The Obturator Nerve Reflex after Thulium Laser vs. Monopolar Transurethral Resection of Bladder Tumors: A Randomized Clinical trial

Vahid Abedi Yarandi[1], Fatemeh Khatami[1], Seyed Mohammad Kazem Aghamir[1]*

Purpose: Obturator nerve reflex is the surgery treatment side effect in patients with bladder cancers. This study was run to determine the obturator nerve reflex by Thulium laser versus monopolar Transurethral Resection of Bladder Tumors (TURBT).

Materials and methods: After receiving the approval code IRCT20190624043991N4, one hundred and eighty-nine patients with bladder tumors from 2010 to 2016 were assessed, and among them, 35 patients were randomly assigned into two groups in a blinded manner; the first group (16 patients) received thulium laser and the second group (19 patients) were patients undergoing monopolar transurethral resection of bladder tumor after spinal analgesia. Clinical data, including different variables such as; age, tumor characteristics, gender, operation duration, types of leg jerking, and intraoperative complications, were recorded. The site of the obturator nerve was determined by nerve stimulation, anatomical landmarks, and ultrasonography. Leg jerking was compared in both groups.

Results: Of the 35 patients, 28 cases were male, and 7 points were female. The mean ± SD (range) of age was 62.0 ± 6.9 (40-75) years in the Thulium laser group and 64.0 ± 7.1 (41-77) years in the monopolar TURBT group. The mean operation time was not different between the two groups significantly ($P > 0.05$). Leg jerking was reported in 25% and 63.1% of the patients in Thulium laser and monopolar TURBT groups, respectively ($P < 0.05$).

Conclusion: Thulium laser is a more feasible and effective method to prevent leg jerking in patients with bladder cancer; so, it is recommended more than monopolar Transurethral.

Keywords: monopolar TURBT; thulium laser; non-muscle-invasive bladder tumor; leg jerking

INTRODUCTION

Bladder cancer is one of the most common cancers worldwide, and about 430000 new cases of bladder cancer were reported in 2012 [(1)]. One of the treatment strategies for bladder cancer is transurethral resection of the bladder tumor (TUR-BT), resulting in long-term survival rates of 40%-60% [(2)]. However, TUR-BT is unfortunately associated with some essential substantial morbidities and complications such as obturator nerve reflex (ONR) and consequently adductor muscles contraction that we call "Leg Jerking"[(3, 4)]. It happens because the obturator nerve extends through the lateral wall of the bladder[(5,6)]. It may result in bladder perforation that is a risky event in these patients[(4, 5)]. General anesthesia and local muscle relaxant injections are the suggested preferred methods of anesthesia in these patients.

Different laser types are recommended for bladder cancers or upper urinary tract urothelial tumors[(7)]. Holmium yttrium aluminum garnet laser (Ho: YAG) is effective but has disadvantages, including limited tissue collection for pathological studies[(8,9)]. In 2005, the new technique of thulium laser (Tm: YAG) was suggested surgically generating a wavelength of 2 µm, which is much more helpful for resection in an aqueous medium [(10)]. The use of thulium laser came to be the appropriate option in reducing leg jerking[(11,12)]. This study was performed to compare the obturator Nerve reflex by Thulium laser versus monopolar Transurethral Resection of Bladder Tumor.

MATERIALS AND METHODS

The Ethics Committee approved the study of the School of Medicine- Tehran University of Medical Sciences (IR.TUMS.MEDICINE.REC.1396.4657) and the Iranian Registry of Clinical Trials (IRCT20190624043991N4). This study was designed based on clinical trial policies, and two groups of patients were blindly randomized into the two different intervention groups. After completing informed consent forms by patients, 189 patients with bladder tumors were referred to the study from 2010

[1]Department of Urology, The Affiliated Changzhou No. 2 People's Hospital of Nanjing Medical University, Changzhou 213003, Jiangsu, China.
[2]Dalian Medical University, Dalian, Liaoning, China.
*Correspondence: Lifeng Zhang, Department of Urology, The Affiliated Changzhou No. 2 People's Hospital of Nanjing Medical University, Changzhou 213003, Jiangsu, China.
Tel:+86 519 88123501. E-mail: nj-likky@163.com.
**Department of Urology, The Affiliated Changzhou No. 2 People's Hospital of Nanjing Medical University, Changzhou 213003, Jiangsu, China.
PHONE:+86 519 88123501. E-mail: zuoli1978@hotmail.com.
Received September 2019 & Accepted July 2021

Table 1. Grade of Leg Jerking

Grade 1	Horizontal leg jerking at site without movement
Grade 2	Horizontal and vertical leg jerking with movement
Grade 3	Horizontal and vertical leg jerking with movement from location

to 2016. Inclusion criteria were filling out the consent form, high risk of general anesthesia for surgery, and bladder tumor presence at the obturator nerve site, which included posterior-lateral, trigone area (**Figure 1**). Patients in their clinical examination and their previous clinical records had no history of neurologic disease (such as multiple sclerosis, stroke, and Parkinson's disease, diabetes, or discopathy that can affect spinal reflexes. The patients were excluded if there were muscle invasion, tumor recurrence, metastasis, present neurologic disease or history of neurologic disease, patient death, and failure to cooperate and follow-up for treatment. But the grade of leg jerking (a novel grade that we describe bettering comparison in different categories) effect was not significant (**Table 1**). The site of the obturator nerve was determined by nerve stimulation, anatomical landmarks, and ultrasonography. The obturator nerve is found by probing through the known location of the nerve[4].

Inside a box were two similar folded papers (A and B), each patient took one of them. The nurse has written it down, and all have been done blindly and randomly. When the operating room was reached, standard anesthesia monitors were used, and the patients were preloaded intravenously with 500 ml 0.9% normal saline. Spinal anesthesia was performed in both groups with a 25 G Quincke needle in the space L3-4 or L4-5 in a sitting position.

After confirming the presence of clear flowing cerebrospinal fluid in the syringe barrel, 10 mg of 0.5% bupivacaine was administered. The patients were in Trendelenburg position for 5 or 10 minutes at an angle of 15 °. If the block of the sensory level was above the T10 level, the patients were placed in the lithotomy position, and the thulium laser or monopolar TURBT was performed.

The thulium laser was used in the first group (16 patients), while monopolar TURBT was performed in a blinded manner in the second group (19 patients).

Clinical data, including age, gender, tumor features, operation duration, types of leg jerking, and some intraoperative complications, were recorded. Leg jerking and period of the procedures were compared. Thulium laser was eradicated by the recruited device (Siemens Company, Germany) with extension and power of 5 mm and 200j/sec. The bladder was half-filled during the procedure, and TURBT was started. The same surgeon did all procedures.

Data analysis was performed among 35 cases, including 16 in Laser and 19 in the standard group. Data analysis was performed by SPSS (version 22.0) software [Statistical Procedures for Social Sciences; Chicago, Illinois, USA]. Inter-group comparisons were performed using the One-Way Analysis test of variance or Independent-Sample-T test for continuous variables and Chi-Square and Fisher tests for categorical variables. P-values less than 0.05 were considered to be statistically significant.

RESULTS

All 35 patients were randomized to receive the thulium laser (n = 16) or the monopolar TURBT (n = 19). Patient and tumor features before surgeries were alike in both groups and are reported in Table 2. There were 28 male and seven female patients. All patients had sufficient specimens for making an accurate diagnosis, including tumor grading and staging. Of the 35 patients, 25 had low-grade tumors, and 10 had high-grade tumors (**Table 2**).

The mean operation time was no difference between the two groups significantly ($P > 0.05$; Table 3). In four patients in the thulium, the laser group experienced intraoperative leg jerking, including 3 with horizontal leg jerking at the site without movement (Grade 1), 1 with horizontal and vertical leg jerking with movement (Grade 2), and no patient with horizontal and vertical leg jerking with movement from the location. In the monopolar TURBT group, 12 patients experienced intraoperative leg jerking, including 5 with horizontal leg jerking at the site without movement (Grade 1), 3 with horizontal and vertical leg jerking with movement (Grade 2), and 4 with horizontal and vertical leg jerking with movement from location ($P < 0.05$; **Table 3**). There was no complication of bladder perforation and severe bleeding in the thulium laser group, but one patient had bladder perforation, and one patient had severe bleeding during the monopolar TURBT ($P > 0.05$; **Table 3**). No mortality was reported during the operations.

DISCUSSION

Obturator nerve stimulation during TURBT under spinal anesthesia may lead to obturator reflex, adductor

Table 2. Demographic and tumor features in patients with non muscle-invasive bladder tumor, treated with thulium laser or monopolar TURBT.

Variable	Thulium laser (n =16)	Monopolar TURBT (n =19)
Male	13 (81.3)	15 (78.9)
Female	3 (18.8)	4 (21.1)
Age, years	62.0 ± 6.9 (40-75)	64.0±7.1 (41-77)
Tumor size, cm	3.3 ± 1.6 (1.5-5.0)	3.5 ± 1.1 (1.7-5.0)
Tumor location		
Right side	9 (56.3)	10 (52.6)
Left side	7 (43.8)	9 (47.4)
Tumor grade		
Low grade	11 (68.8)	14 (73.7)
High grade	5 (31.2)	5 (26.3)

Data reported as n (percent) or mean±SD (range).

Table 3. Operative features of patients with non-muscle-invasive bladder tumor, treated with thulium laser or monopolar TURBT

Variable	Thulium laser (n=16)	Monopolar TURBT (n=19)	*P*-value
Operation duration	32.0 ± 13.5 (25-80)	34.0 ± 11.8 (28-82)	*P* =. 64
Leg Jerking Grade			
Grade 1	3 (18.8)	5 (26.3)	*P* = *.007
Grade 2	1 (6.2)	3 (15.8)	
Grade 3	0 (0)	4 (21.1)	
Total	4 (25)	12 (63.1)	
Complications			
Severe bleeding	0 (0)	1 (0.1)	*P* =. 36
Bladder perforation	0 (0)	1 (0.1)	*P* = .36
Incomplete Surgery	0 (0)	0 (0)	*P* > 0.05

Data reported as n (percent) or mean ± SD (range). * P-value less than 0.05 is considered as the significantly meaningful one.

contraction, and leg jerking with complications such as bladder perforation, bleeding more than incomplete tumor resection[4,8]. Some studies report that the thulium laser is superior to TURBT[13]. However, none of the TURBT side effects were seen in our patients in the laser group. Our result confirmed that the use of thulium laser would lead to higher efficacy than the monopolar TURBT method. Different modalities, such as partial filling of the bladder during TURBT, reduction of resectoscope current intensity, resecting the tumor on the thinner slices, utilization of bipolar or Laser resectoscopes, and using general anesthesia and muscle relaxants together, are used to avoid different complications during surgery to reduce the rate of jerking legs[14-16].

Migliari et al. reported that Thulium laser could be the potential alternative to TURBT and nowadays is considered the standard for diagnosis and treatment of Non-muscle invasive bladder cancer (NMBIC)[17]. In his study, the thullium laser provided a detailed report of neoplastic depth contamination, indicating the possibility of a second resection within 90 days. Before delivery, all different parts of bladder cancer can be combined with thulium lasers, which has the advantage of monopolar energy, especially when the tumor is in the lateral wall of the bladder, the bladder dome, or the perimeatal region[17,18].

Figure1. CT scan of a patient with a non muscle-invasive bladder tumor

The Nd: YAG does not significantly affect the treatment of lower urinary tract transitional cell carcinoma. Ho: YAG and Tm: YAG seem to offer alternatives in the treatment of bladder cancer, but to prove their potential effects in more significant prospective, randomized controlled studies with long-term follow-up should be done[19,20]. Ozer et al.[21] showed that bipolar bladder tumor resection was not superior to monopolar resection significantly than an obstructive reflex and bladder perforation. However, we found a significant difference was also demonstrated by Balci et al.[22], stating that efficacy and safety of monopolar and bipolar methods are comparable in patients with bladder tumors. Venkatramani and his colleagues reported that bipolar TURBT is not superior to monopolar resection in leg jerking, bladder perforation, and bleeding[23]. This same result was also found in our research study. In our tertiary care center, a large number of patients are operated on for bladder malignancies. Most of these patients are elderly with various comorbidities. Spinal anesthesia is preferred over general anesthesia in these patients. However, the ON stimulation during the procedure with subsequent obturator jerk makes spinal anesthesia less popular among our surgeons.

H Liu has shown that the 2-micron laser resection method effectively reduces operative and postoperative complications compared to TURBT but has no other benefits in tumor recurrence. However, patients with multiple non-muscle-invasive bladder tumors were randomized to receive the TURBT or the 2-µm Laser in a non-blind clinical trial. At the same time, our study was designed as a blind randomized clinical trial[7]. Moreover, Yunjin performed a systematic meta-analysis review and stated that laser techniques are practical, safe, and effective and provide an alternative treatment for non-muscle-invasive bladder tumors. Because some limitations cannot be met, well-designed RCTs are needed to confirm their results[20]. Mario W. Kramer, in a systematic review, concluded that lasers are potentially useful options for conventional TURBTs, but systematic evaluation using standard classification systems and well-designed RCTs are needed to compare results meaningfully[24].

CONCLUSIONS

Totally, according to the obtained results in the current study, the use of Thulium laser is a more feasible and effective method to prevent leg jerking in patients with a bladder tumor, and the use of this method is suggested. However, further studies with a larger sample size

are required to attain more definite results.

ACKNOWLEDGMENTS

Special thanks to Urology Research Center (URC), Tehran University of Medical Sciences (TUMS). Thanks to Mrs. Bita Pourmand as well.

CONFLICT OF INTEREST

All authors declare that there is not any conflict of interest.

REFERENCES

1. Antoni S, Ferlay J, Soerjomataram I, Znaor A, Jemal A, Bray F. Bladder cancer incidence and mortality: a global overview and recent trends. Eur Urol. 2017;71:96-108.
2. Ibrahim SM, Mohamed E, Elsharawy I, Kamal K. Transurethral resection of bladder tumor (TUR-BT) then concomitant radiation and cisplatin followed by adjuvant gemcitabine and cisplatin in muscle invasive transitional cell carcinoma (TCC) of the urinary bladder. J Egypt Natl Canc Inst. 2007;19:77-86.
3. Golan S, Baniel J, Lask D, Livne PM, Yossepowitch O. Transurethral resection of bladder tumour complicated by perforation requiring open surgical repair–clinical characteristics and oncological outcomes. BJU international. 2011;107:1065-8.
4. Augspurger RR, Donohue RE. Prevention of obturator nerve stimulation during transurethral surgery. The Jou of Urol. 1980;123:170-2.
5. Jo SY, Chang JC, Bae HG, Oh J-S, Heo J, Hwang JC. A morphometric study of the obturator nerve around the obturator foramen. J Korean Neurosurg Soc.. 2016;59:282.
6 Locher S, Burmeister H, Böhlen T, Eichenberger U, Stoupis C, Moriggl B, et al. Radiological anatomy of the obturator nerve and its articular branches: basis to develop a method of radiofrequency denervation for hip joint pain. PAIN MED. 2007;9:291-8.
7. Liu H, Wu J, Xue S, Zhang Q, Ruan Y, Sun X, et al. Comparison of the safety and efficacy of conventional monopolar and 2-micron laser transurethral resection in the management of multiple nonmuscle-invasive bladder cancer. J Int Med Res. 2013;41:984-92.
8. Kramer MW, Bach T, Wolters M, Imkamp F, Gross AJ, Kuczyk MA, et al. Current evidence for transurethral laser therapy of non-muscle invasive bladder cancer. World J. Urol. 2011;29:433-42.
9. Soler-Martínez J, Vozmediano-Chicharro R, Morales-Jiménez P, Hernández-Alcaraz D, Vivas-Vargas E, García-Vaquero IS, et al. Holmium laser treatment for low grade, low stage, noninvasive bladder cancer with local anesthesia and early instillation of mitomycin C. The Jou of Urol. 2007;178:2337-9.
10. Bach T, Xia S, Yang Y, Mattioli S, Watson G, Gross A, et al. Thulium: YAG 2 µm cw laser prostatectomy: where do we stand? World J. Urol. 2010;28:163-8.
11. Bolat D, Aydogdu O, Tekgul ZT, Polat S, Yonguc T, Bozkurt IH, et al. Impact of nerve stimulator-guided obturator nerve block on the short-term outcomes and complications of transurethral resection of bladder tumour: A prospective randomized controlled study. Can Urol Assoc J. 2015;9:E780.
12. Shah NF, Sofi KP, Nengroo SH. Obturator nerve block in transurethral resection of bladder tumor: a comparison of ultrasound-guided technique versus ultrasound with nerve stimulation technique. Anesth. Essays Res. 2017;11:411.
13. Kati B, Izgi M. A nightmare during endoscopic bladder tumor resection: obturator reflex. J Turgut Ozal Med Cent. 2017;24:371-4.
14. Ploussard G, Daneshmand S, Efstathiou JA, Herr HW, James ND, Roedel CM, et al. Critical analysis of bladder sparing with trimodal therapy in muscle-invasive bladder cancer: a systematic review. Eur Urol. 2014;66:120-37.
15. Smith ZL, Christodouleas JP, Keefe SM, Malkowicz SB, Guzzo TJ. Bladder preservation in the treatment of muscle-invasive bladder cancer (MIBC): a review of the literature and a practical approach to therapy. BJU international. 2013;112:13-25.
16. Russell CM, Lebastchi AH, Borza T, Spratt DE, Morgan TM. The role of transurethral resection in trimodal therapy for muscle-invasive bladder cancer. Bladder Cancer. 2016;2:381-94.
17. Migliari R, Buffardi A, Ghabin H. Thulium laser endoscopic en bloc enucleation of nonmuscle-invasive bladder cancer. J. Endourol. 2015;29:1258-62.
18. Xu H, Ma J, Chen Z, Yang J, Yuan H, Wang T, et al. Safety and Efficacy of En Bloc Transurethral Resection With 1.9 µm Vela Laser for Treatment of Non–Muscle-invasive Bladder Cancer. Urol. 2018;113:246-50.
19. Teng J-f, Kai W, Lei Y, Qu F-j, Zhang D-x, Cui X-g, et al. Holmium laser versus conventional transurethral resection of the bladder tumor. LWW; 2013.
20. Bai Y, Liu L, Yuan H, Li J, Tang Y, Pu C, et al. Safety and efficacy of transurethral laser therapy for bladder cancer: a systematic review and meta-analysis. World J. Surg. Oncol 2014;12:301.
21. Ozer K, Horsanali MO, Gorgel SN, Ozbek E. Bladder injury secondary to obturator reflex is more common with plasmakinetic transurethral resection than monopolar transurethral resection of bladder cancer. Cent Eur J Urol. 2015;68:284.
22. Balci M, Tuncel A, Keten T, Guzel O, Lokman U, Koseoglu E, et al. Comparison of monopolar and bipolar transurethral resection of non-muscle invasive bladder cancer. Urol. Int. 2018;100:100-4.
23. Venkatramani V, Panda A, Manojkumar R, Kekre NS. Monopolar versus bipolar transurethral resection of bladder tumors: a single center, parallel arm, randomized, controlled trial. The Jou of Urol.

2014;191:1703-7.
24. Kramer MW, Wolters M, Cash H, Jutzi S, Imkamp F, Kuczyk MA, et al. Current evidence of transurethral Ho: YAG and Tm: YAG treatment of bladder cancer: update 2014. World J. Urol. 2015;33:571-9.