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Research Article

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Comparative Study of 2um Laser versus Ho lmium Laser for the Resection of Non-Muscle Invasive Bladder Cancer

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Abstract

Objective: To compare the safety and efficacy of conventional monopolar transurethral resection of bladder tumor (TURBT), 2-micron continuous-wave laser and holmium laser resection techniques in the management of primary non-muscle invasive bladder tumor (NMIBT).

Methods: From January 2009 to January 2013, patients newly diagnosed primary NMIBC were enrolled in this study. The patients were divided into conventional TURBT group (n=70), holmium laser group (n=70) and 2-micron laser group (n=70) randomly. Operative time, postoperative bladder irrigation, catheterization time, hospitalization time, complications included obturator nerve reflex, bladder perforation, blood transfusion, and 2-year tumor recurrence rate were documented in all patients.

Results: Characteristics of patients and tumors in all three groups were compared before surgery. There was no significant difference in operative time among the three groups. Compared with the conventional TURBT group, both 2-micron and holmium groups had less intra operative and postoperative complications, including obturator nerve reflex, bladder perforation, and postoperative bladder irritation. There were no significant differences among the three groups in the blood transfusion rate and incidence of urethral stricture. Patients in the 2-micron and holmium groups had less catheterization and hospitalization time than those in the conventional TURBT group. There was no significant difference in the 2-year tumor recurrence rate among the three groups.

Conclusion: Our results demonstrated that the use of 2-micron (thulium) laser and holmium laser in the management of NMIBT were superior to conventional monopolar TURBT, while there were no significant differences between 2-micron laser and holmium laser. However, 2-micron laser and holmium laser did not have an obvious advantage over conventional TURBT in 2-year tumor recurrence rate. A longer follow-up period and larger numbers of patients are necessary to demonstrate the present result in the future.

Keywords: Non-muscle invasive bladder tumor; Holmium laser; 2-micron laser; Transurethral resection of the bladder tumor

Introduction

The incidence of bladder cancer ranks first among all urinary tract tumors. The majority of invasive bladder urothelial carcinomas are non-muscle invasive type ones. Currently, the standard surgical treatment of NMIBT is transurethral resection of the bladder tumor [1]. Back in 1976, lasers were added to the endourological armetarium for bladder tumor treatment. Despite nowadays' standard procedure for staging and treating non-muscle invasive bladder tumor by transurethral resection of bladder tumors (TURB) via a wire loop, laser resection techniques for bladder tumor came back in focus with the introduction of Ho:YAG and not to mention recently Tm:YAG lasers. Today, Ho:YAG and Tm:YAG seem to offer alternatives in the treatment of bladder cancer, but still to prove their potential in larger prospective randomized controlled studies with long-term follow-up [2].

A hundred patients with superficial bladder cancer admitted in the authors' unit from January 2011 to January 2013 were included. Bladder transitional cell carcinomas were confirmed in all patients by cystoscopic biopsy. Patients were then divided into two groups, either receiving 2um laser transurethral resection (50 patients) or holmium laser transurethral resection (50 patients). Clinical efficacy and treatment characteristics were compared in the two groups.

Patients and Methods

General characteristics

A hundred patients with superficial bladder cancer admitted in the authors' unit from January 2011 to January 2013 were included. The experimental process got the approval of hospital ethics committee. Superficial bladder transitional cell carcinomas were confirmed in all patients by postoperative pathology.Seventy-one patients had newly 0diagnosed bladder cancers, 29 had recurrent cancers, 31 had sidewall tumor,and 18 patients were found with multiple tumors. Fifteen patients had tumors with a diameter greater than 2.5 centimeter. patients included must meet the following criteria: ① Radiological examination revealed bladder lesions; ② Cytoscopic biopsy confirmed bladder transitional cell carcinoma, patient should be excluded if the ureter was invased by the tumor; ③ Patients had tumors with clinical stage of Ta or T1. There was no significant difference in the baseline characters in the two groups (Table 1).

Procedures

Patients in the 2um laser group underwent general anesthesia with the lithotomy position. The RevoLix 2um laser equipment (German LISA Laser, maximum power 70w, wavelength 2.01um), and the 550um Percu-Fib direct (end-firing) fiber were used with the 2um laser set to continuous wave mode. The camera system was connected to the TV

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Variable	TURBT (n=70)	2-micron laser (n=70)	Holmium laser (n=70)	P value
Sex				
Male	48	50	45	0.905
Female	22	20	25	0.913
Age (y)	56.25 ± 5.84	58.32 ± 6.13	60.53 ± 6.20	0.821
Tumor number (n)	2.52 ± 1.21	2.74 ± 1.52	2.43 ± 1.32	0.735
Tumor size (cm)	1.53 ± 0.20	1.62 ± 0.32	1.58 ± 0.51	0.650
Tumor location				
Lateral	25	23	28	0.721
Other	45	47	42	0.658
Stage				
Ta	35	40	37	0.745
T1	27	23	28	0.825
CIS	8	7	5	0.652
Grade				
PUNLMP	18	20	15	0.712
Low	46	40	48	0.786
High	6	10	7	0.642

TURBT=transurethral resection of bladder tumor; PUNLMP=papillary urothelial neoplasms of low malignant potential.
Table 1: Characteristics of patients and tumors.

screen. The entire bladder was carefully examined to determine the tumor location, size, number and presence or absence of tumor pedicle, as well as the location of the ureter opening. Bladder mucosa was cut to deep muscle layers at a distance of 2cm from the tumor, the tumor and its associated muscle tissue were exposed and removed from the roots. Vaporization was used to stop the bleeding and smoothen the tumor wounds. For large tumors, the tumor body was first diced using the laser followed by vaporization of the bladder mucosa 2cm from the tumor until normal muscle layer was seen. Vaporization cutting depth can be completely controlled according to tumor location using the left and right or up and down sweeping brush. Tissue specimens were taken randomly from the base of the tumor and the wound edge for pathological analysis.

Holmium laser group

Patients in the 2 μm laser group underwent general anesthesia with the lithotomy position. A 26F reflux plasma prostate resectoscope (Olympus, Japan) was used. Holmium laser (Raykeen DHL-1, China, maximum output 60W, maximum ureter frequency 30 Hz, wavelength 2.1 μm), the fiber was set into the resectoscope working channel. Tumor characters described previously were carefully examined. Laser output power (30-60W) was tailored according to the characteristics of the tumor. The resection process was accompanied with continuous infusion with 0.9% sodium chloride. For smaller, pedunculated tumors, direct vaporization of tumor pedicle or the tumor base and suction of the tumor tissue for biopsy should be the procedure of choice before dealing with submucosa and muscular tissues. For larger tumors or those with wide bases, tumor parts that hinder the exposure should be cleared before resection deep into the root. Mucosa 2 cm around the tumor was cauterized. Base and wound edge biopsies were sent for pathologic examination.

Indwelling catheters were given according to the blood loss and postoperative urinate color in both groups. Three-chamber balloon catheter was preserved for bladder irrigation in those patients with large wounds. Postoperative antibiotics were given for 2 ~ 3 days. Intravesical instillation was conducted immediately after the procedure (within 24 hours), following chemotherapies were done in the outpatient settings. Patients underwent cystoscopy and biopsy for every three months, to detect the recurrence of bladder cancer, treatment schedule was adjusted accordingly.

Outcome

Operative time, blood loss, postoperative urinary retention time, hospital stay, complications and tumor recurrence were documented in both groups.

Statistical analysis

Statistical analyses were done using SPSS l7.0 (Chicago, IL, USA), measurement data was analyzed with the T test and count data was analyzed with x^2-test, $P < 0.05$ was considered statistically significant.

Results

Preoperative and postoperative outcomes of two groups were compared (Table 2). The mean operation time in 2um laser group (20.21 ± 5.45min) was shorter than holmium laser group (32.33 ± 6.07 min, P<0.05). No significant difference was found in blood loss between 2um laser group (11.60 ± 1.63 ml) and holmium laser group (13.26 ± 2.63 ml, P>0.05). One patient in Holmium laser group had postoperative bleeding; Minor bladder perforation occurred in 4 patients in 2 μm laser group. No significant difference was found in postoperative catheter retention time between 2um laser catheter group (2.69 ± 0.45 days) and the holmium laser group (2.45 ± 0.72 days, P> 0.05); Postoperative bladder irrigation was done in 4 and 5 patients in 2 μm laser group and the holmium group, respectively. No postoperative hospital stay was found in 2 μm laser group (3.43 ± 0.43 days) and the holmium laser group (3.29 ± 0.47 days, P>0.05). During the follow-up of 3 to 24 months, urethral stenosis occurred in 2 patients in holmium laser group and 1 patient in 2 μm laser group. There were 6 patients experienced recurrence in 2 μm laser group within 12 months with a one-year recurrence rate of 12%; while 7 patients in holmium laser group had recurrence with a one-year recurrence rate of 14%. There was no significant difference in the incidence of urethral stricture and one-year recurrence rate between the two groups (Table 2).

Variable	TURBT	2-micron laser	Holmium laser	P value
Operative time	27.32 ± 6.62	24.15 ± 5.25	26.24 ± 7.20	0.165
Blood transfusion	2	0	0	0.250
Obturator nerve reflex	11	0	0	<0.01*
Bladder perforation	5	0	0	<0.01*
Catheterization time (d)	3.27 ± 0.46	2.46 ± 0.42	2.35 ± 0.51	<0.01*
Hospitalization time (d)	4.42 ± 0.55	3.43 ± 0.45	3.26 ± 0.44	<0.01*
Bladder irrigation	14	5	6	<0.01*
Urethral stricture	4	2	3	0.320

*Statistically significant. TURBT=transurethral resection of bladder tomor.

Table 2: Intraoperative and postoperative outcomes of conventional TURBT, 2-micron laser and holmium laser group.

Discussion

Bladder cancer is one of the most common urological tumors, with superficial bladder cancer (Tis, Ta, T1) accounting for 75 to 85 percent, of which about 70% are Ta, 20% are T1 and 10% are bladder carcinoma in situ [3]. Over the past 30 years, it is generally believed that TURBT (transurethral electric resection of bladder tumor) are specifically suitable for superficial bladder cancers, and should be recommended as the surgical treatment of choice. The need for advanced technical conditions and high proficiency operators limits the wide application of this procedure. Common complications of the procedure include bladder hemorrhage, perforation and water intoxication, which might pose the need to switch to open surgery. These complications may be attributed to a too-deep cutting or the occurrence of obturator nerve reflex. In recent years, lasers have been widely used in urology clinical practice for its safety and ideal bleeding control advantages [4]. Currently Holmium laser (HO: YAG laser) and 2um laser have been more widely used and [5]. Jiang et al. [6] found transurethral holmium laser resection to be better at bleeding control, better accuracy, and less frequency of obturator nerve reflex in removing non-muscle invasive bladder urothelial carcinoma, campared with transurethral plasma (TURis). Therefore, it was considered a safe and reliable surgical approach. Holmium laser treatment of non-muscle invasive bladder cancer has shown similar short-term recurrence-free survival (RFS) with TURBt, but has less intraoperative and postoperative complications and shorter recovery time [7]. Soler et al. [8] has carried holmium laser treatment on the low level non-muscle invasive bladder urothelial carcinoma under local anesthesia and achieved satisfying outcome. Moreover, Patients undergoing this procedure can be discharged only 3 hours after the operation, but further evidence was still needed for the lack of randomized controlled trials. Flexible cystoscopy was recommended by some along with holmium laser as the first choice for recurrent low-grade non-muscle invasive bladder cancers (G_1 / 2, T_a / 1), but patients with invasion in the ureter infringement should be ruled out. They also found advantages of holmium laser, such as better local tumor control and less complication for advanced bladder cancer (G_3), outweigh its side effect of the increase rate of tumor recurrence [9]. Clinical study comparing 2 μm laser, holmium laser and TURBT found that the laser group had significantly less bleeding, and no difference in the rate of tumor recurrence was observed [10].

Thulium and holmium laser were first used in urology for prostate surgeries. Xia [11] and Sascha [12] has carried out enucleation of prostate using 2 μm laser and holmium laser, respectively, comparing with transurethral resection of the prostate (TURP), in terms of symptoms, bleeding time and catheter indwelling time, the former two showed clear advantages. Due to its clear benefits, laser ablation has been more and more widely used in bladder cancer surgeries in recent years. Wang [13] reported advantages of green laser in superficial bladder tumor resection, including good efficacy, less bleeding and clear surgical vision. Huang [14] demonstrated good effect of holmium laser on bladder tumor, even better than TURBT. In summary, advantages of thulium laser and holmium laser in bladder cancer resection are listed follows: ① Laser energy had no electric field effect and will not stimulate the obturator nerve to cause reflex, thus avoiding bladder perforation, which especially fits for cancers located in the sidewall [15]. ② Direct vaporization can be used for small tumors, while for larger tumors, the cutting function of the laser can be used for resection, thus reducing operation time. ③ Coagulation effect of the laser can block blood and lymphatic vessels to reduce the spread of tumor cells [15]. ④ The shallow tissue penetration of 2um laser and holmium laser make it possible to precisely control the level of vaporization, further reducing the risk of bladder perforation and damage to the surrounding tissue.⑤Laser technology, with endoscopic operating lever adjusting the direction, can be applied with channels of cystoscopy, ureteroscopy and soft lenses, which is designed for treatments in various parts of the bladder lesions. ⑥ Laser surgical procedure is relatively simple and requires less learning period.⑦ Less bleeding, shorter catheter indwelling and fewer hospital days make it particularly suite for patients with poor tolerance, such as elderly patients with implanted cardiac pacemakers and patients with poor cardiopulmonary conditions.⑧ En-bloc resection of the tumor facilitates the pathological analysis for tumor staging, as well as range and depth of tumor invasion. Furthermore, whole resection of the tumor can minimize the opportunity of tumor cells shedding and planting [7]. ⑨ Immediate postoperative intravesical irrigation can decrease tumor recurrence rate. Intravesical chemotherapy within 24 hours after TURBT can reduce the recurrence rate by 40%. Howvever, accidental intraoperative bladder perforation would affect the implementation of immediate infusion [16].

Holmium laser and 2 μm laser share the merit of well-organized cutting with minimal damage to the surrounding tissue.

Holmium laser is a pulsed solid-state laser with a 2.14-nm wavelength, it can be quickly absorbed by the water in the tissue. The tissue penetration depth of holmium laser is 0.4 mm without deep tissue damage [17]. Its ability to generate vaporization provides a satisfactory cutting, hemostatic and enucleation ability. The wavelength of thulium laser was 1.75 to 2.22 μm, also known as the 2 μm laser. The wavelength is close to the water peak absorption value (1.92 μm). In addition, the thickness of carbonized tissue produced by thulium laser was only 50 μm, which is superior to holmium laser. Under continuous wave mode, thulium laser is more effective on tissue cutting, vaporization and hemostasis while sparing deep tissue [18]. The issue penetration depth of thulium laser is only 0.3 mm, thus can avoid surrounding tissue damage. Furthermore, tissue coagulation of 0.2 mm is formed during vaporization, which brings ideal hemostatic effect while with leaving operators' vision intact and clears [19]. The solidified layer left after the removal of tissue was about 1 mm thick, thus will not cause serious tissue edema and necrosis. Water absorption rate of the 2 μm laser is 2.5 to 3 times than holmium laser, indicating a much stronger cutting effect of 2 μm laser. Its continuous operating mode is also distinct from pulsed modes of holmium laser and its "vaporization add cut" approach was superior to the "explosive tearing" mode of holmium laser [20]. The light of 2um laser is forward light and relatively sharp, which may predispose to bladder perforation. Four out of 50 patients in our study had mild bladder perforation. Additionally 2 μm laser would cause thin crusts around the wounds hampering the vision during dissection. Similarly, the residual flocs on the wound and specimens will influence the cutting effect of 2 μm laser. On the other hand, for patients with bladder or urinary tract stones, lithotripsy can be done by holmium laser.

The study found some common characteristics and advantages of holmium laser and 2 μm laser, as well as unique features of each approach. The two modalities were both safe and effective with equivalent clinical values. There are distinctions in the conduction of the surgery procedures. Further investigations are warranted to provide stronger evidence in the choice between these two modalities.

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