Original Article

Holmium laser transurethral resection of bladder tumor: Our experience

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Abstract

Purpose: To compare the safety and efficiency of conventional monopolar and holmium laser *en bloc* transurethral resection of bladder tumor (CM-TURBT and HoL-EBRBT) while managing primary nonmuscle-invasive bladder cancer.

Materials and Methods: From January 2012 to October 2015, fifty patients with primary nonmuscle-invasive bladder cancer underwent endoscopic surgery. Among them, 27 patients underwent CM-TURBT and 23 patients underwent HoL-EBRBT. Clinical data, included preoperative, operative, and postoperative management and follow-up, were recorded.

Results: Patient demographics and tumor characteristics in both groups were compared before surgery. There was no significant difference in operative duration among the groups. Compared with the CM-TURBT group, HoL-EBRBT group had less intraoperative and postoperative complications, including obturator nerve reflex ($P < 0.01$), bladder perforation ($P < 0.01$), as well as bleeding and postoperative bladder irritation ($P < 0.01$). There were no significant differences among the two groups in the transfusion rate and occurrence of urethral strictures. Patients in the HoL-EBRBT group had less catheterization and hospitalization time than those in the CM-TURBT group ($P < 0.01$), and there were no significant differences in each risk subgroup as well as the overall recurrence rate among the CM-TURBT and HoL-EBRBT groups.

Conclusions: HoL-EBRBT might prove to be preferable alternatives to CM-TURBT management of nonmuscle-invasive bladder cancer. HoL-EBRBT however did not demonstrate an obvious advantage over CM-TURBT in tumor recurrence rate.

Key Words: Holmium laser *en bloc* tumor resection, laser transurethral resection of the bladder tumor, nonmuscle-invasive bladder tumor, trans-urethral resection of bladder tumor

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Received: 03.03.2016, **Accepted:** 04.05.2016

INTRODUCTION

Bladder cancer is the second most common cancer of the urinary tract. Approximately 75–85% of the newly diagnosed bladder cancers are confined to the mucosa or submucosa, which is known as nonmuscle-invasive bladder cancer (NMIBC).[1]

Transurethral resection of the bladder tumor (TURBT) followed by adjuvant intravesical chemotherapy or

Access this article online	
Quick Response Code:	Website: www.urologyannals.com
	DOI: 10.4103/0974-7796.190815

How to cite this article: D'souza N, Verma A. Holmium laser transurethral resection of bladder tumor: Our experience. Urol Ann 2016;8:439-43.

immunotherapy, is the gold standard for these tumors.[2] However, TURBT is known to cause complications such as bleeding, obturator nerve reflex (ONR), and bladder perforation.[3] Hence, alternative procedures such as bipolar plasma kinetics and laser surgery were developed to improve the safety and efficacy of TURBT. Laser techniques without deep penetration cause less pain and bleeding. In addition, the power of the laser can be adjusted according to the tumor size.

This study was undertaken to compare the safety and efficiency of conventional monopolar and holmium laser *en bloc* transurethral resection of bladder tumor (CM-TURBT and HoL-EBRBT) while managing primary nonmuscle-invasive bladder cancer.

MATERIALS AND METHODS

We performed a prospective study, on patients with NMIBC, who came to our hospital, from January 2012 to October 2015. The inclusion criteria were a localized papillary tumor at cystoscopy fewer than five in number, with imaging studies showing no extravesical extension, lymphatic metastasis, or invasion of adjacent organs. Patients were excluded if they had muscle-invasive bladder tumors (based on histopathology report postresection), nonpapillary, or extensive tumors (>3 cm).

A detailed history of all patients was obtained, and standard physical examinations were performed before surgery. Ultrasonography (USG), computed tomography, and cystoscopy were performed for diagnosing and staging the disease preoperatively.

The patients were alternatively allotted to undergo CM-TURBT or HoL-EBRBT. All procedures were performed under spinal anesthesia by a single surgeon.

CM-TURBT was done with 26F Iglesias resectoscope (Karl Storz, Tuttlingen, Germany) using 1.5% glycine as irrigation fluid; cutting and coagulation power were set at 120W and 70W , respectively. The tumor was resected with a 1 cm mucosal margin.

HoL-EBRBT was performed with 100W Holmium laser system (VersaPulse PowerSuite, Lumenis, Yokneam, Israel) employing 550 micron end-firing fiber to deliver the laser, using 26F resectoscope (Richard Wolf, Knittlingen, Germany). *En bloc* resection was performed with a 1 cm margin from the tumor base. The laser was set to deliver the energy of 1–2 J and frequency of 40–50 Hz. Normal saline irrigation was used in all cases of this group.

After tumor resection, biopsies were obtained from the tumor base from at least two places and the mucosal margin in both the groups.

All tissues were sent for histopathological evaluation to determine the tumor grade and stage. At the end of the procedure, all patients were catheterized with three-way Foley's catheter and normal saline irrigation was commenced and continued till hematuria disappeared. Mitomycin-C (40 mg) was instilled into the bladder of all patients postoperatively, within 6 h of surgery, except those in whom bladder perforation was suspected. Patients with suspected bladder perforation were administered six cycles of intravesical *Bacillus* Calmette–Guérin instillation (120 mg), 4 weeks postprocedure. Patients were discharged when they were able to void normally after removal of the catheter.

Patients were followed for 3 years using USG, urinary cytology and cystoscopy at every 3 months for first 2 years and 6 monthly in the last year.

Results were statistically analyzed using the SPSS® statistical software package, version 13.0 (SPSS Inc., Chicago, IL, USA) for Windows®. Data were presented as mean ± standard deviation or mean and range. Between groups comparison was performed using one-way analysis of variance for continuous variables and the Chi-square test for categorical variables. A $P < 0.05$ was considered to be statistically significant.

RESULTS

A total of 59 patients underwent endoscopic surgery under spinal anesthesia for bladder cancer from January 2012 to October 2015. Of these, nine had invasive cancer on final histology, postresection, and hence excluded from the study [Figure 1]. The remaining 50 patients who underwent either CM-TURBT ($n = 27$) or HoL-EBRBT ($n = 23$) had their preoperative tumor characteristics similar in both groups, as presented in Table 1. In all cases, the adequate specimen was obtained to stage and grade the disease.

Of the 50 patients, 9 had a papillary urothelial neoplasm of low malignant potential, 36 had a low-grade papillary urothelial carcinoma, and 5 had high-grade papillary urothelial carcinoma [Table 1]. No residual tumor tissue was found from the tumor base or the mucosa around the tumor margin. There were 31 cases with Ta stage and 19 cases with T1 stage tumors.

The mean duration of surgery was not significantly different between the two groups [Table 2]. None of the patients in HoL-EBRBT group experienced intraoperative ONR, but in the CM-TURBT group all patients with lateral tumors ($n = 11$) experienced ONR for a total of twenty-six times

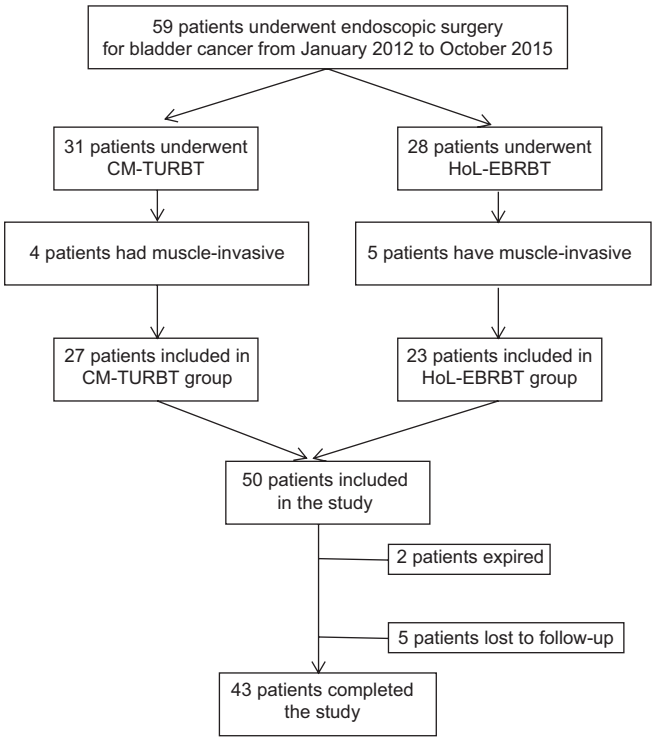

Figure 1: CONSORT diagram of the study. HoL-EBRBT: Holmium laser *en bloc* transurethral resection of bladder tumor, CM-TURBT: Conventional monopolar transurethral resection of bladder tumor

Table 1: Patients demographics

Variable	CM-TURBT	HoL-EBRBT
n	27	23
Sex		
Male	18 (66.7)	15 (65.2)
Female	9 (33.3)	8 (34.8)
Age, years	67.1±8.3 (39.0-77.0)	66.3±9.8 (38.0-76.0)
Tumor number	2.6±1.2 (2.0-5.0)	2.5±1.5 (2.0-5.0)
Tumor size, mm	14.1±2.3 (5.0-31.0)	15.8±3.1 (4.0-30.0)
Tumor location		
Lateral	11 (40.7)	10 (43.5)
Other	16 (59.3)	13 (56.5)
Stage		
Ta	16 (59.3)	15 (56.2)
T1	11 (40.7)	8 (34.8)
Tumor grade		
PUNLMP	5 (18.5)	4 (17.4)
Low	20 (74.1)	16 (69.6)
High	2 (7.4)	3 (13.0)

Data presented as *n* (%) or mean±SD (range). PUNLMP: Papillary urothelial neoplasms of low malignant potential, SD: Standard deviation, HoL-EBRBT: Holmium laser *en bloc* transurethral resection of bladder tumor, CM-TURBT: Conventional monopolar transurethral resection of bladder tumor

($P < 0.01$), despite reducing the bladder distension and electrocautery power during resection of lateral tumors. There were no cases of bladder perforation in the HoL-EBRBT group, but three patients experienced bladder perforation in the CM-TURBT group [$P < 0.01$; Table 2]. All these perforations occurred during ONR and were diagnosed on the table and were managed conservatively by prolonged catheterization for 2 weeks. No mortality was reported during any operation. A significantly higher proportion of patients in the CM-TURBT group experienced symptoms of bladder irritation postoperatively, compared with patients in the HoL-EBRBT group [$P < 0.01$; Table 2], following mitomycin C instillation. The durations of postoperative bladder irrigation, catheterization, and hospitalization were all significantly lower in HoL-EBRBT group compared with the CM-TURBT group ($P < 0.01$). There were no significant between-group differences in the occurrence of urethral strictures.

During the 3-year follow-up period, two patients died at 26 months and 23 months after the surgery (both died due to cardiovascular disease) and five were lost to follow-up at various intervals [Figure 1]. In all these patients, there was no evidence of tumor recurrence, till the time of the last follow-up.

There was no significant difference in the cumulative tumor recurrence rate between the two groups. Postoperative follow-up after 12, 24, and 36 months showed recurrence rates of 8.69%, 17.39%, and 30.43% in the HoL-EBRBT group and 11.11%, 25.92%, and 37.04% in the CM-TURBT group, respectively, by surveillance cystoscopy.

DISCUSSION

There has been a surge in the use of lasers for minimally invasive treatment of urological diseases, in recent years. Although TURBT remains the standard for NMIBC, the use of lasers for treating bladder cancer has been proven to be safe and minimally invasive. Noninvasive, small lesions are especially amenable to management with laser energy, and the clearance rates are comparable to those achieved by standard electrocautery resection.[4-6] Beisland and Seland,[7] in a randomized study, reported a local recurrence rate of 7% for Nd:YAG-treated stage T1 tumors, versus 43% for similar tumors treated with standard electrocautery. Beer *et al.*[8] reported a similar local recurrence rate in their series of 252 consecutive patients treated with a laser for superficial lesions.

Initially, the main limitation of laser treatment of bladder cancer was inadequate tissue for pathologic examination, which restricted its application in the treatment of bladder tumor. However, now holmium laser can ensure *en bloc* resection of the bladder tumor, and provide enough tissue for histologic examination.[9-11] Holmium laser has a wavelength of 2100 nm, and a short extinction length due to the strong absorption by water molecules. At this wavelength, the tissue penetration depth of the laser is about 400 μm, which is reasonably safe. Holmium laser generates steam bubbles in the irrigant at the fiber tip, separating the tissue layers by tearing them apart and simultaneously coagulating small- and middle-sized vessels to a

Table 2: Intra- and post-operative characteristics

Variables	HoL-EBRBT (*n*=23)	CM-TURBT (*n*=27)	Statistical significance
Operative duration, min			
Per patient	58.2±15.8 (20.5-90.0)	55.6±13.5 (18.4-85.2)	NS
Per tumor	11.6±4.6	14.4±5.2[a]	NS
ONR	0 (0)	11 (40.7)[b]	<0.01
Bladder perforation	0 (0)	3 (11.1)	<0.01
Bladder irritation	5 (21.8)	14 (51.8)	<0.01
Intravesical chemotherapy			
MMC	23 (100)	24 (88.9)	
BCG	0 (0)	3 (11.1)	
Postoperative bladder irrigation time, h	8.5±1.3 (2.3-24.0)	14.8±2.1 (3.2-48.2)	<0.01
Period of catheterization, days	2.24±0.43 (24.3-112.0)	4.51±0.92 (34.5-144.3)	<0.01
Period of hospitalization, days	3.21±0.34 (2.5-6.1)	5.82±0.65 (4.2-7.2)	<0.01
Postoperative urethral stricture	2 (8.7)	2 (7.4)	NS

Data presented as mean±SD (range) or *n* (%). [a]One-way analysis of variance for continuous variables; Chi-squared test for categorical variables, [b]ONR occurred 24 times in these ten patients. ONR: Obturator nerve reflex, SD: Standard deviation, HoL-EBRBT: Holmium laser *en bloc* transurethral resection of bladder tumor, CM-TURBT: Conventional monopolar-transurethral resection of bladder tumor, MMC: Mitomycin C, BCG: *Bacillus* Calmette-Guerin, NS: Not significant

depth of 2–3 mm, showing rapid tissue effect as well as excellent hemostasis.[9-15] Holmium laser vaporization, though less invasive, will not provide tissue for histopathological evaluation.

CM-TURBT is associated with potential risks, including the occurrence of ONR during surgery, especially for lesions located in the lateral bladder wall, which may lead to bladder perforation. When TURBT was applied to remove lateral tumors, the current flow passing through the obturator nerve may cause ONR, which results in sudden muscle contractions and bladder perforation. Furthermore, the temperature ranged from 100°C to 300°C at the treatment site thereby causing thermal injury.[16] On the other hand, when the laser is applied to remove the tumor tissue, no current flow occurs during the procedure and hence does not stimulate the obturator nerve, especially in patients with NMIBC, even if the tumors were located in the lateral bladder wall. Therefore, bladder perforation induced by ONR can be avoided using laser techniques. In addition, thermal injury at the treatment site is minimized as the temperature of the treatment site ranged from 40°C to 75°C, causing minimal thermal injuries which could be attributed to the absence of a strong local electrical field.[17]

This study demonstrated that HoL-EBRBT is associated with significantly fewer intraoperative complications during the resection of bladder tumors than CM-TURBT. The tumor cutoff size was comparable with other studies.[9-11] ONR and bladder perforation rate were significantly lower in the HoL-EBRBT group than the CM-TURBT group. In fact, no ONR was observed in the HoL-EBRBT group. This was similar to those observed in a meta-analysis done by Bai *et al.*[18] Thus, HoL-EBRBT can avoid ONR and effectively reduce the risk of bladder perforation. The postoperative irrigation rate was lower and the catheterization time as well as hospital stay were shorter in HoL-EBRBT group compared to CM-TURBT group. This might be because the holmium laser possesses the property of accurate cutting and excellent hemostasis, providing a bloodless operation field throughout the procedure. Furthermore, patients in the HoL-EBRBT group had lesser postoperative pain and analgesic requirement and were discharged earlier from the hospital. Therefore, those patients had a high degree of overall satisfaction with minimal complications.

In our study, there was no significant difference in the 1-year recurrence free survival between the two groups. However, the 2nd and 3rd year recurrence free survival favored the HoL-EBRBT group. This might partly be because of the insufficient resection depth of lateral-wall tumor during CM-TURBT, to reduce the risk of bladder perforation.[19] In HoL-EBRBT, the holmium laser can instantly coagulate the blood and lymph vessels, reducing the chance of intraoperative dissemination of the cancer cells.[20] Besides, holmium laser can resect neoplasm as well as adjacent tissues *en bloc* without touching the tumor, reducing the possibility of recurrence *in situ*.[4] A few researchers are even of the view that the recurrence rate of holmium laser treatment for bladder tumors is lower than that of CM-TURBT because of an active immune effect of the holmium laser.[21]

CONCLUSION

HoL-EBRBT is a promising technique in the treatment of NMIBC. It showed several advantages over CM-TURBT regarding the ONR, bladder perforation, bladder irrigation, catheterization time, hospital stay, and 3-year recurrence free survival. HoL-EBRBT is safe and efficient for the treatment of NMIBC and can be used as an alternative procedure for CM-TURBT regarding low-grade papillary urothelial

carcinoma or low-grade early TNM-stage urothelial carcinoma. However, a larger randomized series with long-term follow-up is required to confirm these initial findings.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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