, Kapoor R, Mandhani A. Asymptomatic prostatic inflammation in men with clinical BPH and erectile dysfunction affects the positive predictive value of the prostate-specific antigen. Urol Oncol 2014;32:946-51.
23. Yli-Hemminki TH, Laurila M, Auvinen A, et al. Histological inflammation and risk of subsequent prostate cancer among men with initially elevated serum prostate-specific antigen (PSA) concentration in the Finnish prostate cancer screening trial. BJU Int 2013;112:735-41.