Original Article

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Are Clinically Significant Cancer Detection Rates Different in Peripheral Zone Lesions Undergoing Transrectal MR-TRUS Targeted Prostate Biopsy with Local Anesthesia and Sedoanalgesia?

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Abstract

Objective: We aimed to compare clinically significant prostate cancer (csPC) detection rates between patients who underwent targeted prostate biopsy under sedoanalgesia and those who underwent biopsy under local anesthesia with intrarectal local anesthetic instillation (IRLI).

Materials and Methods: We analyzed targeted biopsy data from 2015 to 2021 at our center. csPC detection rates of sedoanalgesia (n=56) and IRLI (n=257) groups in targeted biopsy in peripheral zone (PZ) lesions compared after Mahalanobis distance matching within the propensity score caliper method. Four variables-age, prostate specific antigen density, index lesion prostate imaging-reporting and data system score, and the number of lesions-were selected as covariates for the matching procedure.

Results: After matching, 96 patients from the IRLI group and 50 patients from the sedoanalgesia group were included in the analysis. In the IRLI group, csPC was detected in 33 (34.4%) patients, whereas in the sedoanalgesia group, it was detected in 21 (42%) patients. No statistically significant difference was found between the two groups (p=0.365).

Conclusions: csPC detection rates for local and sedoanalgesia are similar in PZ lesions while performing targeted transrectal biopsy.

Keywords: Prostate cancer, targeted biopsy, local, sedoanalgesia, anesthesia

Introduction

Transrectal or transperineal prostate biopsy performed under the guidance of transrectal ultrasound (TRUS) is the most commonly used method for diagnosing prostate cancer (1). The 2022 European Association of Urology (EAU) Prostate Cancer Guidelines state that biopsy with an 18 gauge needle and periprostatic block (PPB) is the standard practice; however, differing anesthesia techniques have been reported in the literature.

For men with a high prostate specific antigen (PSA) level or abnormal findings on digital rectal examination (DRE), 10 or 12 systematic biopsies guided by TRUS are recommended to diagnose suspected prostate cancer. Systematic biopsy without imaging has a low rate of detecting clinically significant prostate cancer (csPC) but a high rate of detecting clinically insignificant prostate cancer (2), which can lead to undertreatment in some patients and overtreatment in others (3,4). The current EAU guidelines strongly recommend performing multiparametric magnetic resonance imaging (mpMRI) before systematic biopsy (1). Performing mpMRI can prevent unnecessary biopsies in some patients and enable targeted biopsies in cases of suspicious lesions (5). The PRECISION study demonstrated that mpMRI is superior to standard systematic biopsies in detecting csPC in men who had not previously undergone prostate biopsy, regardless of whether a targeted biopsy was performed (6). However, the MRI-FIRST and 4M studies found that the difference in the success rate of csPC detection between the two methods was statistically insignificant (7,8). In the MRI-FIRST study, combined biopsy demonstrated a significantly higher success rate in diagnosing csPC than targeted or systematic biopsy alone (7). In the 4M study, the diagnostic rate of clinically insignificant

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prostate cancer was significantly lower with targeted biopsy (8). Current EAU guidelines recommend combined biopsy for patients with a suspicious lesion on mpMRI and targeted biopsy only for patients with a negative biopsy history (1).

Systematic prostate biopsy and transrectal MR-targeted prostate biopsy under TRUS guidance (TRUSG) are commonly performed under local anesthesia. Local anesthesia can be applied as intrarectal local anesthetic instillation (IRLI), PPB, or pudendal nerve block. Many studies in the literature have compared these techniques (9,10,11,12). Other studies have compared general anesthesia methods with local anesthesia or placebo methods, primarily based on pain scores (13,14).

In this study, we aimed to compare csPC detection rates between patients who underwent TRUS-MR targeted prostate biopsy under pseudoanalgesia and those who underwent biopsy under local anesthesia with IRLI. The gel used for local anesthesia contained 6 mL of 2% lidocaine and chlorhexidine.

Materials and Methods

Patients

This study consists of a retrospective analysis of data from patients who underwent MR-TRUS-targeted transrectal prostate biopsy at the Department of Urology, Gazi University Faculty of Medicine Hospital between December 2015 and October 2021. In this medical center, lesions located in the peripheral zone (PZ) are routinely biopsied under local anesthesia. However, lesions located in the transitional zone (TZ), central zone (CZ), and anterior fibromuscular stroma (AFS) are biopsied under sedoanalgesia. Biopsy-naïve patients and had lesions located in TZ and/or CZ and/or AFS underwent combined biopsy (targeted + systematic) under sedoanalgesia, and these patients were included in the study sample if they had a concurrent PZ lesion (n=56). Patients with only PZ lesions who underwent biopsy with IRLI were also included in the study sample (n=257). Biopsy results of lesions outside the PZ in the pseudoanalgesia group were excluded from the analyzes.

MRI and Targeted Biopsy

Patients with elevated PSA levels or abnormal DRE findings who were scheduled for a prostate biopsy underwent mpMRI, which was conducted before biopsy using a 3.0 Tesla (T) MRI device (Magnetom Verio; Siemens Health Care, Erlangen, Germany). All examinations were reported according to PI-RADS v2 or v2.1. Patients with PI-RADS ≥3 lesions underwent TRUSG-MR targeted biopsy. All PI-RADS ≥3 lesions were marked on T2 sequences by a radiologist with extensive experience in this field, and the lesions were outlined on the prostate boundaries and drawings made by a urologist using the BioJet fusion system (D&K Technologies, Barum, Germany) software in conjunction with the Flex Focus 500 ultrasound system (BK Medical, Herlev, Denmark). All targeted biopsies were performed by two experienced urologists. All patients also underwent a standard 12-core systematic biopsy simultaneously with the targeted biopsy. All biopsies were evaluated by the same pathologist. The csPC threshold was defined as International Society of Urological Pathology Grade Group ≥2.

Statistical Analysis

Statistical analyzes were performed using R version 4.0.4 and R Studio version 1.4.1106, with the MatchIt package used for matching analysis. Four variables-age, PSA density, index lesion PI-RADS score, and the number of lesions-were selected as covariates for the matching procedure. Propensity scores were calculated using logistic regression with biopsy technique (local vs. general anesthesia) as the dependent variable and the selected covariates as predictors. A matching caliper was created using propensity scores, and the nearest Mahalanobis distance was used for actual matching based on defined covariates. Before conducting this analysis, the treatment assignment, independence assumption, ignorability assumption, balance checking, overlap assumption, and caliper specification were met. The chi-square test was used to determine the statistical difference among categorical variables. All analyzes used a significance level of α=0.05.

The study protocol was approved by the Clinical Research Ethics Committee of Gazi University Faculty of Medicine (decision no: 104 , date: 07.02.2022).

Results

The clinical and radiological patient data are summarized in Table 1. Propensity distance matching was performed for homogenization for comparison (Table 2, Figure 1). After matching, 96 patients from the local anesthesia group and 50 patients from the sedoanalgesia group were included in the analysis. In the local anesthesia group, csPC was detected in 33 (34.4%) patients, whereas in the sedoanalgesia group, it was detected in 21 (42%) patients. No statistically significant difference was found between the two groups (p=0.365; Table 3). Regarding anesthesia complications, no adverse events were reported. However, some patients experienced fever within 48 h after the procedure. In the local anesthesia group, 3 patients (3.1%) developed fever, whereas in the sedoanalgesia group, 2 patients (4.0%) experienced the same symptoms. These patients were subsequently treated with parenteral antibiotics

Table 1. Clinical and radiological features of the patients

n	**313**
Age [median(range)] (years)	63 (58-68)
PIRADS n (%)	
3	91 (29.1%)
4	152 (48.6%)
5	70 (22.4%)
Total PSA [median(range)] (ng/dL)	6.4 (4.8-9.1)
MRI prostate volume [median(range)] (mm^3)	54 (40-175)
PSA density [median(range)] ($ng/dL/mm^3$)	0.116 (0.078-0.170)
Lesion length [median(range)] (mm)	12 (9-15)
The number of lesions n (%)	
Solitary	239 (76.4%)
Multiple	74 (23.6%)

PSA: Prostate specific antigen

Table 2. Before and after match analysis						
	Pre-match			Post-match		
	Local anesthesia (n=257)	Sedoanalgesia (n=56)	p-value	Local anesthesia (n=96)	Sedoanalgesia (n=50)	p-value
Age			0.75			0.735
Median	63	62.5		63.5	64	
Q1, Q3	57, 68	59, 67		59, 68	59, 68	
PSA density			0.015			0.449
Median	0.110	0.142		0.124	0.134	
Q1, Q3	0.077, 0.16	0.096, 0.202		0.087, 0.162	0.091, 0.183	
PI-RADS			0.182			0.909
3	80 (31.1%)	11 (19.6%)		15 (15.6%)	9 (18.0%)	
4	123 (47.9%)	29 (51.8%)		57 (59.4%)	28 (56.0%)	
5	54 (21.0%)	16 (28.6%)		24 (25.0%)	13 (26.0%)	
The number of lesions			0.192			0.710
Solitary	200 (77.8%)	39 (69.6%)		70 (72.9%)	35 (70.0%)	
Multiple	57 (22.2%)	17 (30.4%)		26 (27.1%)	15 (30.0%)	
PSA: Prostate specific antigen, PI-RADS: Prostate imaging-reporting and data system						

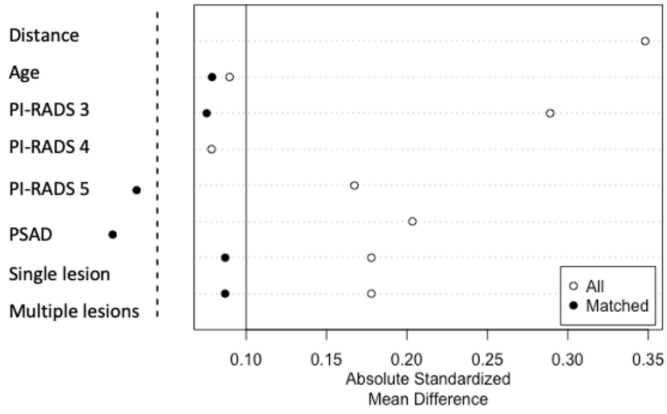

Figure 1. Distribution chart before and after the match

PI-RADS: Prostate imaging-reporting and data system, PSAD: Prostate specific antigen density

Table 3. csPC detection rates by anesthesia type			
	csPC	Benign	p-value
Local anesthesia n=96	33 (34.4%)	66 (65.6%)	0.365
Sedoanalgesia n=50	21 (42.0%)	29 (58.0%)	
csPC: Clinically significant prostate cancer			

after hospitalization. In addition, urinary retention occurred in 4 patients (4.1%) in the local anesthesia group and 2 patients (4.0%) in the sedoanalgesia group.

Discussion

Regardless of the application method (systematic/targeted), route (transrectal, transperineal), and anesthesia type, the most important goal of prostate biopsy is to determine the presence and degree of cancer. Although many studies have compared the detection rates of csPC for different application methods (7,8) and routes (15), research on the effect of anesthesia type on csPC detection rates is limited. Previous research has focused on the effect of anesthesia type on patient comfort and procedure-related complications. In our literature search, we found no studies that investigated the effect of anesthesia type (local vs. sedoanalgesia) on the csPC detection rate of targeted biopsies.

Biopsies taken under general anesthesia are more comfortable for both the patient and the physician (16). However, because of the significant time and cost associated with biopsies under general anesthesia, we only perform transrectal prostate biopsies under local anesthesia on patients with PZ lesions in our clinic. Local anesthesia causes fewer cardiac and pulmonary complications; however, it is unclear whether patients are under higher stress levels during the procedure than if they were under general anesthesia. General anesthesia can increase cardiopulmonary complications but may be less stressful for the patient (16). In our clinic, if there is a PIRADS ≥3 lesion with an anterior location, we perform targeted biopsy under sedoanalgesia. In targeted prostate biopsies performed transrectally on an anterior lesion, the biopsy needle must travel a longer distance in the prostate, causing more pain. Thus, real-time ultrasound and MRI matching may be disrupted because of patient movement, resulting in decreased biopsy quality.

We conducted a retrospective analysis of MR-TRUS-targeted prostate biopsy data and found no statistically significant difference in csPC detection rates between the local anesthesia and pseudoanalgesia groups for biopsies taken from PZ lesions. Similarly, Hogan et al. (17) compared prostate cancer detection rates in transperineal prostate biopsies based on anesthesia type and found no statistically significant difference between the general and local anesthesia groups. In a recent study by Kim et al. (18), sedation anesthesia was found to have a cancer detection rate statistically significantly higher than IRLI in 12-core systematic biopsies (34% vs. 29.2%, p=0.024). In the

same study, logistic regression analysis showed that sedation anesthesia was an independent predictor of cancer detection in patients with PSA levels <10 ng/mL (18). However, no data on the csPC detection rates were presented in the study. In the present study, we only compared csPC detection rates, and unlike the work of Kim et al. (18), we compared pseudoanalgesia and local anesthesia groups of patients who underwent targeted biopsy. We attribute the differing results of this study and those of Kim et al. (18) to these two factors. In a study by Temiz et al. (19), the authors compared the cancer detection rates of PPB and IRLI in 10-core systematic biopsy procedures and found a statistically significant difference in favor of PPB (25.4% vs. 19.8%, p=0.001). In the same study, patients in the IRLI group had significantly higher pain scores, as measured by the visual analog score (VAS). The authors explained the lower cancer detection rate in the IRLI group by theorizing that clinicians may not adequately sample the apex and far lateral parts of the prostate because of the relatively high pain experienced by patients in this group (19).

Prostate biopsies performed under local anesthesia are often well tolerated by patients. In their daily practice, clinicians tend to prefer local anesthesia for prostate biopsy because general anesthesia is associated with a risk of cardiopulmonary depression and increased cost (16). A meta-analysis of 47 randomized controlled studies found that a combination of PPB and intravenous sedation is the most effective method for reducing biopsy-related pain, followed by spinal anesthesia (20). In a study by Irani et al. (21) in which sextant TRUS biopsies were performed without anesthesia in 81 patients, an average patient pain value of 3 [on a scale of 0 (no pain)-10 (unbearable pain)] was measured using VAS, and the procedure was described as moderately uncomfortable. In the same study, 6% of patients stated that the procedure should be performed under general anesthesia, and 15% stated that they would prefer to undergo the procedure under any type of anesthesia if they needed to undergo a biopsy again (21). Pasali et al. (22) compared the types of local and regional anesthesia applied during transrectal prostate biopsy. The pain scores of the IRLI group were significantly higher than those of the PPB and caudal regional anesthesia groups (22). A meta-analysis of 25 randomized controlled studies found that PPB is an effective and safe method to reduce biopsy-related pain, whereas IRLI is less effective than PPB and not significantly different from a placebo method (23). In our routine practice, we do not use PPB for patients undergoing targeted prostate biopsy because we are concerned about possible mismatches in the registration of MRI and real-time ultrasound images due to the anatomical changes that occur after injection of local anesthetic into the periprostatic area. Therefore, we use IRLI for patients undergoing targeted biopsy.

Study Limitations

The most important limitation of our study is its retrospective design. Another limitation is that the biopsies were not performed by a single clinician.

Conclusion

While performing transrectal targeted prostate biopsy for lesions located in the PZ, csPC detection rates for local and sedoanalgesia are similar. Both types of anesthesia can be effectively used according to patient and physician preference.

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Ethics

Ethics Committee Approval: The study protocol was approved by the Clinical Research Ethics Committee of Gazi University Faculty of Medicine (decision no: 104 , date: 07.02.2022).

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