

**Transrektal ultrasonografi eşliğinde yapılan prostat biyopsilerinin retrospektif analizi***Retrospective analysis of transrectal ultrasonography guided prostate biopsy***Ekrem Akdeniz<sup>1</sup>, Mustafa Suat Bolat<sup>1</sup>, Necmettin Sahinkaya<sup>1</sup>, Omer Alici<sup>2</sup>**<sup>1</sup> Samsun Training and Research Hospital, Department of Urology, Samsun, Turkey<sup>2</sup> Samsun Training and Research Hospital, Department of Pathology, Samsun, Turkey**Özet**

**Amaç:** Transrektal ultrason eşliğinde prostat iğne biyopsisi, prostat kanseri tanısında standart prosedür haline gelmiştir. Biz bu çalışmada prostat hastalıklarının tanısında transrektal iğne biyopsi yönteminin etkinliğini ve histopatolojik sonuçlarını araştırmayı amaçladık.

**Gereç ve Yöntem:** Ocak 2011- Aralık 2014 tarihleri arasında kliniğimizde transrektal ultrason eşliğinde on kor prostat biyopsisi yapılan 643 olgunun yaşları, klinik özellikleri, prostat spesifik antijen (PSA) seviyeleri ve histopatolojik sonuçları hasta dosyalarından retrospektif olarak değerlendirilerek veriler analiz edilmiştir.

**Bulgular:** Hastaların yaş ortalaması 66.09 ± 7.65 yıl olarak bulundu. Serum prostat spesifik antijen (PSA) değeri 46,69 ± 410,72 ng / ml idi. Parmakla rektal muayene pozitifliği 175 (27.2%) hastada mevcuttu. En sık patolojik tanı benign prostat hipertrofisi (BPH) 313 (% 48.7) olarak bulundu. Prostat kanseri, prostatit, prostatik intraepitelial neoplazi (PIN) ve atipik small asiner proliferasyon (ASAP) oranları sırasıyla 139 (% 21.6), 114 (% 17.8), 51 (% 7.9) ve 26 (% 4) olarak bulundu. Prostat kanseri grubunda ortalama serum PSA düzeyi diğer gruplara göre yüksek bulundu. Prostat kanseri insidansı 65 yaş üzeri hastalarda anlamlı derecede yüksek izlendi.

**Sonuç:** Yüksek PSA seviyesi ve parmakla rektal muayene bulguları olan hastalar prostat kanseri açısından yüksek riskli grup olarak kabul edilmelidir. Transrektal ultrason eşliğinde prostat iğne biyopsisi prostat hastalıklarının malign benign ayrımı açısından güvenli ve etkili bir yöntemdir.

**Anahtar Kelimeler:** Patoloji, Prostat, Prostat spesifik antijen

**Abstract**

**Objective:** Transrectal ultrasound guided prostate needle biopsy has become standard procedure in prostate cancer diagnosis. We aimed to investigate the efficacy of transrectal ultrasound guided prostate needle biopsy on prostatic diseases and review histopathological outcomes.

**Materials and Methods:** Six hundred and forty-three patients were evaluated in our clinic. Transrectal ultrasound guided prostate needle biopsies for suspicious prostate cancer diagnosis were evaluated retrospectively.

**Results:** Mean age of patients was 66.09±7.65, mean serum prostate specific antigen value 46.69±410.72 ng/mL and digital rectal examination positivity was 175(27.2%). Of the biopsy results 313(48.7%) were benign prostatic hypertrophy, 139(21.6%) were carcinoma of the prostate, 114(17.8%) were prostatitis, 51(7.9%) were prostatic intraepithelial neoplasia and 26(4%) were atypical small acinar proliferation of prostate, respectively. Mean serum prostate specific antigen level in carcinoma of the prostate group was statistically significantly higher in other groups. Prostate cancer incidence was statistically significantly high in the older than 65 years group than younger than 65 years group.

**Conclusions:** Patients with elevated prostate specific antigen and digital rectal examination findings should be considered as high risk group and should be followed closely in terms of prostate cancer and transrectal ultrasound guided prostate needle biopsy is safe and effective procedure for this group of patients who have extend from benign to malign conditions.

**Key Words:** Pathology, Prostate, Prostate Specific Antigen

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## **Introduction**

Prostate cancer is the most prevalent type of cancer in men of the western world and it is top second lethal cancer after lung cancer (1,2). Transrectal ultrasound guided prostate needle biopsy has become standard procedure in prostate cancer diagnosis (3). After Astaldi did fist prostate biopsy in 1937, Hodge described standard sextant prostate biopsy in 1989 (4,5). Recently, ten core needle biopsy is recommended as the standard by European Association of Urology (EAU) (6).

Affection of prostatic tissue by hormonal changes and obstruction at the bladder neck due to these changes are two common features of both neoplastic and benign pathologies. Malignant and benign prostate diseases have similar clinic presentations and affect men over 50 years of age. Therefore, it is not possible to differentiate one another only by listening clinical complaints. Main tools for differential diagnosis in these diseases are Digital Rectal Examination (DRE) and serum Prostate Specific Antigen (PSA) levels. Unfortunately, since methods including detecting hypoechoic lesions in Transrectal Ultrasound (TRUS) solely do not have enough specificity and sensitivity, in today's practice, final diagnosis is possible only by histopathologic assessment.

Indications for prostate needle biopsy are suspicious findings on DRE and abnormal serum PSA levels (6). Other indications for prostate biopsy are suspicious lesion in TRUS, origin evaluation for bone metastases of unknown primary, residual tumor assessment of incidentally detected prostate carcinomas on transurethral prostatectomy material. In this study, we aimed to investigate the efficacy of transrectal ultrasound guided prostate needle biopsy and the relationship between histopathological results with clinic and laboratory results.

## **Material and Method**

This study was carried out by Pathology and Urology Clinics of Samsun Training and Research Hospital between January 2011 and December 2014. Medical datas are obtained from patients that underwent TRUS guided prostate core needle biopsy with suspicious prostate cancer diagnosis were evaluated retrospectively. Of these, 643 patients were accrued to the study. Patients were scheduled for prophylactic ciprofloxacin 500 mg, bid, orally 48 hours prior to biopsy and until five days after

the biopsy. A 7.5 MHz rectal probe was used for biopsy. During the procedure, patients were positioned in the left sided decubitus position with knee-hip flexion. An 18 G 25 cm automatic cutting needle (Bard<sup>®</sup> Max-Core<sup>®</sup>, Tempe, Arizona, USA) were used to obtain the biopsies. For the periprostatic LA injection, 10 mL of 2% prilocaine hydrochloride (Citanest, Zenica Medical, Paris, France) was used. A 22 G 20 cm Chiba needle (Matek medical, Ankara, Turkey) was inserted through the needle guide under TRUS guidance. Ten core biopsy protocol was used for prostate tissue sampling. However, extra biopsies were taken from places with abnormal rectal findings and hypoechoic lesions in ultrasound. Each biopsy material was stored in different bottles that include %10 formaldehyde and was transferred to the pathology department. Age, clinical features, serum PSA values and biopsy findings were recorded. Results were analyzed using SPSS 17.0 (SPSS Inc, Chicago, IL, USA) software. Results are presented as means±standard errors of means and  $p < 0.05$  was considered as significant. Descriptive group datas were compared using the unpaired Student t-test and Pearson chi-square test. The study was performed in accordance with the ethical principles in the Good Clinical Practice guidelines, in addition to applicable local regulatory requirements and the protocol was approved by local ethics review boards. All the patients read the patient information form about the study procedure and written informed consents were obtained.

## **Results**

Six hundred and forty-three patients were accrued to this study. Characteristics of patients are given in Table 1. Mean age of patients was  $66.09 \pm 7.65$ , mean serum PSA value  $46.69 \pm 410.72$  ng/mL and DRE positivity was 175 (27.2%). Biopsy results were benign prostate hypertrophy (BPH) 313 (48.7%), carcinoma of the prostate 139 (21.6%), prostatitis 114 (17.8%), Prostatic Intraepithelial Neoplasia (PIN) 51 (7.9%) and Atypical Small Acinar Proliferation (ASAP) of prostate 26 (4%) respectively. Relation between histopathological findings and mean age, mean serum PSA levels and DRE positivity is described in Table 2. Mean serum PSA level in prostate carcinoma group was statistically significantly higher than other groups. Relation between histopathological findings of patients with age group and PSA group distribution, is

described in Table 3. Prostate cancer incidence was statistically significantly high in the older than 65 years group than younger than 65 years group.

### Discussion

Prostate diseases affect mostly middle-aged men, and they have same clinical features. Most prevalent prostate diseases in this study were BPH (48.7%), following prostate cancer (21.6%) in thesecond rank, later PIN (7.9%) and ASAP (4%), respectively. Mean age of patients was  $69.63 \pm 8.50$  years in prostate cancer group,  $64.76 \pm 7.12$  years in BPH group,  $65.95 \pm 6.98$  years in prostatitis group,  $66.33 \pm 6.55$  years in PIN group and finally  $63.23 \pm 7.94$  years in ASAP group. Prostate diseases are most common in men 60-70 years of age and prostate cancer is most common in men that are older than 65 years (7). In our study, mean age of patients with prostate cancer is consistent with the literature.

Despite growing technology, early diagnosis of prostate cancer is still a challenging problem. Because curative treatment of localized prostate cancer is possible, early diagnosis of this disease is even more important. TRUS-guided transrectal prostate needle biopsy has taken its place as the gold standard in the diagnosis of prostate cancer in clinical practice.

DRE is still the oldest and most valid diagnostic tool for prostate cancer. This type of examination may change depending on the experience and interpretation of the clinician. In our study, only 1 of 13 (7%) patients was diagnosed prostate cancer, even though, his DRE was positive, and serum PSA level was  $< 2.5$  ng/mL. In the literature, rate of diagnosed cancer for biopsies that were carried out only after positive DRE finding is 35% (8). In patients with serum PSA levels greater than 2 ng/mL, sole positive predictive value of DRE in diagnosing prostate cancer changes between 5-30% (9). Abnormal DRE findings are related with high Gleason score and when suspicious DRE findings are present, it is strongly emphasized that needle biopsy should be carried out without detection of the serum PSA levels (10,11). In our study, a total of 175(27.2%) patients were found to have abnormal DRE findings, and 67 (38.2%) of them had prostate cancer. This data indicates that even though DRE is an insufficient tool itself and it is still an irreplaceable element in diagnosis of prostate cancer. It should always be done in

**Table 1.** Characteristics of Patients

Characteristics	Results
Age, mean $\pm$ SD, year (min-max)	66.09 $\pm$ 7.65 (42-87)
Total PSA, mean $\pm$ SD	46.69 $\pm$ 410.72 (0.20-7640)
Total PSA group, (n,%)	
$\leq 4$	65 (10.1)
4.01-10	337 (52.4)
10.01-20	153 (23.8)
20.01-50	55 (8.6)
>50.01	33 (5.1)
DRE(n,%)	
Positive	175 (27.2)
Negative	468 (72.8)
Histopathology(n,%)	
BPH	313 (48.7)
Cancer	139 (21.6)
Prostatit	114 (17.8)
PIN	51 (7.9)
ASAP	26 (4)

routine prostate examination.

Ever since the determination of serum PSA levels entered urology practice, important developments were recorded in diagnosis, treatment and follow-up of prostate cancer (12). PSA is specific for prostate; however, it is not specific for prostate cancer. Any disruption in prostate tissue integrity (BPH, prostatitis, prostatic infarct) leads to PSA blending into the circulation, therefore, results in an increase in serum PSA concentration (13). In our study, mean PSA serum level was  $182.39 \pm 872.30$  ng/mL in prostate cancer group,  $7.59 \pm 5.01$  ng/mL in BPH group,  $13.88 \pm 12.75$  ng/mL in prostatitis group,  $9.85 \pm 5.06$  ng/mL in PIN group,  $8.17 \pm 5.5$  ng/mL in ASAP group, respectively. According to statistical evaluation, there were statistically significant difference in serum PSA levels between biopsy positive group and biopsy negative group.

In our study, detection rates of prostate cancer according to serum total PSA levels were as follows: 12.3% in PSA  $< 4$  ng/ml group, 13.35% in PSA 4-10 ng/mL group, 16.34% in 10.1-20 ng/mL group, 54.54% in 20.1-50 ng/mL group and 93.93% in  $> 50$  ng/mL group. Same rates were reported as 11%, 15.2%, 27.8%, 59.6% and 93.7% in same groups at Teoh et al study in which 2026 patients were accrued. In the Prostate Cancer Prevention Trial Study, in patients with normal DRE findings, serum PSA level  $< 4$

**Table 2:** Characteristics of Histopathological Findings

Characteristics	Age mean±SD, year	Total PSA mean±SD,ng/mL	DRE positivity,%
BPH	64.69±7.04	7.59±5.01	74 (42)*
Cancer	69.78±8.57	182.39±872.3*	70 (40)*
Prostatit	65.95±6.98	13.88±12.75	11(6.6)
PIN	66.33±6.55	9.85±5.06	14 (8)
ASAP	63.23±7.95	8.17±5.5	6 (3.4)

**Table 3.** The relationship between histopathological groups with age and PSA groups.

Characteristics	BPH	Cancer	Prostatit	PIN	ASAP
Age groups (n,%)					
<65 years	146(22.7%)	41(6.4%)	45(7%)	18(2.8%)	15(2.3%)
≥65 years	167(25.9%)	98(15.2%)*	69(10.7%)	33(5.2%)	11(1.8%)
PSA groups (n,%)					
≤4	52(8.1%)	8(1.2%)	1(0.1%)	2(0.3%)	2(0.3%)
4.1-10	194(30.2%)	45(7%)	53(8.2%)	27(4%)	18(2.8%)
10.1-20	62(9.6%)	25(3.9%)	42(6.5%)	20(3%)	4(0.6%)
20.1-50	5(0.7%)	30(4.7%)	16(2.5%)	2(0.3%)	2(0.3%)
>50	0	31(4.8%)	2(0.3%)	0	0

ng/mL detection rate of prostate cancer was calculated as 15.2% (14,15). Results of our study show similar features as well. In the literature, detection rate of prostate cancer was reported as 24.5% in PSA<4 ng/ml group and 19.1% in PSA 4-10 ng/mL group (16,17). Gerstenbluth et al, grouped PSA levels into three as follows; 20-20.9, 30-39.9 and 40-49.9 ng/mL, then detection rate of prostate cancer in these groups were 73.6%, 90.3% and 93.8% respectively (18). In our study prostate, cancer detection rate is lower than that of described in the literature.

When total Gleason score of prostate cancer diagnosed patients was evaluated, percentages of patients were as follows 38.84% in Gleason score 6 groups, 18.72% in Gleason score 7 groups, and 42.44% in Gleason score 7 and higher. In Teoh et al's study the patient percentages according to Gleason score grouping were 35.6%, 21.2%, and 42%, respectively (14). Our results in the presented study are in concordance with results of Teoh et al's study.

In the presented study, we reported that serum PSA levels of prostatitis patients were lower than that of prostate cancer patients, however, higher than that of BPH patients. Chung at al showed in their study that in patients with prostatitis mean serum PSA level is 10.95±8.71ng/mL (19). In our study, we demonstrated that prostatitis causes statistically significantly elevated serum PSA lev-

els.

Prostate cancer-related death rate decreases thanks to early diagnostic procedures (20). Because recently doctors can detect large numbers of local prostate cancers by developed prostate core biopsy techniques (21). Patients with high serum PSA levels and positive DRE should be considered as risk group and should be put under close follow-up for prostate cancer until the contrary is proven. The fundamental aim for prostate core biopsy is to reduce the number of prostate cancer-related death and to increase the patient's quality of life.

**Conclusion**

Patients with elevated PSA and DRE findings should be considered as high risk group and should be followed closely in terms of prostate cancer until proven otherwise. The main objective should be to reduce deaths from prostate cancer and improve the patient's quality of life. Although serum PSA levels of prostatitis patients were lower than that of prostate cancer patients and higher than that of BPH patients, transrectal ultrasound guided prostate needle biopsy is the only safe and effective procedure in prostate cancer diagnosis with clinic and laboratory findings.

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