

Factors affecting complications of transrectal ultrasound-guided prostate biopsy: A cohort study with 403 patients in a single center

Transrektal ultrason eşliğinde prostat biyopsisinin komplikasyonlarını etkileyen faktörler: Tek merkezde 403 hasta ile yapılan kohort çalışma

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Abstract

Aim: Prostate cancer is among the common cancer types in male population. Transrectal ultrasound (TRUS) guided prostate biopsy is considered the gold standard for diagnosis of prostate cancer. Complications in this tissue sampling method were analyzed in the present study.

Methods: A descriptive study with retrospective design was planned. A total of 403 patients who had 12 core TRUS guided prostate biopsy for the first time in December 2016 -November 2018 period were evaluated. Age of the patients, digital rectal examination finding, prostate specific antigen (PSA) levels, prostate volumes and complications were analyzed.

Results: Average age, serum total PSA level and prostate volume of patients were 63.2±8.53 years, 21.6±18.19 ng/mL and 65.63±20.19 cc, respectively. Genitourinary system infection was observed in 7.2% of the patients after the procedure. In terms of non-infection complications, 23.1% of patients had hematuria, 16.1% hematospermia and 2.2% rectal bleeding. On the other hand, 4.2% of the patients had vasovagal episodes and 0.7% had acute urinary retention. Of all patients, 8.9% were hospitalized due to observed complications.

Conclusion: We conclude that TRUS-guided prostate biopsy is a reliable diagnostic tool with low complication rates in patients with prostate cancer pre-diagnosis.

Keywords: Biopsy, Complications, Prostate, Transrectal ultrasound

Öz

Amaç: Prostat kanseri erkek popülasyonda yaygın izlenen kanser türleri arasında yer almaktadır. Prostat kanseri tanısında transrektal ultrasonografi (TRUS) eşliğinde prostat biyopsi altın standart olarak gösterilmektedir. Çalışmamızda bu doku örnekleme metodunun komplikasyonları analiz edilmiştir.

Yöntemler: Çalışmada Aralık 2016 ile Kasım 2018 tarihleri arasında ilk defa TRUS eşliğinde 12 kor prostat biyopsisi yapılan 403 olgu değerlendirildi. Hastaların yaşları, parmakla rektal muayene bulguları, prostat spesifik antijen (PSA) düzeyleri, prostat hacimleri ve komplikasyonları değerlendirilmiştir.

Bulgular: Hastaların ortalama yaşı, serum total PSA düzeyi ve prostat hacmi sırasıyla 63,2 ± 8,53 yıl, 21,6 ± 18,19 ng/mL ve 65,63 ± 20,19 cc idi. İşlem sonrası hastaların %7,2'sinde genitouriner sistem enfeksiyonu izlendi. Enfektif olmayan komplikasyonlara bakıldığında ise hastaların %23,1'inde hematüri, %16,1'inde hematospermi, %2,2'sinde rektal kanama gözlemlendi. Öte yandan hastaların %4,2'sinde vazovagal epizodlar ve %0,7'sinde ise akut üriner retansiyon ile karşılaşıldı. Çalışmaya alınan hastaların %8,9'u komplikasyonlara bağlı hospitalize edildi.

Sonuç: Prostat kanseri ön tanısı olan hastalarda TRUS eşliğinde prostat biyopsisinin düşük komplikasyon oranları ile güvenle kullanılabilir bir tanı aracı olduğu düşüncesindeyiz.

Anahtar kelimeler: Biyopsi, Komplikasyon, Prostat, Transrektal ultrason

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Introduction

Prostate cancer is among the most prominent health problems in aging male population. It ranks second after pulmonary malignancies in cancer-linked deaths [1]. Mortality rate due to prostate cancer in the United States for 2006-2010 periods was 23% [2]. It has been reported that 382,000 prostate cancer diagnoses were made in EU countries in 2008, and about 89,000 people lost their lives as a result of this disease [3]. Epidemiology studies in Turkey, on the other hand, showed an incidence rate of 36.3 per 100,000 people for prostate cancer in 2008 [1].

Methods used for diagnostic evaluation of prostate cancer include digital rectal examination, prostate specific antigen (PSA), transrectal ultrasound (TRUS) guided prostate biopsy and recently popular multi-parametric magnetic resonance as well as medical history of patient [4]. However, as in other cancer types, diagnosis is made based on histopathological examination. Today, TRUS guided prostate biopsy is considered diagnostic tool of gold standard by urologists [5]. Along with the increasing awareness for prostate cancer in the society, common use of PSA and aging populations of countries, prostate biopsies have been increasingly used [1]. Based on scientific data in the United States, about 7% of males who are 65 years of age and over take prostate biopsy every year [6].

In parallel to increasing use of prostate biopsies, frequency of undesired side effects from this invasive uro-radiological procedure are also on increase. In this retrospective study, patients who had 12 core TRUS guided prostate biopsy in our center were analyzed and complication frequencies were evaluated.

Materials and methods

A total of 403 patients who had 12 core TRUS guided prostate biopsy first time in December 2016 – November 2018 period and who had complete information in hospital record files were analyzed retrospectively in the present study. Abnormal digital rectal examination findings and/or an elevated serum total PSA levels were considered main biopsy indications. All cases had prophylactic antibiotherapy. Starting from one day before the procedure, twice daily doses of 500 mg ciprofloxacin was administered orally for three days. Before the biopsy procedure, rectum cleaning was carried out through routine enema procedure. After prostate examination in left lateral decubitus position, intrarectal 5% lidocaine pomade application and periprostatic nerve block using 5 cc 2% lidocaine solution guided with ultrasound were applied to all patients. Then, 12-core biopsy specimens were obtained from the base of the right, and left prostate lobes, lateral, and far remote lateral to the midline, medial, and lateral parts of the apex. All these procedures were carried out using 18 Gauge 30 cm biopsy needle and automatic biopsy gun (Angiotech Tru-Core I, Florida, USA) guided by a Diagnostic Ultrasound System 3535 (B&K Medical, Herlev, Denmark) with 7.5 MHz rectal probe. Specimens taken were sent to pathology department in tubes containing 10% formaldehyde solution. Patients were informed about all possible complications and discharged after being kept under observation for two hours.

Patients with neurological disorders, patients who previously underwent prostatic surgery, patients who had pathology in anal region or who were on antithrombotic or anticoagulant medication were excluded.

Age of the patients, digital rectal examination findings, PSA levels, prostate volumes and complications of included patients were evaluated.

Informed consent was taken from all patients and all steps of the study were carried out according to the basic principles of Helsinki declaration. The study was approved by Local Ethics Committee.

Statistical analysis

All statistical analysis was performed using SPSS 21.0 program for Windows (SPSS, Inc., Chicago, IL, USA). Student T test was used to test whether there was any difference between the two groups. $p < 0.05$ was considered statistically significant. The values obtained in the study were given as mean \pm standard deviation (minimum – maximum).

Results

Average age of 403 patients who underwent TRUS guided prostate biopsy examination in the present study was 63.2 ± 8.53 years, and average total PSA level was 21.6 ± 18.19 ng/mL. Average prostate volume of the patients was 65.63 ± 20.19 cm³. In terms of indications for prostate biopsy, 87 patients had only abnormal digital rectal examination findings such as nodule in prostate, asymmetry and irregularities while 204 cases had only high PSA levels. On the other hand, 112 patients had both high PSA levels and abnormal digital rectal examination findings. Histopathological diagnosis of 141 (35%) cases was prostate adenocarcinoma.

With regard the biopsy complications, 93 patients (23.1%) complained of hematuria. Average duration of the complaint was 3.6 ± 3.1 days. Hematuria complaint healed itself in 82 cases without any medical intervention. Remaining 11 patients were hospitalized and bladder irrigation was performed for these patients. Five of these patients had blood transfusion. Hematospermia was observed in a total of 65 patients (16.1%). No treatment protocol was applied for any patients monitored for hematospermia, and symptoms healed within 4-16 days. Rectal bleeding was observed in nine patients (2.2%). All of them lasted for less than two days and no surgical or medical intervention was needed other than intrarectal compression rectal bleeding points by finger. A total of 17 cases (4.2%) had vasovagal symptoms such as sweating, nausea, paleness, head swimming and hypotension. All of these cases were remedied clinically by Trendelenburg position and intravenous liquid support. No patients had myocardial infarction or cerebrovascular disorder due to vasovagal stimulus. Urinary retention, another complication observed after the procedure, was detected in three patients (0.7%). Emergency suprapubic cystostomy catheter was placed in three patients under local anesthesia. After alpha blocker, analgesic and antimicrobial treatment, cystostomy of all patients were taken, which showed that all cases improved without needing surgical intervention.

Infective pathology was observed in 29 patients (7.2%) after TRUS guided prostate biopsy procedure. Six of these cases had orchitis, two had epididymitis and 21 had prostatitis. A total

of 23 patients had fever over 38.5 °C at least once. In 16 of the patients who had infective complication, urine culture was positive. Cultures of nine patients were positive for Escherichia coli, four for Enterococcus, two for Klebsiella and one for Pseudomonas. Urosepsis developed in only one patient. All complications taken together, 36 patients (8.9%) were treated by hospitalization.

Hematuria and hemospermia were positively associated with high PSA and prostate volume (p<0.001). On the other hand, hemospermia was more common in young patients and hematuria was found more frequently in older patients (p<0.001). No association was found between rectal bleeding and age, PSA, prostate volume (p=0.892, p=0.874, p=0.647, respectively). Increased incidence of vasovagal symptoms with decreasing age was observed (p=0.035). On the other hand, no correlation was found between PSA and prostate volume of these patients (p=0.836, p=0.706, respectively). In addition, acute urinary retention was positively associated with increased age, PSA and prostate volume (p<0.001). When the infectious pathologies were examined, it was determined that only the high PSA values were correlated (p=0.034) (Table 1).

Table 1: Overview of complications following prostate biopsy

| Complications | Variable | Complication mean±SD | No-complication mean±SD | p |
|-------------------------|------------------------------------|----------------------|-------------------------|--------|
| Hematuria | Number | 93 | 310 | |
| | Cancer diagnose after biopsy | 38 | 103 | |
| | Age(y) | 66.26±6.47 | 62.28±8.86 | <0.001 |
| | PSA(ng/mL) | 32.03±21.13 | 18.59±15.99 | <0.001 |
| | Prostate volume (cm ³) | 82.25±25.62 | 60.64±15.05 | <0.001 |
| Hemospermia | Number | 65 | 338 | |
| | Cancer diagnose after biopsy | 26 | 115 | |
| | Age(y) | 61.12±7.25 | 63.60±8.71 | <0.001 |
| | PSA(ng/mL) | 34.90±23.45 | 19.14±15.80 | <0.001 |
| | Prostate volume (cm ³) | 90.15±26.60 | 60.90±14.59 | <0.001 |
| Rectal bleeding | Number | 9 | 394 | |
| | Cancer diagnose after biopsy | 4 | 137 | |
| | Age(y) | 63.33±2.54 | 63.20±8.62 | 0.892 |
| | PSA(ng/mL) | 21.88±2.47 | 21.69±18.39 | 0.874 |
| | Prostate volume (cm ³) | 65.01±2.50 | 65.64±20.41 | 0.647 |
| Vasovagal symptoms | Number | 17 | 386 | |
| | Cancer diagnose after biopsy | 6 | 135 | |
| | Age(y) | 58.94±8.42 | 63.39±8.50 | 0.035 |
| | PSA(ng/mL) | 22.55±6.39 | 21.65±18.54 | 0.836 |
| | Prostate volume (cm ³) | 63.82±7.40 | 65.71±20.57 | 0.706 |
| Acute urinary retention | Number | 3 | 400 | |
| | Cancer diagnose after biopsy | 1 | 140 | |
| | Age(y) | 76.01±6.92 | 63.10±8.48 | <0.001 |
| | PSA(ng/mL) | 52.33±44.45 | 21.46±17.87 | <0.001 |
| | Prostate volume (cm ³) | 88.33±20.21 | 65.46±20.12 | <0.001 |
| Infective pathology | Number | 12 | 374 | |
| | Cancer diagnose after biopsy | 29 | 129 | |
| | Age(y) | 61.58±5.87 | 63.32±8.70 | 0.291 |
| | PSA(ng/mL) | 27.72±22.06 | 21.22±17.80 | 0.034 |
| | Prostate volume (cm ³) | 69.13±21.01 | 65.36±20.13 | 0.332 |

SD: standard deviation, PSA: prostate specific antigen

Discussion

A detailed analysis of medical literature shows that the first prostate needle biopsy was performed in 1930 by Ferguson. This first attempt was carried out using transperineal approach with an 18-gauge needle. However, longer distance traversed difficulty of manipulations, patients' disturbances due to perineal susceptibility and longer procedures in transperineal biopsies directed clinicians to find different approaches. With subsequent multicenter, large cohort studies, many superior aspects of transrectal prostate biopsies have been shown and this biopsy procedure has been a common practice in modern clinics. Among the mentioned superior features of transrectal biopsies are shorted distance to sampling area, ease of manipulation, less susceptibility of rectum and shorter time needed for the procedure [7,8].

In post-World War II period, Sonar (Sound Navigation and Ranging) machines that function using data obtained from

advancing of sound energy in a medium, its refraction, reflection and absorption have been started to be used in health practice. Parallel to scientific advancements, there were groundbreaking developments in uro-radiology area. In terms of use of sonographic evaluation in prostate tissue, Wild and Reid used TRUS the first time in 1957, and Watanabe et al. [9] put this method in clinical practice in 1974. TRUS allows clinicians to take specimens appropriate for zonal anatomy of prostate. With specific design of machines for pelvic organs using emerging technologies, both prostate gland and seminal vesicles could be visualized with high resolution in transverse and sagittal planes [10].

Before these revolutionary developments in scientific world, prostate biopsies were performed physically with the guidance of a finger in many centers. With TRUS going into practice, extremely significant changes took place in data about prostate cancer. Scientific analyses revealed that even in patients for whom abnormal digital rectal examination findings, about half of the patients with negative outcomes in biopsies carried out by the guidance of a finger in fact was found to have cancer based on TRUS guided prostate biopsies [11]. An extremely critical historical procedure seems to have started in prostate cancer diagnosis with the introduction of systemic sextant prostate biopsy (6-core) with the guidance of TRUS by Hodge et al. in 1989 [12]. However, there was no standardization for taking specimen in TRUS guided prostate biopsies. Studies conducted revealed that 6-core prostate biopsy was extremely inadequate in the diagnosis of prostate cancer [1]. Clinical studies showed that prostate cancer could be missed in 15-34% of patients who had sextant biopsy [13,14]. Subsequent studies showed that increasing the number of TRUS guided biopsy specimens to 12 markedly increased the success rate in finding malignant tissues [15]. In recent approaches of TRUS guided biopsies, specimens are taken from peripheric zone and lateral regions where 70% of malignancies arise, whereas routine sampling is not carried out in transitional zone in which cancer rate is as low as 1.9-2.1%. Besides, it is clear that no biopsy method is 100% successful in making prostate cancer diagnosis. In patients who had prostate cancer diagnosis clinically which could not be verified by tissue sampling, on the other hand, repeating prostate biopsies and increasing the number of specimens are quite common approaches adopted by many clinics [1,15].

Although TRUS guided prostate biopsies are commonly used in medicine, different preparation procedures have been used. This invasive procedure causes complications varying from hematuria to urosepsis with different frequencies. These complications are caused by many factors such as position given to patient, physical contact of probe to anal region and damage as a result of making hole in rectum mucosa for the purpose of sampling. However, complication frequencies have been considerably decreased in recent years as a result of great care observed during preparation stage before biopsy, introduction of automatic biopsy guns, routine use of antibiotic prophylaxis and increasing knowledge of clinicians. Based on recent reports, 64-78% of cases have minor post-operative complications such as hematuria, urinary retention, hemospermia and vasovagal

reaction while 0.3-3.0% have major complications such as urosepsis and Fournier gangrene [16].

Hematuria and hematospermia are most common post-operation complications of TRUS guided prostate biopsy. In their studies covering 2049 cases, Efesoy et al. [1] found that hematuria and hematospermia complication rates in TRUS guided prostate biopsy were 66.3 and 38.8%, respectively. On the other hand, Rietbergen et al. [17] examined 1687 prostate biopsies and reported that 23.6% of the patients had hematuria and 45.3% had hematospermia after the procedure. Hematuria and hematospermia observed after TRUS guided prostate biopsies generally heal themselves without needing a treatment. However, in 0.25–0.7% of the cases hematuria leading to clot retention and/or requiring transfusion can be seen [1]. In the present study, 23.1% of the patients had hematuria and 16.1% had hematospermia. Hematuria healed itself in 82 cases without needing any intervention, while 11 cases (2.7%) needed hospitalization. On the other hand, no treatment was performed for any patients who had hematospermia complication, and symptoms regressed within 4-16 days. Dede et al. [18] reported a rectal bleeding rate of 8% for TRUS guided prostate biopsy. Similarly, frequency of this complication was reported as 10% by Naughton et al. [19]. On the other hand, a lower incidence rate of 2.3% was reported for rectal bleeding by Berger et al. [20] in a large patient series including 5957 patients. Among the treatment modalities for rectal bleeding is intrarectal compression is applied on rectal bleeding points by finger, ultrasound probe or anoscope. Nevertheless, endoscopic sclerotherapy is another treatment option in cases for which hemostatic control cannot be achieved. In the present study, rectal bleeding was observed in 2.2% of the patients. Bleeding did not last longer than two days in any patient and no patients needed blood transfusion.

Infective pathologies are other complications that could develop after prostate biopsies. All clinicians today have a consensus over the use of prophylaxis for TRUS guided prostate biopsies. However, there is no agreement on type, dose and duration of antibiotic treatment and on combined approaches [21,22]. In cases without prophylaxis administration, incidence rates of infective pathologies range from 20 to 50%, and some of these clinic cases could lead to mortality [23]. With the introduction of antibiotic prophylaxis these rates decreased to 0.1-10.0% [18]. After TRUS guided prostate biopsy, very different infective pathologies such as pyuria, prostatitis, epididymitis, orchitis, asymptomatic bacteriuria and urosepsis could develop. Of all these pathologies of prostate biopsy, urosepsis is the most serious complication [1,22]. Erkoç et al. [24] studied 1280 cases for complications after TRUS guided prostate biopsy and observed a 6.5% infective complication rate. Similarly, Wu et al. [25] found 8.23% incidence rate for this complication. Infective pathology rate was 7.2% in the present study.

Vasovagal episodes are other complications observed after TRUS guided prostate biopsy. Most of them are considered to develop as a result of anxiety. However, they could also develop as a result of decrease in blood supply to brain due to vasodilation which develops in gastrointestinal veins as secondary to distension in rectum. For affected cases,

Trendelenburg position and intravenously applied liquid hydration are sufficient treatment modalities for most patients [22]. It is estimated to be 8% after the procedure [26]. This rate was 4.2% in our series. All cases recovered clinically using Trendelenburg position and intravenous liquid support. Another complication of TRUS guided prostate biopsy is lower urinary system symptoms. These complaints arise due to trauma and edema caused by the procedure. An average of 0.8-40% of cases who had TRUS guided prostate biopsy were reported to have lower urinary system symptoms and 0.2-9.1% were reported to have acute urinary retention [1]. In the present study, 0.7% of the cases had acute urinary retention. Suprapubic cystostomy was performed in these patients.

Retrospective nature and limited number of cases were the main limitations of the present study.

In conclusion, based on the findings of the present study, it could be stated that with its low complication rates, TRUS guided prostate biopsy is a reliable diagnostic tool for prostate cancer.

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