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Safety, Feasibility, and Oncological Outcomes of En-Bloc Transurethral Resection of Bladder Tumor Using Superpulse Thulium Fiber Laser-Initial Series

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Laser; Bladder tumor; Transurethral resection of bladder tumors

1. Abstract

1.1. Objective: To assess the safety and efficacy of Thulium fiber laser En bloc transurethral resection of bladder tumors.

1.2. Methods: We performed a retrospective analysis of Thulium fiber laser (TFL) En-bloc TURBT (Transurethral resection of bladder tumor) done by a single surgeon at our institute from September 2020 till March 2022. All cases were newly diagnosed superficial bladder tumors < 5 cm in size. En-bloc TURBT was done using 550 µ laser fibers at 1.5 J and 20 Hz. In all cases tumor size and site, laser on time, intraoperative visibility, degree of laser vibration and any complications like obturator nerve reflex, bladder perforation and bleeding were recorded. Tumor stage, grade and presence of detrusor muscle was noted in each case. Average follow up was 18 months.

1.3. Results: 10 cases of laser En-Bloc TURBT were done during the study period. Mean tumor size was 2.65 with mean laser on time of 421.2s. Good visibility and minimal fiber vibration was noted in each case. All cases were discharged home same day, none requiring postoperative catheterization or bladder irrigation. There were no obturator nerve reflex or bladder perforation reported.

1.4. Conclusion: Our initial attempt with TFL-En-Bloc TURBT on a small number of cases has shown that it's safe and efficient. Further trials need to be done to assess tumor recurrence after En-Bloc TURBT.

2. Introduction

Transurethral Resection of Bladder Tumor (TURBT) is considered the gold standard surgical treatment for Non-Muscle Invasive Bladder Cancer (NMIBC). [1, 2]. Due to high recurrence rates in NMIBC, a properly performed TURBT plays critical role in preventing tumor recurrence. The standard TURBT technique involves piecemeal resection of the tumor, which theoretically increases the risk of tumor seeding contributing to increased recurrence rates [3]. Other concerns with TURBT include bladder perforation, obturator nerve reflex (ONR) and inadequate staging due to absence of Detrusor Muscle (DM) in the specimen in 30% to 50% of cases [4, 5]. Presence or absence of DM in the initial pathology specimens have been shown to significantly determine risk of recurrence [6].

To overcome these shortcomings one piece or En-bloc TURBT has been introduced as an alternative approach for management of small bladder masses. Various energy sources including modified electrodes and various lasers (Nd-YAG, Ho: YAG, Green light laser) have been used for performing En-bloc TURBT. Several case series and review articles have reported the feasibility, safety, and efficacy of laser En-bloc resection of bladder tumors. A steeper learning curve and limited data on utilization of laser energy for En-bloc TURBT limits the widespread adoption of this technique [7-14].

Recently, the Thulium fiber laser (TFL) has been approved by FDA for intracorporeal laser lithotripsy and is being increasingly used across North America. Ability to deliver a pulsed laser at more optimal wavelength and shallower depth of tissue penetration with better hemostatic properties has generated increasing interest in soft tissue applications of this laser [15]. Ex vivo studies have assessed soft tissue effects of TFL, and clinical studies have compared TFL-prostate enucleation with transurethral resection of prostate (TURP) [16, 17]. Recently a phase-II trial of TFL En-Bloc TURBT has been completed in Russia with encouraging results [18]. We present our early case series assessing safety, feasibility, and pathological and oncological outcome of TFL En-Bloc TURBT.

3. Material and Methods

After obtaining an IRB approval, a prospective analysis of patients undergoing TFL En-Bloc TURBT From August 2020 till March 2022 was conducted. Patients with NMIBC based on preoperative office cystoscopy were selected for En-Bloc TURBT. Written informed consent was obtained from all patients. Those patients with suspicion of muscle invasion or demonstration of locally advanced or node positive or metastatic disease on preoperative imaging, previous history of TURBT, and those with large tumors (> 5 cm) were also excluded from the analysis.

All patients were evaluated with a detailed history and presenting complaints, duration of symptoms, and comorbid conditions were noted. All patients underwent routine preoperative blood tests, contrast enhanced computed tomography scan, chest X ray, and Urine cytology. Office cystoscopy was done in all patients before booking for laser En-Bloc TURBT. This was done to assess both feasibility as well as relation to ureteral orifice.

3.1. Surgical Technique

All En-Bloc TURBT were done by a single surgeon using Super Pulse TFL (Soltive™ Olympus®) with the patient in standard lithotomy position under general anesthesia. Cystoscopic evaluation confirmed site, size, number of tumors and their relation to ureteral orifices were noted in each case. A 26 Fr continuous irrigation resectoscope with a laser bridge was used through which a 550µ laser fiber was passed. Laser settings were 1.5 Joules and 20 Hertz delivering 30 watts for every case.

After identifying the tumor, a circumferential incision is first marked around the tumor base at a margin of approximately 5 millimeters (Figure 1). For tumors closer to the ureteral orifice the margin is made closer to the tumor base. The resection started at 6 o'clock and first proceeds towards 3 o'clock and then from 6 o'clock towards 9 o'clock. Focus was then diverted to a deeper resection to identify the deep muscle, after which the plane of laser resection stays above the deep muscle with slow brushing movements from 3 o'clock to 9o'clock. Gentle counter traction with the beak of the cystoscope exposes the correct plane of enucleation to separate the tumor from the deep muscle (Figure 2). Unique properties of TFL helps in achieving simultaneous coagulation and hence better hemostasis. Tumors on the anterior wall and dome are considered difficult sites for En-bloc resection. At the Dome resection is done 1st from 12 o'clock to 3 o'clock and then from 12 o'clock to 9 o'clock position. At the dome, gravity aids in exposing the plane between the tumor and deep muscle. The key to this procedure is to remain in a uniform plane under the tumor at the detrusor level throughout the resection avoiding under resection or perforations (Figure 3).

After En-bloc resection of all lesions either Ellik's evacuator or graspers were used to extract the tumors intact. In cases with large tumors after En-bloc resection, the tumor is divided into 2 pieces, first the superficial part of the tumor is resected using electrosurgical loop and then the deep part of the tumor attached to detrusor muscle is extracted intact along with the sheath. All cases underwent immediate intravesical installation of 2 GM gemcitabine and a foley catheter remined in place for 2 hours and removed in all patients before discharge. Cases lacking DM in the initial specimen were planned for Re-look En-Bloc TURBT. All patients were followed with three-month office cystoscopy every 3 months for the first year. Patients found to have recurrent tumors underwent repeat SP-TFL En-bloc TUARBT if feasible.

Adequacy of resection was assessed by completeness of resection and presence of detrusor muscle in the resected specimens. In all cases we measured laser on time, visibility scores (from 1 to 5, where 1 is clear visibility not needing any intervention and 3 needing continuous irrigation to maintain vision, and 5 is very poor visibility interfering with procedure), degree of laser vibration interfering with precision (from 1 to 5, where 1 is no vibration and precise incision, 2 is minor misfire and 5 is significant misfire interfering with procedure). All cases were assessed for intraoperative complications such as obturator nerve reflex, bladder perforation, and severe bleeding. Postoperative pathology (tumor stage and grade) along with presence or absence of deep muscle was noted in each case.

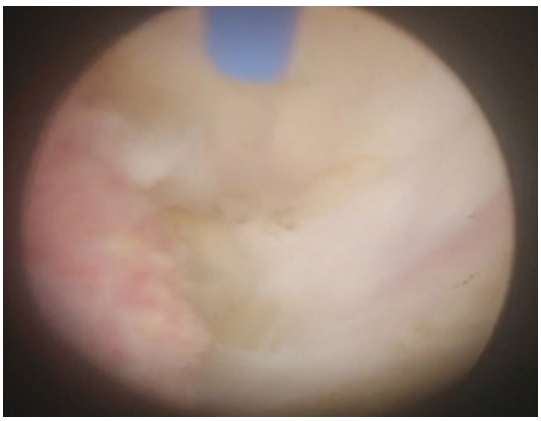

Figure 1: En-Bloc TURBT started with circumferential incision along the tumor base and staying above the detrusor muscle.

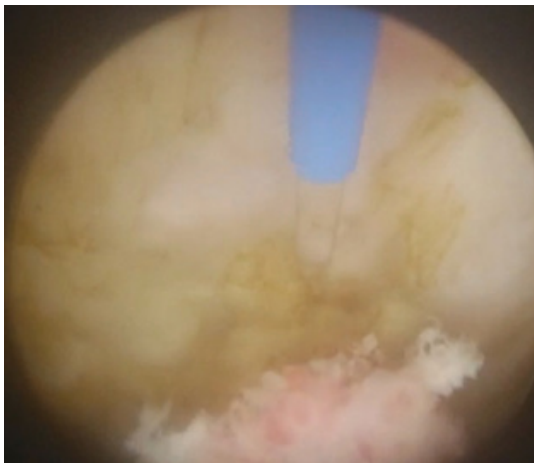

Figure 2: Staying above the detrusor and gradually separating the tumor from the base.

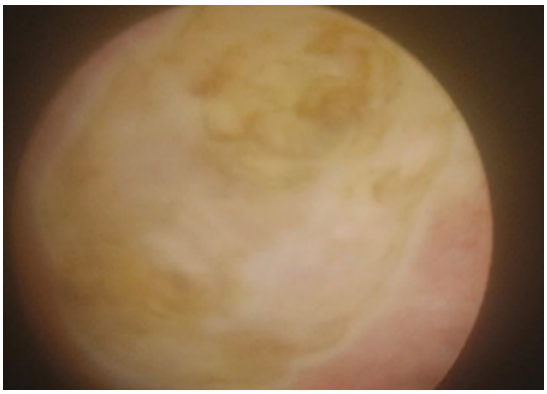

Figure 3: Tumor bed showing presence of detrusor muscle in the bed and good hemostasis

3.2. Statistical Analysis

For demographic and categorical variables, frequency and proportions were calculated. Mean and standard deviation (SD) was calculated for continuous variables.

4. Results

A total of 10 cases of SP-TFL were done with a mean age of 63.4 years during the study period. Mean BMI was 30.6 kg/sqm (Table 1). 7 cases were single tumor, whereas 3 were multiple tumors. Tumor size ranged from 1.17-3.3 centimeter with a mean of 2.65centimeter. 7 tumors were on the lateral wall, whereas 3 tumors were on the dome (Table 2). 7 cases had papillary tumors with narrow stalk whereas 3 cases had a solid tumor with a broad-based stalk. In 4 cases the tumors were close to the ureteral orifices, one case requiring ureteral stenting. Laser on time ranged from 240 to 985 seconds with a mean of 421.2 seconds. Average visibility of 1.2 was reported in all cases (Table 2). Visibility scores were 1 in 8 cases and 2 in 2 cases. Bleeding score was 1 in all the cases. Minimum laser fiber vibration was seen in all cases leading to precise incision. None of the cases had fiber degradation. No case required postoperative catheterization, post-operative bladder irrigation or hospitalization. None of the case required reoperation (Table 3).

One patient was found to have muscle invasive disease and later underwent radical cystectomy. Tumors were low grade in 8 cases and high grade in 2 cases. DM was present in 8 cases in the initial En-Bloc TURBT (Table 3). 2 cases with absent detrusor muscle underwent relook TURBT at 2 weeks and deep muscle was identified.

Table 1: Patient demographics and tumor characteristics

Age (Year), Mean (Median)	63.4 (63 years)
Gender	M-8 F-2
BMI, Mean kg/sqm	30.6
Tumor size (cm), Median, IQR	1.17-3.3cm (2.65 cm)
Location	5-Left lateral wall 3-Right lateral wall 2-Dome
Tumor type Solid Papillary	 3 7
Close to ureteral orifice	Encroaching-4 Far-6
Tumor focality Single Multiple	 7 3 (2 lesion in 2 cases; 4 lesions in 1 case)
Laser fiber used	550um -4 cases, 375um-1 case
Laser settings	1.5 J x 20Hz=30W

Table 2: Perioperative outcome

Laser on time, sec	(240-985sec), 421.2 sec
Catheter duration	0
Bladder irrigation	none
Hospitalization duration (Hours), Median, IQR	3.6 hours
Complications	
Hematuria	0
Perforation	0
ONR	0
Re-operation or readmission	0
Visibility score	0-8 cases
	2- 2 case
Bleeding score	0 in all cases
Stent placement	1 case
Incision precision (degree of fiber vibration)	1-3 cases 0-7 cases
Fiber degradation	0 case (1 case had fiber breakage on insertion)

Table 3: Pathologic and oncologic outcome

Specimen extraction	Through scope sheath in all Intact – 8 Chips, but base separated- 2
Tumor stage	Ta-6 T1-3 T2-1
Tumor grade	LG-7 HG-3 (1 had Plasmacytoid TCC)
Presence of DM	DM present - 8 DM absent -2 (Present on re-resection in both)
Recurrence on follow up at 6 months	No rec -5 Rec-2-Repeat En bloc TURBT
Recurrence at 12 months	Focal recurrence at new site – 1 No rec - 6 3 patients planned for surveillance cystoscopy

5. Discussion

Conventional TURBT, despite being gold standard treatment of NMIBC, is associated with various limitations like poor specimen quality and tumor cell fragmentation due to piecemeal resection increasing the risk of tumor implantation and recurrence [19]. Piecemeal resection can also miss DM in the specimen. Importance of presence of DM in TURBT specimens has been stressed upon in various studies and patients often require relook TURBT in case of absence of DM in the TURBT specimens [6, 20-22]. To overcome these limitations, concept of En-Bloc TURBT was established, and various energy sources (electrosurgical and laser) were tried. In contrast to electrical surgical techniques, laser surgery is associated with less thermal damage to specimen. There has been a surge in the use of different kind of lasers (Nd-YAG, Ho: YAG, Green light laser) for soft tissue application in various urological diseases. Various trials have assessed safety and efficacy of Laser En-Bloc TURBT, and similar to our study have found lesser risk of bleeding, bladder perforation, ONR, shorter catheterization duration and hospital stay [7-14]. A steeper learning curve and limited data on utilization of laser energy for En-bloc TURBT limits the widespread adoption of this technique.

En-Bloc TURBT was first described by Kitamura et al in 1980 using a polypectomy snare [23]. Over last 4 decades, with availability of different energy sources at different times, mainly for prostate surgeries, urologists have attempted their application in bladder tumors and En-Bloc TURBT has generated frequent interest among the urologists [7-14]. Particularly, last decade has seen renewed interest in En-Bloc TURBT among the urologists, more so after the availability and refinement of high-power lasers [13, 24-26]. En-Bloc TURBT defends the basic principle of cancer surgery and theoretically should improve accurate histological assessment of specimen, decrease tumor seeding and hence could reduce recurrence rates and may decrease or obviate the need for relook TURBTs. A European multicenter trial has shown that DM was present in 97% of specimens removed by electric En-Bloc TURBT and in 100% of specimens removed by laser En-Bloc TURBT [7]. In our study, DM was present in 8/10 cases (80%).

Various lasers have been tried for En-BlocTURBT, like Ho: YAG, Green light laser, Thulium: YAG, Rivolux laser and Vela Laser [13, 14, 24-26]. Over years great improvements in the existing laser technologies has happened, adding a new laser called SP-TFL in the urologist's armamentarium [15]. Experimental trials and few clinical studies have shown its benefits over the gold standard Ho: YAG laser particularly for lithotripsy [15-17]. SP-TFL has soft tissue applications as well due to its higher water absorption coefficient leading to excellent tissue hemostasis [17, 18]. Studies comparing TFL prostate enucleation to open simple prostatectomy and TURP have shown comparable outcomes and reduced perioperative morbidity (reduced blood loss, hospital stay and catheter duration) in the thulium group [17, 27].

Enikeev et al in a phase-II trial compared TFL-En-Bloc TURBT with TURBT. They found that TFL group is more likely to contain deep muscle, has higher six-month recurrence free survival, and lesser complications. Similar to our study, no ONR was seen in En-Bloc TURBT (compared to 17.2% in conventional TURBT group) and no bladder perforation in En-Bloc TURBT (compared to 10.3% in TURBT group) [18].

Most studies on laser En-Bloc TURBT have mean tumor size less than 3 cm [24-26]. Similar to other studies mean tumor size in our study was 2.65 cm. Main difficulty with larger tumors is the requirement of fragmentation before retreiving the specimen defeating the whole purpose of en bloc resection. In our study in 8 cases, the Specimen was either retrieved intact through the sheet or using Ellik's evacuator. In 2 cases with large tumor, after En-bloc TURBT, the superficial part was resected using monopolar TURBT and collected separately, and the deep part was removed intact through the sheath. Some surgeons believe that when En-Bloc TURBT is done for larger tumors, morcellation is beneficial as negative suction during morcellation can reduce tumor fragment implantation [13]. In our initial attempt at TFL-En-Bloc TURBT, we selected tumors mainly located on lateral walls, but later with increasing experience, also included tumors on the dome. Most authors believe that tumors located at favorable locations were more suitable for En-Bloc TURBT, whereas various surgeons have also tried En-Bloc TURBT for tumors located at dome and anterior wall as well [13, 24]. Moreover, as the depth of penetration of TFL is only 0.2 millimeter, using TFL for resection of tumors at the dome or anterior wall should not be associated with increased risk of intraperitoneal bladder perforation. Our study being an early attempt at En-Bloc TURBT with a new laser technology we selected cases with tumor size less than 3 centimeter. Various studies have shown that

multiplicity of tumors is not a contraindication for laser En-Bloc TURBT [24, 25]. In our series, 3/10 patients have multiple tumors.

ONR resulting in bladder perforation can occur in TURBT due to flow of electric current through the obturator nerves while resecting tumors on the lateral walls. In laser En-Bloc TURBT, as there is no flow of electric current, there is no risk of ONR. Like other studies we didn't encounter any ONR or bladder perforation.

Minimal vibration of fiber was seen during bladder tumor resection using TFL, leading to precise cutting. Moreover, there was efficient hemostasis (Bleeding scores zero) in all cases. None of the cases required postoperative bladder irrigation, or use of electrocautery for fulguration of bleeding points. In other studies, as well, efficient hemostasis has been seen with this laser [15-17].

All our cases were discharged within few hours of the procedure and none of them required postoperative catheterization. Recent review by Li et al. has shown that catheter duration is reduced by more than 1 day in laser En-Bloc TURBT cases compared to monopolar TURBT [14].

The most important marker of adequacy of TURBT is presence of the detrusor muscle. This is important for accuracy of tumor staging as well as has been shown to reduce recurrence free survival [6, 20-22]. In our study, 8 cases had DM present in first resection and other 2 cases had DM present in relook En-Bloc TURBT. Similar to our results (80%), studies with laser En-Bloc TURBT have reported detrusor muscle in 78%-100% of cases [6].

We understand that this is an initial trial of few cases of TFL-En-Bloc TURBT. With increasing confidence and encouraging results we are planning to do more cases. The major limitation of our study is a smaller number of cases. Another major limitation of laser En-Bloc TURBT is its application in larger tumors. More work needs to be done regarding specimen retrieval in laser En-Bloc TURBT. Moreover, further long-term trials are needed to compare if there is any difference in recurrence rates between laser En-Bloc TURBT and conventional TURBT. This can have major impact on patient care, as cases done by laser En-Bloc TURBT may not need frequent surveillance cystoscopy.

6. Conclusion

En-Bloc TURBT has been tried for more than two decades, but still the data are limited in the absence of a proper randomized controlled trial. Renewed interest in Laser En-Bloc TURBT has been generated particularly after the availability of high-power lasers like Ho: YAG and TFL. Our initial attempt with TFL-En-Bloc TURBT on a small number of cases has shown that it's safe and efficient. Further studies need to be done to evaluate any change in tumor recurrence after En-Bloc TURBT.

7. Consent and IRB approval

Written informed consent obtained from the patients. All patient identifiers removed from all the images. IRB approval obtained.

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