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Effect of alpha-blocker use on morbidity and lower urinary tract symptoms in patients undergoing transrectal ultrasound-guided prostate biopsy

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Abstract

Objective: To evaluate voiding dysfunction and morbidity after transrectal ultrasound (TRUS)-guided prostate biopsy and to investigate whether pre-intervention alpha-blocker treatment had any effect on morbidity and voiding dysfunction.

Material and methods: The study included 197 consecutive patients who underwent TRUS-guided prostate biopsy between January 2014 and January 2018. The patients were divided into two groups, those receiving alpha-blocker (silodosin) and those not receiving alpha-blocker treatment before the procedure (controls). All patients were evaluated before and one week after the procedure with the International Prostate Symptom Score (IPSS), measurements of maximum flow rate (Q_{max}), post-void residual urine volume (PVR) and prostate volume, and procedure-related complications were also recorded. All analyzed parameters were compared by within-group and between-group evaluations.

Results: There was no significant difference between the two groups in terms of IPSS, Q_{max} and prostate volume values before biopsy. In the follow-up evaluation performed on the seventh day after biopsy, IPSS, PVR and prostate volume were found to be increased, whereas Q_{max} was decreased in the control group ($p < 0.05$). In the silodosin group, an increase in prostate volume was observed, but there were no significant changes in IPSS, Q_{max} and PVR values. Acute urinary retention (AUR) after the biopsy procedure developed in two patients (2%) in the silodosin group, and in nine patients (9.1%) in the control group ($p = 0.02$). No significant difference was found between the two groups in terms of biopsy-related complications, except for AUR.

Conclusion: We believe that alpha-blocker treatment initiated before biopsy may be advantageous in preventing voiding dysfunction that may develop after the procedure.

Keywords

Alpha-blockers, complications, lower urinary tract symptoms, TRUS-guided prostate biopsy

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Introduction

According to global data, prostate cancer is the most common type of cancer among men and the most common cause of mortality after lung/bronchial cancers.[1] In the current era, prostate biopsy is performed in a greater number of men due to various reasons, including the widespread use of prostate-specific antigen (PSA) testing for the diagnosis of this cancer, the increased awareness of the population about this disease, the availability of early diagnosis

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and treatment programs, and the aging global population.[2] The gold-standard method to establish a histopathological diagnosis of prostate cancer is the use of prostate biopsy performed with the guidance of transrectal ultrasonography (TRUS).[3] Over the last few decades, pre-biopsy patient preparation and biopsy technique have undergone significant changes and improvements, making the undesired side effects of TRUS-guided prostate biopsies more tolerable; thereby facilitating the use of this procedure.[3] Nowadays, TRUS-guided biopsy has become an easy-to-apply daily procedure that may be performed in polyclinic settings. However, due to the invasiveness of the procedure, self-limited minor complications, such as hematuria, hematospermia and transrectal bleeding, are not uncommon, while very rare major complications that may even be fatal are also reported. Thus, researchers continue to conduct studies and research to further simplify the procedure and/or understand and reduce complications.[4]

In addition to undesirable side effects, the direct effect of TRUS-guided biopsy on voiding dysfunction constitutes another problem. In patients undergoing prostate biopsy, an increase in the severity of lower urinary tract symptoms (LUTS) may occur, and sometimes even acute urinary retention (AUR) may develop in an estimated 0.2%–2.6% of patients.[4] Although the exact pathophysiology of voiding dysfunction developing after biopsy is unknown, it is considered that the trauma during the procedure may increase bladder outlet resistance, leading to voiding difficulties by causing prostate edema.[5]

We hypothesized that alpha-blocker treatment initiated before the biopsy procedure would reduce bladder outlet resistance and prevent voiding dysfunction in these patients. Therefore, we aimed to evaluate the effect of this treatment on LUTS and biopsy-related complications.

Material and methods

Study design

After obtaining approval from Ankara Numune Training and Research Hospital Ethics Committee (Approval number: 2014/766) and informed consent from all participants, patients that presented to our tertiary healthcare institution from January 2014 to January 2018 and underwent TRUS-guided biopsy, due to abnormal findings in digital rectal examination (diffuse stiffness, nodule, and diffuse asymmetry) and/or elevated prostate-specific antigen (PSA) (>2.5 ng/ml), were included in this prospective study. Patients with urinary tract infection, urethral stricture, rectal disease (anal fissure, anal fistula, or hemorrhoid), severe coagulation disorder, diabetes mellitus or neurologic disease, and those with a history of alpha-blocker therapy, prostate surgery, prostate biopsy or AUR were excluded from the study. The final study group included 197 consecutive patients who underwent TRUS-guided prostate biopsy. These patients had been prospectively randomized into two groups, the first group ($n=99$) was started on 8 mg silodosin 10 days before biopsy and continued this alpha-blocker treatment for 10 days after the procedure, while the second group ($n=98$) did not receive alpha-blocker treatment before biopsy and were assigned as controls (Figure 1).

Measurements

Detailed medical history was obtained from all patients included in the study. Age, current chronic diseases, and medications used were recorded. Then, a comprehensive urogenital examination and neurological examination were performed. The International Prostate Symptom Score (IPSS) form was completed through face-to-face interviews with the patients. Patients' urine analysis and urine culture results, and their total and free PSA values were obtained. The PSA and free PSA measurements of the patients were undertaken by the radioimmunoassay method with the UniCel® DxI 800 Immunoassay System (Beckman Coulter, Inc. USA). The maximum urinary flow rate (Q_{max}) of the patients was calculated using uroflowmetry. The postvoid residual urinary volume (PVR) measurements were obtained by abdominal ultrasonography. For prostate size measurement and prostate biopsy, the patients were placed in the left lateral decubitus position and all procedures were performed by the same urologist using a Hitachi EUB-400® ultrasonography device with a 6.5 MHz biplanar transrectal probe.

Biopsy procedure

Prostate biopsies were scheduled after urinary culture negativity was confirmed in each patient. Fleet's enema adult® (monobasic and dibasic sodium phosphate) was recommended 2 h before biopsy. Antibiotic prophylaxis was initiated with 500 mg oral ciprofloxacin in all patients 3 days before biopsy, and was continued on the day of the procedure and 3 days after the procedure. All patients underwent periprostatic nerve block with 10 mL of 2% prilocaine before biopsy. A standard 12 core prostate biopsy was performed with an 18G needle

Follow-up

All patients included in our study were called for a follow-up visit on the seventh day after the procedure, and the IPSS form was completed again. Urine analysis, uroflowmetry, PVR and prostate size measurements were also repeated. The patients were questioned for urinary retention, hematuria, rectal bleeding, biopsy-related urinary tract infection, fever, vasovagal symptoms and hypotension, and the results were recorded. The inter- and intra-group comparisons were made in terms of prostate size, voiding dysfunction and complication rates.

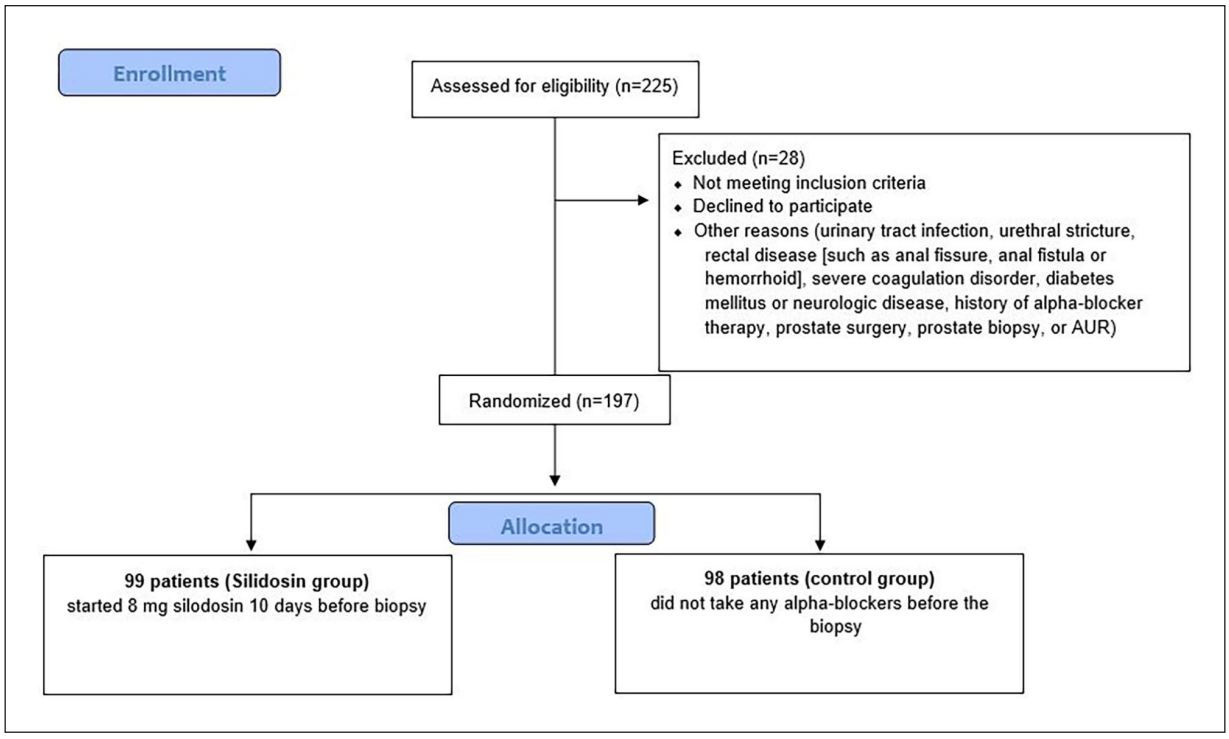

Figure 1. Flow chart of the study.

Statistical analysis

All statistical analyses were performed using the Statistical Package for the Social Sciences, version 20.0 (SPSS, Chicago, IL, USA). The results were expressed as mean ± standard deviation. Normality of distribution of quantitative variables was checked with the Shapiro-Wilk test. The two groups were compared using Chi-square tests including the Fisher's exact test for categorical data, and the independent samples *t*-test for quantitative data. Within-group time-bound comparisons of quantitative variables were performed with the paired samples *t*-test. A *p*-value below 0.05 was considered to be statistically significant.

Results

The mean age of the 197 consecutive patients was 62.4 ± 7.6 years. There was no statistically significant difference between the two groups with regard to age, PSA, prostate volume, Q_{max} and PVR before biopsy. On post-biopsy day 7, AUR developed in 11 (5.5%) patients, of which two were in the silodosin group (2/99, 2%) and nine were in the control group (9/98, 9.1%). AUR was managed by urethral catheter placement. When the prostate volumes of the patients were compared according to the presence/absence of AUR, the mean prostate volume of the 11 patients who developed AUR was 63.8 ± 18.4 ml, while those without AUR ($n = 186$) had a mean value of 48.3 ± 25.5 ml, indicating a significant difference ($p = 0.04$).

When the changes in the data of the 98 patients in the control group before and after the biopsy procedure were compared, there was a significant increase in mean IPSS, a significant decrease in Q_{max}, and a significant increase in PVR and prostate volume compared to the baseline values ($p < 0.05$). In the silodosin group, an increase in prostate volume was observed compared to baseline values, while there was no significant change in IPSS, Q_{max} and PVR (Table 1).

In the evaluation of TRUS-guided biopsy-related complications among all patients, the most common complication was observed as rectal bleeding that had developed in 31 (16.5%) patients. This was followed by hematuria that had occurred in 24 (12.8%) patients. The comparison of groups with regard to complications are given in Table 2.

Discussion

While the curative treatment of localized prostate cancer is possible today, local invasive or metastatic prostate cancer treatment requires a multimodal approach, and treatment results remain unsatisfactory.[6] From this point of view, it is important to be able to diagnose prostate cancer while it is still in the localized stage. In the diagnosis of early stage and organ confined prostate cancer, a TRUS-guided prostate biopsy is accepted as the standard approach which has the advantage of being available worldwide.[7] Although this procedure is largely considered as a safe and well-tolerated method, it is associated with minor complications, and very rarely, major complications.[8] The invasive nature

Table 1. Baseline and post biopsy seventh day characteristics and voiding functions of the silodosin and control groups.

Variables	Silodosin ($n=99$)	Control ($n=98$)	p-Value
Age (years)	62 ± 7.4	63.2 ± 8.2	0.52
PSA (ng/ml)	8.1 ± 5.7	9.8 ± 6.1	0.47
Prostate volume (ml)			
Baseline	41.8 ± 11.1	45.4 ± 12.6	0.37
Post-biopsy day 7	47.3 ± 24	50.3 ± 14.1	0.29
p Value*	<0.001	<0.001	
Voiding functions			
Q_{max} (mL/s)			
Baseline	12.1 ± 6.2	12.6 ± 7.0	0.81
Post-biopsy day 7	12.3 ± 6.9	9.3 ± 6.9	0.03
p Value*	0.06	<0.001	
PVR (mL)			
Baseline	107.8 ± 70.4	92.1 ± 79.9	0.17
Post-biopsy day 7	100.3 ± 93.5	125.3 ± 63.5	0.03
p Value*	0.73	0.006	
IPSS			
Baseline	13.8 ± 8.8	12 ± 9.4	0.26
Post-biopsy day 7	12.4 ± 10.5	14.4 ± 10.1	0.17
p Value*	0.57	0.002	

PSA: prostate-specific antigen; IPSS: international prostate symptom score; PVR: post-void residual urine; Q_{max}: maximum flow rate.
The results are shown as mean ± standard deviation.
*Paired t-test.

Table 2. Complications following prostate biopsy and comparison between the two groups.

Complications	Silodosin ($n=99$)	Control ($n=98$)	p-Value
Rectal bleeding, n (%)	16 (16.1)	15 (15.3)	0.52
Hematuria, n (%)	12 (12.1)	12 (12.2)	0.47
Urinary tract infection, n (%)	5 (5)	9 (9.1)	0.07
Hematospermia, n (%)	5 (5)	6 (6.1)	0.48
AUR, n (%)	2 (2)	9 (9.1)	0.02
Vasovagal syncope, n (%)	3 (3)	2 (2)	0.31

AUR: acute urinary retention.

of the procedure and rectal route of application are among the factors that are associated with the complications of TRUS-guided prostate biopsy. Before various advances with the method itself and its application, numerous publications evaluating the results of TRUS-guided prostate biopsy had reported serious complications (especially major infections) and even procedure-related deaths.[9]

In addition to known complications of the procedure, such as pain, hematuria, hematospermia, infection and sepsis, it has been reported that TRUS-guided biopsy may result in voiding difficulties in patients, with frequency ranging from 0.8% up to 40%.[10,11] In their prospective study, Bozlu et al.[12] randomized 66 patients that underwent TRUS-guided 12-core prostate biopsy into two groups. The first group had received tamsulosin as an alpha-blocker and the other group consisted of non-treatment controls. The authors reported lower frequency of AUR and voiding difficulties on the seventh day after the procedure in the tamsulosin group compared to the control group (3% vs 9.1% for AUR and 9.1% vs 42.4% for voiding difficulties). In another prospective study reporting follow-up findings from the post-interventional seventh day after TRUS-guided biopsy, Chung et al.[13] found that PVR was increased and Q_{max} was decreased compared to baseline measurements in both groups (patients with and without alpha-blocker treatment). Furthermore, in the alpha-blocker group, PVR was decreased and Q_{max} was increased when compared to the control group. The authors did not detect a significant IPSS change in either group. In our study, similar to the results reported by Chung et al., we observed that the Q_{max} value was decreased and the PVR value was increased on the seventh day of post-biopsy follow-up. However, there was no statistically significant change in the Q_{max} and PVR values compared to the baseline values in the silodosin group ($p > 0.05$). We consider that this may be due to the masking of the

alpha-blocker effect in the silodosin group by the edema of the prostate caused by biopsy. On the other hand, we found that the IPSS score was increased in the control group but did not change in the silodosin group. These results support the suggested development of voiding difficulties in relation with the conduct of the biopsy. One particular novel result of the present study—which has not been evaluated previously—was that, on the seventh post-biopsy day, there was a significant increase in prostate volume in both groups when compared to baseline values ($p < 0.001$). This change in prostate volume after biopsy supports the hypothesis that post-biopsy prostate edema may have developed in previous studies; therefore, our belief is that the increase in the prostate size occurs secondary to prostate edema.[5,10]

In studies in the literature, it has been reported that AUR develops at a frequency ranging from 0.2% to 9.1% after prostate biopsy.[5,14] In a prospective study conducted with 204 patients, Zisman et al.[10] reported that AUR developed in five (2.5%) patients, and the authors emphasized that prostate size was a risk factor for the development of AUR after biopsy. Similarly, Zaytoun et al.,[4] in a research including 1438 cases, reported a significant relationship between prostate size and AUR development. In our study, AUR had developed in 11 (5.5%) patients overall, of which two were in the silodosin group (2/99; 2%) and nine were in the control group (9/98; 9.1%). The frequencies reported in either group were consistent with the literature. In addition, we detected findings supporting the hypothesis of Zisman et al., that prostate size was a risk factor for the development of AUR. Indeed, while the mean prostate volume of the 11 patients who developed AUR was 63.8 ± 18.4 ml, the 186 patients who did not develop AUR had significantly lower prostate volume (48.3 ± 25.5 ml) ($p = 0.04$). Therefore, prostate size before biopsy was determined as an important factor in the development of AUR after the procedure.

Among the studies focusing on the frequency of complications in TRUS-guided prostate biopsy, the prevalence of minor and major complications were reported as 69.7% and 0.01%, respectively, in the 5802-patient series of Raaijmakers et al.[14] and the 5957-patient series of Berger et al.,[15] respectively. In our study, no serious complications were observed in any of the patients. In the evaluation of complications frequency, rectal bleeding was found to be the most common complication in either group, followed by hematuria. No statistically significant difference was observed between the two groups in terms of complication frequency.

The current study has certain limitations. The relatively small group of patients prevented us from making definitive conclusions; however, the inclusion/exclusion criteria were utilized to ensure that analyses were performed accurately. Therefore, the reduction in the number of cases included was unavoidable and necessary. In addition, the current study did not have a placebo arm, which can be considered as another limitation. Thus, our results should be supported by further comprehensive and prospective studies.

Conclusion

In this study, TRUS-guided prostate biopsy was shown to cause voiding dysfunction. We consider that, although pre-biopsy initiation of alpha-blocker treatment had no effect on other morbidities, it may be able to prevent post-procedural voiding dysfunction and AUR. Future studies will determine whether prophylactic alpha-blocker treatment before biopsy can be integrated into routine practice, especially in high-risk patients with high IPSS and large prostate volume, as an additional measure –similar to the use of antibiotic prophylaxis before the biopsy procedure.

Authorship contributions

Concept – GE, RS; Data collection and/or processing – RS; Analysis and/or interpretation – RS; Literature review – GE; Writing – RS; Critical review – RS.

Declaration of conflicting interests

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Ethical approval/patient consent

This research was approved by the local clinical research ethics committee of Ankara Numune Training And Research Hospital on February 26 with an approval number 2014/766

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References

1. Siegel R, Naishadham D and Jemal A. Cancer statistics, 2013. *CA Cancer J Clin* 2013; 63(1): 11–30.
2. Welch HG and Albertsen PC. Prostate cancer diagnosis and treatment after the introduction of prostate-specific antigen screening: 1986-2005. *J Natl Cancer Inst* 2009; 101: 1325–1329.
3. Clements R. The role of transrectal ultrasound in diagnosing prostate cancer. *Curr Urol Rep* 2002; 3: 194–200.
4. Zaytoun OM, Anil T, Moussa AS, et al. Morbidity of prostate biopsy after simplified versus complex preparation protocols: assessment of risk factors. *Urology* 2011; 77(4): 910–914.
5. Borboroglu PG, Comer SW, Riffenburgh RH, et al. Extensive repeat transrectal ultrasound guided prostate

biopsy in patients with previous benign sextant biopsies. *J Urol* 2000; 163: 158–162.
6. Boehm K, Leyh-Bannurah S-R, Rosenbaum C, et al. Impact of preoperative risk on metastatic progression and cancer-specific mortality in patients with adverse pathology at radical prostatectomy. *BJU Int* 2017; 120(5): 666–672.
7. Ghai S and Toi A. Role of transrectal ultrasonography in prostate cancer. *Radiol Clin North Am* 2012; 50: 1061–1073.
8. Loeb S, Vellekoop A, Ahmed HU, et al. Systematic review of complications of prostate biopsy. *Eur Urol* 2013; 64: 876–892.
9. Wu YP, Li XD, Ke ZB, et al. Risk factors for infectious complications following transrectal ultrasound-guided prostate biopsy. *Infect Drug Resist* 2018; 11: 1491–1497.
10. Zisman A, Leibovici D, Kleinmann J, et al. The impact of prostate biopsy on patient well-being: a prospective study of voiding impairment. *Urol J* 2001; 166: 2242–2246.
11. Mkinen T, Auvinen A, Hakama M, et al. Acceptability and complications of prostate biopsy in population-based PSA screening versus routine clinical practice: a prospective, controlled study. *Urology* 2002; 60(5): 846–850.
12. Bozlu M, Ulusoy E, Doruk E, et al. Voiding impairment after prostate biopsy: does tamsulosin treatment before biopsy decrease this morbidity? *Urology* 2003; 62: 1050–1053.
13. Chung SJ, Jung SI, Ryu JW, et al. The preventive effect of tamsulosin on voiding dysfunction after prostate biopsy: a prospective, open-label, observational study. *Int Urol Nephrol* 2015; 47(5): 711–715.
14. Raaijmakers R, Kirkels WJ, Roobol MJ, et al. Complication rates and risk factors of 5802 transrectal ultrasound-guided sextant biopsies of the prostate within a population-based screening program. *Urology* 2002; 60(5): 826–830.
15. Berger AP, Gozzi C, Steiner H, et al. Complication rate of transrectal ultrasound guided prostate biopsy: a comparison among 3 protocols with 6, 10 and 15 cores. *J Urol* 2004; 171(4): 1478–NaN80; discussion 1480; discussion 1480-1.