

The Effect of Obturator Nerve Blockade on Oncological Outcomes of Patients with Lateral Wall Localized Non-Muscle Invasive Bladder Cancer

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What's known on the subject? and What does the study add?

Prior research has established that transurethral resection of bladder tumors (TUR-BT) is the standard approach for non-muscle invasive bladder cancer (NMIBC), particularly those localized to the lateral wall. During this procedure, the stimulation of the obturator nerve can trigger adductor muscle contractions, potentially leading to complications like incomplete tumor resection, inadequate muscle tissue sampling, and bladder perforation. Obturator nerve blockade has been proposed as a method to mitigate these complications by preventing undesirable adductor muscle spasms. Various techniques, including ultrasound guidance, have been explored for obtaining effective obturator nerve blockade. This study contributes to the existing knowledge by investigating the impact of combining spinal anesthesia with ultrasound-guided obturator nerve blockade on oncological outcomes in patients with lateral wall localized NMIBC. The results demonstrate several key findings that add to the understanding of this topic. First, the combination of spinal anesthesia and obturator nerve blockade is associated with lower rates of tumor recurrence and progression compared to spinal anesthesia alone. Additionally, patients who underwent this combined approach had higher rates of complete resection and adequate detrussor muscle sampling in surgical specimens. These findings underscore the potential benefits of incorporating obturator nerve blockade into TUR-BT procedures for lateral wall localized NMIBC, enhancing patient outcomes and reducing perioperative complications.

Abstract

Objective: To investigate the effect of obturator nerve blockade on oncological outcomes of patients with a diagnosis of lateral wall localized non-muscle invasive bladder cancer.

Materials and Methods: One hundred six patients diagnosed with lateral wall localized non-invasive bladder cancer were evaluated between January 2015 and March 2020 in this retrospective, cross-sectional observational study. The patients were divided into two groups: patients receiving only spinal anesthesia and those receiving spinal anesthesia combined with ultrasound-guided obturator nerve blockade. Oncological outcomes of the groups were compared statistically.

Results: We observed recurrent tumors in 25 patients (45.5%) in Group 1 and 11 patients (21.6%) in Group 2. Additionally, we observed tumor progression in eight patients (14.5%) in Group 1 and two patients (3.9%) in Group 2. We observed statistical significance in differences between groups regarding tumor size, recurrence rate, adequate muscle tissue sampling, ability for complete resection, and persistent obturator reflex. The efficacy rate of obturator blockade was 92.1% in Group 2. One-year recurrence-free survival (RFS) was 98.0% and 5-year RFS was 23.5% for Group 1, while for Group 2, they were 97.4% and 57.2%, respectively.

Conclusion: The obturator reflex is a common and challenging reflex that may cause major complications and result in unintended consequences, such as incomplete resection or tumor recurrence with transurethral resection of bladder tumors. In this study, we demonstrated that combining spinal anesthesia with obturator nerve blockade for lateral wall localized non-muscle invasive bladder cancer may prevent tumor recurrence and reduce perioperative complications.

Keywords: Bladder cancer, non-muscle invasive bladder cancer, obturator nerve blockade, adductor contraction, bladder perforation, and nerve block

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Introduction

Bladder cancer is the sixth most common cancer in men in the United States (1). Transurethral resection of bladder tumor (TUR-BT) is an initial diagnostic and therapeutic procedure for non-muscle invasive bladder cancer (NMIBC). The most common complications related to tumor resection include minor bleeding and irritative symptoms in the early postoperative period. Major complications, including uncontrolled hematuria and bladder perforation, may occur in approximately 5% of cases (2).

The obturator nerve is located near the inferolateral bladder wall, and it arises from the anterior rami of the second, third, and fourth lumbar nerves, descends through the psoas major and emerges from the psoas major medial border. The nerve then crosses into the pelvis at the level of the sacroiliac joint. At this point, it courses close to the wall of the bladder (3). TUR-BT localized close to the lateral side of the bladder may stimulate the obturator nerve and trigger adductor contraction, possibly causing inadvertent bladder perforation or an incomplete resection due to the hindrance of the tumor resection. However, spinal anesthesia combined with obturator nerve blockade in the obturator canal may be effective in preventing the adductor spasm (4). Various strategies are recommended to prevent undesirable adductor contractions due to obturator nerve stimulation. For instance, the incidence of obturator nerve stimulation can be reduced through attention to technical strategies, decreasing the intensity of energy, avoiding overdistention of the bladder and using anesthetic paralysis or giving general anesthesia during the resection of lateral wall-localized tumors to decrease the obturator reflex response (5-7).

Most bladder cancers (70-75%) are NMIBC during the initial diagnosis, and tumor recurrence is more common in NMIBC. Nearly 30% of patients have tumor recurrence within the first 3 months of having TUR-BT, and 50% of patients have a recurrent tumor at the 1-year follow-up (8). The major causes of recurrent tumor have been reported to be residual tumor tissue due to an incomplete resection or inability to obtain adequate muscle tissue during TUR-BT (9). The obturator reflex that occurs during TUR-BT may increase the risk of incomplete resection of the tumor, inability to sample the muscle tissue or tumour dissemination via bladder perforation.

In this study, we investigated the effect of obturator nerve blockade on oncological outcomes in patients undergoing TUR-BT for lateral wall-localized NMIBC.

Materials and Methods

We designed a retrospective cross-sectional observational study that was conducted between January 2015 and March 2020. A total of 315 patients with a diagnosis of NMIBC localized

to the lateral wall of the bladder were analyzed at the İzmir Bakırçay University Çiğli Training and Research Hospital Urology Department and Recep Tayyip Erdoğan University Urology Department. Patients with a history of previous TUR-BT, diagnosis of non-urothelial carcinoma, coagulopathy, history of allergic reaction to the local anesthetic agent, presence of muscle invasive bladder cancer, history of chemotherapy or radiotherapy before TUR-BT, presence of variant histopathology, use of bipolar energy for the resection of bladder tumor, the presence of concomitant upper urothelial tract urothelial carcinoma, neuromuscular disease, pregnancy, or history of medication affecting the immune system were excluded. Of the initial 315 patients, 209 were excluded from the study, and the remaining 106 patients were included (Figure 1). After local ethical committee permission was received (Recep Tayyip Erdoğan University Non-Invasive Clinical Research Ethics Committee; number: 2020/131, date: 01.07.2020), data from the patients with a diagnosis of NMIBC were recorded retrospectively from the hospital patient record system. Patients' demographic characteristics, localization, largest tumor size, histopathological type of tumor, presence of recurrence and/or progression, time to recurrence from initial TUR-BT, presence of muscle tissue in the surgical specimen, inability to complete resection, death from cancer, and both perioperative and postoperative complications were recorded for further statistical analyses.

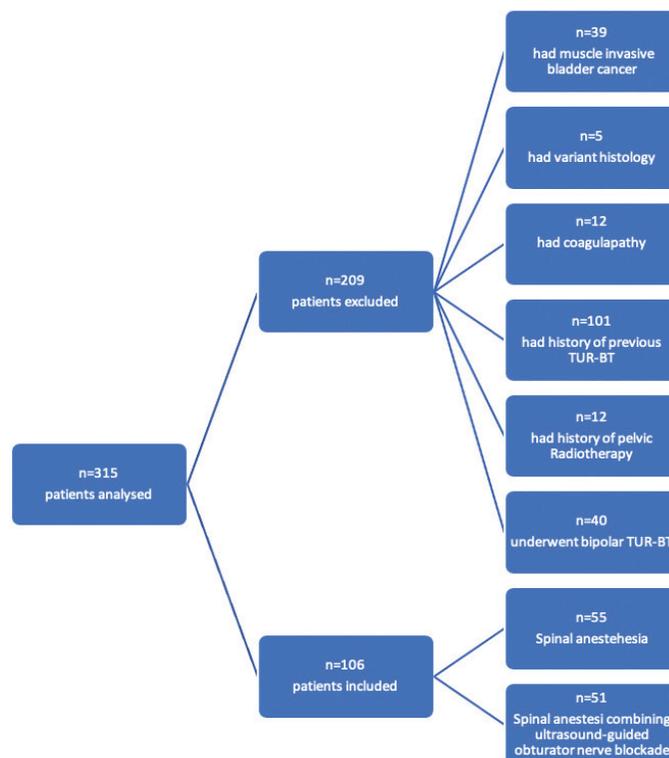


Figure 1. Clinical course of the study

All TUR-BT procedures were performed using monopolar energy for the resection of the tumor with a 26 Fr Karl-Storz resectoscope under 30-degree optical vision with adjustment to 120 joules for cutting and 80 joules for coagulation. Spinal anesthesia was performed in the operating room with the patient in a sitting position. The 25-gauge Quincke needle was inserted at the level of the L3-4 or L4-5 intervertebral space, and 10-15 mg of 2-3 mL 0.5% hyperbaric bupivacaine was administered through the needle into the subarachnoid space before the patient was repositioned to a supine position. After waiting for 10 min, and when sensorial blockade up to the T10 dermatome was observed, a lithotomy position was performed. Additional obturator nerve blockade with ultrasound guidance was performed according to the localization of the tumor. First, the antero-medial side of the femur was demonstrated with a two-dimensional 38 mm, 6-13 MHz ultrasound probe (Mindray, M7, Biomedical Electronics Co., Shenzhen, China). Afterward, a high-frequency probe was placed proximal to the adductor longus muscle to determine the adductor longus, brevis, and magnus muscles. When the obturator nerve was demonstrated between the muscle groups, the position of the nerve was confirmed by setting the current of the stimulator (Braun Stimuplex HNS11, B. Braun, Melsungen, Germany) to 1.5-2 mA and the duration of 0.1 ms. Using ultrasound vision, a 50 mm needle (21-gauge, 50 mm Stimuplex A, B. Braun, Melsungen, Germany) was inserted parallel to the long axis of the probe and guided to the anterior branch of the obturator nerve. After adductor contractions were observed at 0.3-0.5 mA, a maximum of 10 mL 2% lidocaine was injected through the needle. Surgery began 10 min later. During the surgery, patients were monitored using non-invasive blood pressure, pulse, and SpO₂ intraoperative electrocardiography.

Meta-analyses have reported no statistically significant differences between bipolar and monopolar TUR-BT in terms of obturator reflex and bladder perforation rates (10,11). In our study, all patients underwent monopolar TUR-BT due to the presence of controversial results in comparisons of bipolar versus monopolar techniques and current urology guidelines giving strong advice to use monopolar TUR-BT (12). Patients were divided into two groups according to the anesthesia used. While only spinal anesthesia was performed in Group 1, spinal anesthesia was combined with ultrasound-guided obturator nerve blockade according to the localization of the tumor for Group 2. The groups were compared statistically in terms of oncological outcomes. In patients with an incomplete resection, another TUR-BT was performed 4-6 weeks after the first TUR-BT. Intravesical immunotherapy using Bacillus Calmette-Guerin (BCG) was performed based on pathological results and recommendations of the European Urology Guidelines for non-muscle invasive bladder cancer.

The first follow-up was performed with all patients the third month after the initial TUR-BT, and subsequent follow-ups were performed every 3 months up to 2 years, then every 6 months up to 5 years and 1 per year after 5 years. A detailed history, physical examination, cystoscopic examination, and urinary cytology were collected at each follow-up (12).

Statistical Analysis

All statistical analyses were conducted using the SPSS Statistics 26.0 (IBM Inc., Armonk, NY, US) software package. Categorical variables were described with frequencies and percentages; continuous variables were described with means and standard deviations. The Kolmogorov-Smirnov test was used to evaluate the normality of the distributions, and the Mann-Whitney U test was used to compare groups and quantitative independent data. The chi-square test was used for qualitative independent data. Spearman's correlation analysis was applied for correlation, and the Kaplan-Meier test was used to calculate survival statistics. A p-value less than 0.05 was chosen as the criterion for statistical significance.

Results

The mean age of the patients was 64.71±11.70 years. The mean follow-up time was 39.75±14.61 months. There were 85 (80.2%) male patients and 21 (19.8%) females. A total of 40 patients (37.7%) underwent a second TUR-BT after the initial TUR-BT due to incomplete resection or absence of muscle tissue sampling in the surgical specimens. In terms of complications, three patients (2.8%) had bladder perforation, six patients (5.7%) had hematuria and 10 patients (9.4%) had cystitis. All patients who had bladder perforation were extraperitoneal and managed with catheterization. No patient needed open laparotomy for bladder perforation.

In Group 1, 55 patients (51.9%) underwent TUR-BT with only spinal anesthesia, and 51 patients (48.1%) underwent TUR-BT using spinal anesthesia combined with ultrasound-guided obturator nerve blockade (Group 2). In all, the efficacy rate of the obturator nerve blockade was 92.1%. The patients' initial characteristics, which were collected during the first diagnosis, are summarized in Table 1. Recurrent tumor was observed in 25 patients (45.5%) in Group 1 and 11 patients (21.6%) in Group 2. Additionally, tumor progression was observed in eight patients (14.5%) in Group 1 and two patients (3.9%) in Group 2. For all patients, the 1-year overall recurrence-free survival (RFS) was 99.0%, whereas the overall 5-year RFS was 49.3%. In Group 1, the 1-year RFS was 98.0% and the 5-year RFS was 23.5%. In Group 2, the 1-year and 5-year RFSs were 97.4% and 57.2%, respectively (Figure 2).

Single-dose adjuvant chemotherapy was administered to 22 patients (40.0%) in Group 1 and 18 patients (35.3%) in Group 2. Adjuvant intravesical immunotherapy was administered to 20 patients (36.4%) in Group 1 and 21 patients (41.2%) in Group 2.

Table 1. Patients' initial characteristics at diagnosis	
Age, mean ± standard deviation (SD), years	64.71±11.70
Gender, n (%)	
Male	85 (80.2%)
Female	21 (19.8%)
Diabetes mellitus, n (%)	
Present	87 (82.1%)
Absent	19 (17.9%)
Hypertension, n (%)	
Present	66 (62.3%)
Absent	40 (37.7%)
Tumor size, mean ± SD, mm	3.21±1.43
Tumor localization, n (%)	
Left	62 (58.5%)
Right	44 (41.5%)
T stage, n (%)	
Ta	72 (67.9%)
T1	34 (32.1%)
Grade, n (%)	
Low grade	68 (64.2%)
High grade	38 (35.8%)
Recurrence, n (%)	
Present	36 (34.0%)
Absent	70 (66.0%)
Progression, n (%)	
Present	10 (9.4%)
Absent	96 (90.6%)

Maintenance immunotherapy could be completed in 14 patients (25.5%) in Group 1 and 10 patients (19.6%) in Group 2. 22 (88.8%) patients had a recurrent tumor and 8 (40.3%) had tumor progression, although received intravesical immunotherapy with BCG in group 1. In Group, 11 (4.7%) patients had a recurrent tumor and 2 (9.5%) had tumor progression, although received immunotherapy with BCG ($p<0.001$). While no death due to bladder cancer was observed in our study, one patient died from acute myocardial infarction. The oncological outcomes of the groups are summarized in Table 2. Statistical significance was observed in differences between the groups in terms of tumor size, recurrence rate, adequate muscle tissue sampling, ability to complete resection, and persistent obturator reflex. In the Spearman's correlation analysis, we observed a positive correlation between obturator nerve blockade and tumor size, adequate muscle tissue sampling, and ability to complete the resection. There were also negative correlations of the obturator nerve blockade with tumor recurrence and persistent obturator reflex (Table 3).

Discussion

In this study, we investigated the effects of an obturator nerve blockade on oncological outcomes in patients who underwent TUR-BT. The results revealed that ultrasound-guided obturator nerve blockade combined with spinal anesthesia was associated with lower rates of tumor recurrence and tumor progression and better rates of RFS, tumor size, adequate muscle tissue, and complete resection. The ultrasound-guided obturator nerve blockade combined with spinal anesthesia correlated positively with tumor size, adequate muscle tissue sampling and complete resection rates and a negative correlation with tumor recurrence and persistent obturator reflex.

TUR-BT is the gold standard method for both the initial diagnosis and treatment of patients with NMIBC. The frequency of severe adductor muscle contractions during the transurethral resection of laterally located bladder tumors has been reported to be approximately 20% (13). Major complications, such as bladder perforation and excessive hemorrhage, incomplete resection of tumor and inadequate sampling of muscle tissue in surgical specimens, may occur during resection due to adductor muscle contractions via stimulation of the obturator nerve (14). To prevent this undesirable adductor reflex, obturator nerve blockade with ultrasound guidance was recommended in several studies (5,15,16). First, Labat (17) described an obturator nerve blockade with a nerve stimulator in 1922. Afterwards, Wassef (18) described the inter-adductor approach, Khorrami et al. (2) described the transvesical approach using a nerve stimulator, Choquet et al. (19) studied the inguinal approach to block the obturator nerve, and several studies have compared sonographic

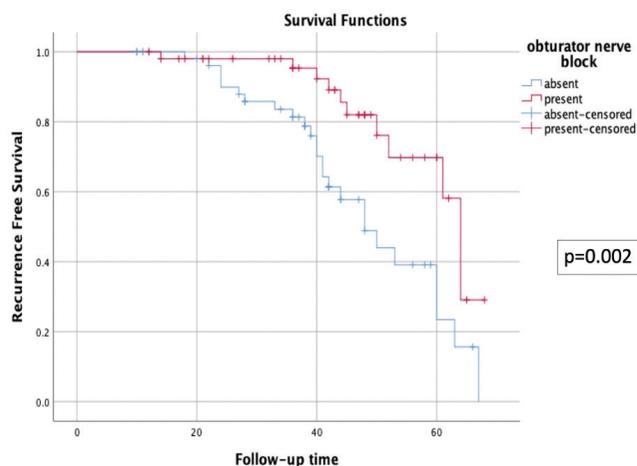


Figure 2. Group Kaplan-Meier curves in terms of recurrence-free survival

	Group 1 n=55	Group 2 n=51	p-value
Tumor size, mean ± standard deviation (SD), mm	2.90±1.43	3.55±1.37	0.030
T stage, n (%)			0.131
Ta	41 (74.5%)	31 (60.8%)	
T1	14 (25.5%)	20 (39.2%)	
Grade, n (%)			0.057
Low grade	40 (72.7%)	28 (54.9%)	
High grade	15 (27.3%)	23 (45.1%)	
Muscle tissue sampling, n (%)			0.010
Absent	15 (27.3%)	4 (7.8%)	
Present	40 (70.2%)	47 (92.2%)	
Resection, n (%)			0.021
Incomplete	10 (18.2%)	2 (3.9%)	
Complete	45 (81.8%)	49 (96.1%)	
Obturator reflex, n (%)			0.003
Absent	38 (69.1%)	47 (92.2%)	
Present	17 (30.9%)	4 (7.8%)	
Recurrence, n (%)			0.010
Absent	30 (54.5%)	40 (78.4%)	
Present	25 (45.5%)	11 (21.6%)	
Progression, n (%)			0.106
Absent	47 (85.5%)	49 (96.1%)	
Present	8 (14.5%)	2 (3.9%)	
Time to recurrence mean ± SD, months	4.44±6.02	7.76±15.66	0.097
Complications, n (%)			0.117
Hematuria	5 (9.1%)	1 (2.0%)	
Cystitis	5 (9.1%)	5 (9.8%)	
Bladder perforation	3 (5.5%)	0	

	Obturator nerve blockade	Presence of muscle tissue	Complete resection	Tumor size	Recurrence	Progression	Time to recurrence	Complication
Obturator nerve blockade	1							
Presence of muscle tissue	0.253**	1						
Complete resection	0.225*	0.532**	1					
Tumor size	0.208*	0.089	0.056	1				
Recurrence	-0.252**	-0.132	-0.058	0.039	1			
Progression	-0.182	-0.102	-0.088	-0.038	0.382**	1		
Time to recurrence	-0.162	-0.055	-0.015	0.038	0.955**	0.393**	1	
Complication	-0.153	0.032	-0.049	0.044	0.179	0.106	0.142	1

Values in bold are statistically significantly different. *p<0.05, **p<0.01

demonstrations of obturator nerve-to-nerve stimulation methods (20). In a recent study, Smith described a combined ultrasound and nerve stimulator approach (21). Despite all of these techniques effectively blocking the obturator nerve, undesirable adductor muscle spasms may still occur during TUR-BT, even when an obturator nerve block is performed correctly, due to variations in the obturator nerve's ramifications (22). The efficacy rate of obturator nerve blockade is between 84% and 96%, according to several studies (23,24). In our study, we performed a combination of ultrasound guidance and nerve stimulator to block the obturator nerve, and our efficacy rate was 92.1%, meaning it was as effective as the rates reported in other studies.

Although an obturator nerve blockade is an intervention that reassures physicians during surgery and reduces the rate of perioperative complications, its contribution to oncological outcomes is not yet clear. Erbay et al. (25) showed that patients with lateral wall-localized NMIBC who underwent spinal anesthesia combined with obturator nerve blockade had longer RFS than patients who received only spinal anesthesia. In addition, rates of complete resection and the presence of muscle tissue in the surgical specimen were higher in patients who received an obturator nerve blockade combined with spinal anesthesia (25). Tekgül et al. (16) reported that patients with a lateral wall-localized bladder tumor and where an obturator nerve blockade was used had a prolonged time to recurrence compared to patients without an obturator nerve blockade. We observed a significantly increased RFS in patients who received an obturator nerve blockade, but we did not find any significant difference in prolonged time to recurrence.

The presence of detrusor muscle tissue in the specimen provides accurate pathologic staging that allows for the determination of an adequate follow-up protocol and potential adjuvant treatment according to tumor grade and invasiveness. Additionally, a complete resection of all tumor tissues significantly reduces the risk of NMIBC recurrence and progression. Understaging of NMIBCs at the first resection due to the lack of detrusor muscle in the resected specimen is reported in up to 49% of patients, compared with 14% for patients with adequate muscle tissue sampling (26,27). In our study, we found lower inadequate muscle tissue sampling and higher detrusor muscle complete resection rates in the obturator nerve blockade group.

The recurrence rate in the first year after an incomplete resection is 15–61% in Ta and T1 tumors (12). The presence of residual tumor tissue after a TUR-BT procedure increases recurrence rates and decreases RFS. One study investigating the presence of residual tumor in the marginal resection after a complete TUR-BT of Ta/T1 transitional urinary bladder cancer reported that 26% of patients had residual tumor tissue after a complete

resection of Ta/T1 bladder tumors (28). This possibility increases further with undesirable conditions, such as the obturator reflex during the resection of tumors located in the lateral wall of the bladder. Our results were similar. In our study, RFS was longer in patients who underwent spinal anesthesia combined with obturator nerve blockade, and no patients had tumor progression. Moreover, we observed that patients who received an obturator nerve blockade had a higher pathological T stage according to the TNM classification and decreased recurrence progression rates compared with patients who did not receive an obturator nerve blockade.

Another challenging complication due to adductor spasm from stimulation of the obturator nerve during resection is bladder perforation. Several studies have reported bladder perforation due to the obturator reflex in 0.9% to 5% of cases (29,30). Bladder perforation can lead to extravesical dissemination of the tumor (31). In our study, only three patients (2.8%) had extraperitoneal bladder perforation, and they were treated with only a urinary catheter. Open laparotomy was not required in any patient with bladder perforation, and no pelvic mass was observed at follow-ups due to extravesical tumor dissemination.

Study Limitations

This study has some limitations. First, due to the retrospective design of the study, randomization could not be included. Second, the study population was small, and due to the population size, we could not reach statistical significance in terms of some variables, such as time to recurrence.

Conclusion

This study revealed that patients with NMIBC localized to the lateral wall of the bladder who received an obturator nerve blockade combined with spinal anesthesia had a significantly increased RFS, decreased major perioperative complication rate, increased rate of complete resection, and adequate detrusor muscle sampling. The obturator nerve blockade combined with spinal anesthesia also contributed to the correct staging of patients with lateral wall-localized NMIBC, which plays a critical role in subsequent treatment.

Ethics

Ethics Committee Approval: After local ethical committee permission was received (Recep Tayyip Erdoğan University Non-Invasive Clinical Research Ethics Committee; number: 2020/131, date: 01.07.2020).

Informed Consent: Informed consent was obtained.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: E.D., A.Ç., Ö.E., Concept: M.O.H., H.E., Design: M.O.H., H.E., Data Collection or Processing: M.O.H., Analysis or Interpretation: M.O.H., Literature Search: M.O.H., Writing: M.O.H., H.E., S.K., H.A.

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