

ORIGINAL ARTICLE

Effect of transurethral partial cystectomy with 2.0 μm laser in treating superficial bladder cancer

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Summary

Purpose: To compare and analyze the efficacy and safety of transurethral partial cystectomy with 2.0 μm laser and transurethral resection of bladder tumor (TURBT) in treating patients with superficial bladder cancer.

Methods: The clinical data of 130 patients with superficial bladder cancer were divided into two groups based on different treatments, with 65 patients in each group, and treated with transurethral partial cystectomy with 2.0 μm laser and TURBT separately. Then, operation conditions such as intraoperative blood loss, operation time, in-dwelling time of urinary catheter and length of hospital stay were recorded and compared between the two groups. Finally, the tumor recurrence in the patients was followed up and recorded.

Results: The operation time ($p < 0.001$) and length of hospital stay ($p = 0.013$) were remarkably shorter, and the intraoperative blood loss ($p < 0.001$) was notably smaller in laser group than those in TURBT group. Laser group had an evidently lower total incidence rate of complications than TURBT group ($p = 0.005$). The patients were reexamined by cystoscopy

at 4 weeks after operation, and the biopsy results indicated that there were markedly more cases of positive findings in TURBT group than those in laser group (no positive findings) ($p = 0.033$). However, laser group exhibited distinctly decreased postoperative levels of IL-6 and TNF- α but an obviously increased IL-10 level compared with TURBT group ($p < 0.001$). Besides, after 6-40 months of follow-up for all the patients, the total recurrence rate was prominently lower in laser group than that in TURBT group ($p = 0.006$).

Conclusions: In contrast with TURBT, transurethral partial cystectomy with 2.0 μm laser for superficial bladder cancer can significantly reduce the operation time and intraoperative blood loss, improve the operative effect, induce fewer postoperative complications and cause milder body injury and inflammatory response at the same time, which is worthy of clinical promotion.

Key words: transurethral partial cystectomy with 2.0 μm laser, transurethral resection of bladder tumor, superficial bladder cancer, efficacy

Introduction

Superficial bladder cancer, one of the common types of tumors of the urinary system, is characterized by a high morbidity rate, local infiltration, distant metastasis and high recurrence rate, becoming a serious disease affecting patient's health and quality of life [1-6]. Operation, simultaneously assisted with intravesical

instillation chemotherapy, is the major treatment of superficial bladder cancer at present, despite many operative methods with respective advantages and disadvantages in clinical treatment. Currently, transurethral resection of bladder tumor (TURBT) is the gold treatment standard of superficial bladder cancer, but problems such as

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Received: 03/04/2020; Accepted: 30/04/2020

postoperative bladder irritation symptoms, tumor recurrence, intraoperative obturator nerve reflex and even bladder perforation always bother urological surgeons [7,8].

In recent years, 2.0 μm laser becomes a frequently applied minimally invasive technique in laser therapy in surgery, and laser vaporesction possesses advantages such as good hemostatic effect, precise cleavage and no electrical stimulation, which can realize full-thickness *en bloc* resection of tumors like open partial cystectomy and obtain satisfying pathological specimens [9,10]. In the present study, the clinical data of 130 patients with superficial bladder cancer who were admitted to and treated in the Department of Urinary Surgery of our hospital from October 2014 to October 2016 were retrospectively analyzed. The therapeutic effects and safety were analyzed and compared between transurethral partial cystectomy with 2.0 μm laser and TURBT, so as to provide more reasonable references for the selection of clinical treatment protocols for patients with superficial bladder cancer.

Methods

General data

A total of 130 patients with superficial bladder cancer treated in our hospital from October 2014 to October 2017 were selected, including 74 males and 56 females aged 35-76 years, with an average age of 56.1 ± 10.4 years. All the patients were assigned into laser group (n=65, transurethral partial cystectomy with 2.0 μm laser) and TURBT group (n=65, TURBT) based on the therapeutic methods. Inclusion criteria: patients with superficial bladder cancer confirmed by cystoscopy and biopsy; those without operative contraindications such as cardiac, hepatic, renal and coagulation dysfunction; and those with a Karnofsky performance status score ≥ 70 points. Exclusion criteria: patients unable to receive operation, or those accompanied with other neoplastic diseases. The differences in baseline data such as age, gender, tumor site, tumor number, tumor size, clinical stage of tumor and complications were not statistically significant before operation between the two groups ($p > 0.05$) (Table 1). This study was approved by the Ethics Committee of Linyi Cancer Hospital. The Declaration of Helsinki was followed, and the duty of disclosure was performed. All the patients enrolled signed the informed consent.

Table 1. Baseline demographic and clinical characteristics of the studied patients

Parameters	Laser group (n=65) n (%)	TURBT group (n=65) n (%)	p value
Age, years	55.78±10.44	56.52±10.81	0.692
Gender			0.595
Male	35 (53.8)	39 (60.0)	
Female	30 (46.2)	26 (40.0)	
Tumor location			0.837
Side wall	25 (38.5)	22 (33.8)	
Neck	3 (4.6)	4 (6.2)	
Trigone	28 (43.1)	32 (49.2)	
Body	9 (13.8)	7 (10.8)	
TNM stage			0.261
T ₁	47 (72.3)	41 (63.1)	
T ₂	18 (27.7)	24 (36.9)	
Pathology grade			0.839
I	14 (21.5)	15 (23.1)	
II	32 (49.2)	34 (52.3)	
III	19 (29.2)	16 (24.6)	
Number of tumors			0.331
1	44 (67.7)	49 (75.4)	
≥ 2	21 (32.3)	16 (24.6)	
Mean tumor size (cm)	2.21±0.31	2.30±0.34	0.117
Systemic disease			0.927
Hypertension	11 (16.9)	13 (20.0)	
Coronary heart disease	6 (9.2)	8 (12.3)	
Diabetes mellitus	8 (12.3)	12 (18.5)	

TURBT: Transurethral resection of bladder tumor, TNM: Tumor, Lymph Node, Metastasis

Operative methods

The transurethral partial cystectomy with 2.0 µm laser was adopted in laser group, in which a laser surgery system with a wavelength of 2 µm was applied. The patients were subjected to epidural anesthesia in the lithotomy position, and isotonic solution was perfused into the urinary bladder under a cystoscope inserted through the urethra. The location, size, morphology and number of tumors were evaluated, then optical fibers were placed into the urinary bladder along the working channel, the parameters of laser energy were adjusted (laser wavelength: 2.013 µm), and the energy (power: 60-70 W) was transmitted via 600 µm optical fibers. Subsequently, a circular marker was made on the mucosa at 1-2 cm peripheral to the tumor, so as to determine the extent of resection. Then, the mucous layer was cut until the muscular layer along the marker line to completely resect the tumor from the basilar part. Later, the bladder serosa was continuously cut from the basilar part, and the bottom muscular layer of the tumor was excluded. After operation, the tissues were flushed with normal saline, an urethral catheter was detained, and anti-infection treatment was applied.

In TURBT group, TURBT was performed by virtue of WA22302D resectoscope (Olympus). After epidural anesthesia, the patients layed in the supine-lithotomy position on the operation table, and the resectoscope was inserted into the urinary bladder from the external urethral orifice after routine disinfection and draping, so as to observe the number, size, location and distance to the ureteral orifice of bladder tumor. Next, the bladder tumor was excised using a diathermy loop on the resectoscope, and the pedicle and basilar part of the bladder tumor were excised until the superficial muscular layer of the urinary bladder. Meanwhile, the pedicle surrounding tissues at 1 cm away from the bladder tumor and wound after resection were subjected to electric coagulation, and the bladder tumor was aspirated by a flusher. When no active bleeding and residual blocks of bladder tumor tissues were observed, the resectoscope was extracted. After operation, the urethral catheter was detained, and anti-infection treatment was conducted.

Intravesical instillation of pirarubicin was started for the patients in both groups within 24 h after operation as follows: once a week for 8 times, once every two weeks for 8 times, once every four weeks for 8 times and once every three months for 8 times.

Observation indexes

Related clinical indicators of operation, including intraoperative blood loss, operation time, in-dwelling time of urinary catheter after operation, drainage volume and length of hospital stay after operation in the two groups were recorded. Moreover, the levels of tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6) and IL-10 in the plasma of radial artery blood were detected before and after operation via enzyme-linked immunosorbent assay (ELISA). Finally, the incidence of postoperative complications such as bladder perforation, irritation symptoms of bladder and obturator nerve reflex was recorded in both groups.

Blood routine, urine routine and renal functions of the enrolled patients were followed up during treatment, and adverse reactions to treatment were inquired. Besides, cystoscopy was conducted routinely every 3 months within 2 years, urinary color Doppler ultrasonography was performed every 6 months, and chest X-ray, B-mode ultrasonography of upper urinary tract and CT scan of pelvic cavity were applied once every year. The tumor recurrence within 2 years was followed up and compared between the two groups, and the time to recurrence was recorded if the tumor recurred. New lesions indicated in cystoscopy reexamination or biopsy suggested tumor recurrence.

Statistics

SPSS 22.0 (IBM, Armonk, NY, USA) was adopted for statistical analyses. The measurement data were expressed by mean ± standard deviation, and two-sample t-test was performed for inter-group comparison. The enumeration data were presented as ratio (%), and χ^2 test was conducted for inter-group comparison. Kaplan-Meier curves and log-rank test were used for survival analysis and $p < 0.05$ suggested statistically significant differences.

Table 2. Comparison of perioperative parameters

Parameters	Laser group (n=65)	TURBT group (n=65)	p value
Operation time (min)	28.6±3.3	41.2±4.7	0.001
Blood loss (ml)	55.7±7.4	75.4±6.1	0.001
Postoperative catheter drainage time (day)	6.1±1.7	5.7±1.4	0.146
In-hospital time (day)	11.7±1.4	12.3±1.3	0.013
Complications, n (%)	13 (20.0)	28 (43.1)	0.005
Obturator nerve reflex	0 (0)	8 (12.3)	
Irritation symptoms of bladder	5 (7.7)	9 (13.8)	
Bladder perforation	4 (6.2)	4 (6.2)	
Urethrostenosis	2 (3.1)	4 (6.2)	
Serum sodium decrease	2 (3.1)	5 (7.7)	

TURBT: Transurethral resection of bladder tumor

Results

Comparison of operative conditions between the two groups of patients

The operation time (28.6 ± 3.3 min vs. 41.2 ± 4.7 min, $p < 0.001$) was remarkably shorter, and the intraoperative blood loss (55.7 ± 7.4 mL vs. 75.4 ± 6.1 mL, $p < 0.001$) was notably smaller in laser group than those in TURBT group. However, there was no statistically significant difference in the indwelling time of urinary catheter between the two groups (6.1 ± 1.7 d vs. 5.7 ± 1.4 d, $p = 0.146$). Besides, laser group had evidently shorter length of hospital stay than TURBT group (11.7 ± 1.4 d vs. 12.3 ± 1.3 d, $p = 0.013$). Varying degrees of complications, including bladder perforation, bladder irritation symptoms, serum sodium decrease and obturator nerve reflex, occurred in both groups after operation. The incidence rates of obturator nerve reflex and irritation symptoms of bladder were lower in laser group than those in TURBT group (0% vs. 12.3% & 7.7% vs. 13.8%). Furthermore, laser group exhibited a clearly lowered total incidence rate of complications in comparison with TURBT group [20.0% (13/65) vs. 43.1% (28/65), $p = 0.005$] (Table 2).

Comparison of positive biopsy rate after operation between the two groups of patients

The patients were reexamined by cystoscopy at 4 weeks after operation, and the wound tissues were taken for biopsy. The pathological results indicated that there were 9 (13.8%) cases of positive findings in TURBT group, and a second TURBT was performed. No positive findings were detected in laser group. The tumor clearance after operation was superior in laser group to that in TURBT group ($p = 0.033$).

Comparisons of IL-6, IL-10 and TNF- α levels before and after operation between the two groups of patients

The levels of IL-6, IL-10 and TNF- α displayed no statistically significant differences before operation between the two groups ($p = 0.515$, $p = 0.397$, $p = 0.735$). After operation, the IL-6 level rose from 13.78 ± 6.08 pg/mL to 35.95 ± 6.70 pg/mL and from 13.10 ± 5.79 pg/mL to 92.03 ± 6.89 pg/mL in the two groups, and it was prominently lower in laser group than that in TURBT group ($p < 0.001$). The postoperative level of IL-10 was increased from 6.32 ± 2.12 pg/mL and 5.98 ± 2.43 pg/mL to 15.15 ± 1.99 pg/mL and 10.38 ± 2.35 pg/mL, respectively, in the two groups, and laser group had a remarkably higher IL-10 level than TURBT group after operation ($p < 0.001$). Finally, the TNF- α level was raised from 30.63 ± 8.12 $\mu\text{g/mL}$ to 45.48 ± 9.24 $\mu\text{g/mL}$ in laser group and from 30.13 ± 8.68 $\mu\text{g/mL}$ to 80.85 ± 9.60 $\mu\text{g/mL}$ in TURBT group after operation, which was obviously lower in laser group than that in TURBT group with a statistically significant difference ($p < 0.001$) (Figure 1).

Comparison of tumor recurrence during follow-up between the two groups of patients

All the patients were followed up for 6-40 months, with an average of 22.6 ± 3.9 months. There were 2 cases of recurrence in laser group within 6 months, one of which was subjected to transurethral partial cystectomy with 2.0 μm laser again and had no recurrence thereafter. The pathological stage was T2 in the other case, so radical cystectomy was conducted alternatively. TURBT group had 5 cases of recurrence, with the pathological stage of T2, 3 of which underwent radical cystectomy, and the remaining 2 were treated with TURBT again because they were intolerant to radical cystectomy. However, the tumor recurred again at 5

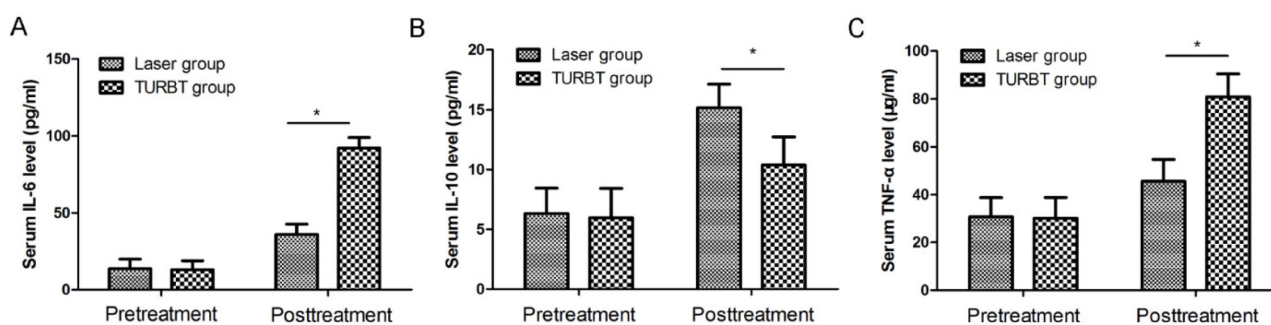


Figure 1. Comparison of IL-6, IL-10, TNF- α levels of patients in the two groups. **A:** Pretreatment IL-6, IL-10 (**B**), TNF- α (**C**) levels of patients had no significant difference between Laser group and TURBT group ($p = 0.515$, $p = 0.397$, $p = 0.735$). IL-6 (**A**), IL-10 (**B**), TNF- α (**C**) levels of patients dramatically increased after treatment. Posttreatment IL-6 (**A**) and TNF- α (**C**) levels of patients in Laser group was significantly lower than that of TURBT group, while IL-10 (**B**) level of patients in Laser group was significantly higher than that of TURBT group (* $p < 0.001$).

and 8 months after operation, and both cases died after giving up operation. During 6-12 months of follow-up, 3 cases of recurrence with T2 pathological stage were observed in laser group, all of which were treated with radical cystectomy alternatively. Among 8 cases of recurrence in TURBT group, 4 cases had no recurrence after TURBT again, while the other 4 cases manifested T2 pathological stage, 3 of which were subjected to radical cystectomy instead and 1 was treated with TURBT + systemic chemotherapy again due to unwillingness to radical cystectomy. The case died of metastatic disease at 9 months after operation. During 12-24 months after follow-up, there were 6 cases of recurrence in laser group without recurrence after transurethral partial cystectomy with 2.0 μm laser again. TURBT group had 9 cases of recurrence, 2 received TURBT again and had no recurrence thereafter, and 4 cases with T2 pathological stage changed to receive radical cystectomy. Twenty-four months later, no recurrence was detected in laser group. Four cases of recurrence were observed in TURBT group, and no recurrence occurred after a second TURBT. There was 1 case of death caused by other organ diseases in laser group at 29 months and 2 cases of death because of other organ diseases in TURBT group at 31 and 40 months. Besides, the total recurrence rate was prominently lower in laser group than that in TURBT group [16.9% (11/65) vs. 40.0% (26/65)], and the difference was statistically significant ($p=0.006$). Kaplan-Meier curves of tumor-free survival rate of patients in laser group and TURBT group is shown in Figure 2.

Discussion

As a common tumor in urinary surgery, bladder cancer accounts for about 3.2% of all the malignant tumors, and superficial bladder cancer accounts for 70-75% of bladder cancers [11-14]. Most cases have involved the muscular layer when discovered due to lack of specific clinical manifestations [15]. Currently, TURBT is adopted to treat the majority of non-muscle-invasive bladder cancer (NMIBC) cases in clinical practice, but such a therapeutic method has its own disadvantages. For example, the possible nerve stimulation and thermal damage to the peripheral and deep bladder tissues during operation can aggravate the injury of patients. Besides, the electric resection may trigger obturator nerve reflex, thus inducing bladder perforation and other complications. Moreover, only the superficial muscular layer of the urinary bladder is resected during the cleavage of tumor tissues, and the bladder tumor root cannot be resected completely, so the bladder tumor may recur after operation [16,17].

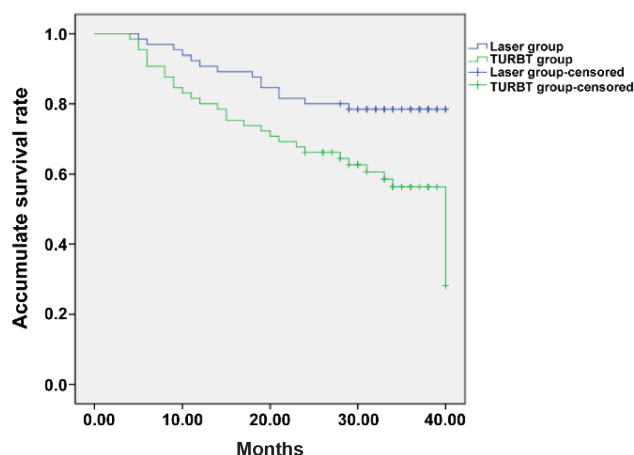


Figure 2. Kaplan-Meier survival curves of patients in Laser group and TURBT group. The tumor-free survival rate of patients in Laser group was significantly higher than that of TURBT group ($p=0.006$).

TURBT has been applied in the field of urinary surgery since 1966, and it is widely utilized to treat urological diseases due to merits, such as small trauma and blood loss and easy manipulation [18]. Laser surgery has been gradually popularized and applied in the treatment of bladder tumor in recent years, satisfactory efficacy and favorable hemostatic effect have been obtained, and the surgical safety is improved [19]. In this study, the efficacy and safety of transurethral partial cystectomy with 2.0 μm laser and TURBT were compared, and the results suggested that transurethral partial cystectomy with 2.0 μm laser can effectively reduce the operation time for NMIBC and promote postoperative rehabilitation. The possible reason is that the 2.0 μm laser causes a small amount of bleeding during the excision of malignant bladder tumor, without serious tissue necrosis, thereby saving operation time and accelerating the recovery of patients [20]. In addition, the intraoperative blood loss in laser group was smaller than that in TURBT group, demonstrating that transurethral partial cystectomy with 2.0 μm laser can prominently decrease the intraoperative blood loss, which is related to the fact that the synchronous application of vaporization and incision during the resection by 2.0 μm laser can efficiently decrease hemorrhage. Meanwhile, it was found that transurethral partial cystectomy with 2.0 μm laser is able to markedly reduce the incidence of postoperative complications of bladder cancer, which is possibly associated with the following factors: The 2.0 μm laser will not induce electric field effect when cleaving the tumor on the lateral wall of urinary bladder, so it will not lead to contraction of muscle groups innervated by obturator nerve. The 2.0 μm laser only penetrates 0.3 mm

of the tissues, and the thickness of solidified layer formed after resection is merely 1.0 mm, so the limited penetrating power to the tissues seldom causes bladder perforation [21,22]. The reason of obturator nerve reflex is that the current stimulation closely adheres to the obturator nerve along the lateral wall of urinary bladder, which triggers the contraction of adductor muscles of thigh innervated by obturator nerve, resulting in dramatic adduction and inner rotation of ipsilateral lower limb and even bladder perforation in serious cases, and causing complications such as injury of the colon and iliac vessels. As for the treatment, the obturator nerve needs to be blocked by local anesthetics including lidocaine or intravenous injection of muscle relaxant for the purpose of anesthesia and prevention at the same time. However, the muscle relaxant will increase the burden on cardiopulmonary function and make the tumor on the lateral wall of urinary bladder hard to be thoroughly resected, rising the probability of tumor recurrence after operation [23]. The 2.0 μm laser, however, will not produce electric current during the cutting of tumor tissues, without stimulation of the obturator nerve.

Inflammatory factors and operative trauma are closely correlated with physical status. For instance, IL-6 can regulate the synthesis and release of CRP, and TNF- α participates in inflammatory responses. Higher levels of both factors denote stronger inflammatory responses in the body and severer trauma. However, the higher the *in vivo* level of anti-inflammatory cytokine IL-10 is, the stronger inflammatory ability of the body will be [24,25]. According to the results in this study, the levels of serum IL-6, IL-10 and TNF- α were elevated in both groups after operation compared with those before operation, implying different degrees of postoperative injury in both groups. In contrast, laser group exhibited notably lowered IL-6 and TNF- α levels and a distinctly raised IL-10 level compared with TURBT group, suggesting

that transurethral partial cystectomy with 2.0 μm laser can significantly ameliorate inflammatory responses and alleviate injury of the patients with superficial bladder cancer.

Studies have revealed that at least 27% (up to 62%) patients with bladder cancer have residual tumors after the first TURBT, and latent or residual tumor foci can be excised by a second TURBT [26,27]. In the present study, the positive biopsy rate was 13.8% (9/65) in TURBT group, while no positive case was detected in laser group at 1 month after operation. Moreover, the postoperative recurrence rate in laser group was notably lower than that in TURBT group, illustrating that the en bloc resection of tumor may affect the recurrence and progression after operation.

There were certain limitations in this study as it was a single-center retrospective study. The sample size was not large enough, the follow-up time was not long enough, and the follow-up content was not comprehensive enough. Therefore, more rigorous and scientific large-sample, multi-center, prospective randomized controlled studies need to be designed in the future to confirm our research results, thus providing references for selecting proper treatment protocols for patients.

Conclusions

In contrast with TURBT, transurethral partial cystectomy with 2.0 μm laser for superficial bladder cancer can significantly reduce the operation time and intraoperative blood loss, obviously improve the operative effect, induce fewer postoperative complications and cause milder body injury and inflammatory response at the same time, which is worthy of clinical promotion.

Conflict of interests

The authors declare no conflict of interests.

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