Transurethral resection and degeneration of bladder tumour

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Abstract

Introduction: We evaluate the efficacy and safety of transurethral resection and degeneration of bladder tumour (TURD-Bt).

Methods: In total, 56 patients with bladder tumour were treated by TURD-Bt. The results in these patients were compared with 32 patients treated by current transurethral resection of bladder tumour (TUR-Bt). Patients with or without disease progressive factors were respectively compared between the 2 groups. The factors included recurrent tumour, multiple tumours, tumour ≥3 cm in diameter, clinical stage T2, histological grade 3, adenocarcinoma, and ureteral obstruction or hydronephrosis.

Results: Follow-up time was 48.55 ± 23.74 months in TURD-Bt group and 56.28 ± 17.61 months in the TUR-Bt group ($p > 0.05$). In patients without progressive factors, no tumour recurrence was found and overall survival was 14 (100%) in the TURD-Bt group; 3 (37.50%) patients had recurrence and overall survival was 5 (62.5%) in the TUR-Bt group. In patients with progressive factors, 8 (19.05%) patients had tumour recurrence, overall survival was 32 (76.19%) and cancer death was 3 (7.14%) in TURD-Bt group; 18 (75.00%) patients had tumour recurrence ($p < 0.05$), overall survival was 12 (50.00%) ($p < 0.01$) and cancer death was 8 (33.33%) ($p < 0.05$) in TUR-Bt group. No significant complication was found in TURD-Bt group.

Conclusion: This study suggests that complete resection and degeneration of bladder tumour can be expected by TURD-Bt. The surgical procedure is safe and efficacious, and could be predictable and controllable before and during surgery. We would conclude that for bladder cancers without lymph node metastasis and distal metastasis, TURD-Bt could be performed to replace radical TUR-Bt and preserve the bladder.

Introduction

Radical cystectomy with pelvic lymph node dissection remains the gold standard to treat muscle-invasive bladder cancer. The multifocal presentation of many of these tumours and the deep extent of invasion into the muscle layer require this approach in most cases.[1-3] Radical cystectomy may cause important changes in the lives of patients, not only in urinary and sexual function, but also in social function, daily living activities, and satisfaction with body image.[4] For the past 30 years, organ preservation strategies have demonstrated good carcinologic and quality-of-life results in breast, larynx, and esophagus cancers.[5] The research for an alternative to radical cystoprostatectomy is not new.[2-4,6-11] Radical transurethral resection of bladder tumour (TUR-Bt) can be successful in well-selected individuals when the procedure is performed correctly. Advantages of this form of therapy include decreased morbidity and greater applicability to populations with significant comorbidity. Disadvantages include significant potential for pathologic mis-staging and undertreatment of significant disease.[12]

Based on our previous experimental data, tumour bed coagulation and degeneration was applied in clinical and patients with bladder tumour were treated by transurethral resection and degeneration of bladder tumour (TURD-Bt) at our department since 2005. The aim of TURD-Bt is to completely remove visible and invisible tumour through the bladder wall by resection, vaporization and degeneration. In the present study, the effectiveness and safety of TURD-Bt were retrospectively evaluated and compared with TUR-Bt.

Methods

Patients

Between September 2005 and August 2011, 56 patients with bladder cancer were treated by TURD-Bt. Patients with bladder cancers without lymph node metastasis, distal metastasis, and with favourable bladder compliance were included in our study. They were compared with a retrospective cohort of 32 patients with bladder cancer treated by conventional TUR-Bt as the control group. Patients with or without disease progressive factors were compared between

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the 2 groups. The following factors were correlated with the rate of disease progression: recurrent tumour, multiple tumours, tumour ≥3 cm in diameter, clinical stage T2, histological grade 3, adenocarcinoma, and ureteral obstruction or hydronephrosis. Cystoscopy and histological diagnosis were routinely performed before the surgery. All patients signed an informed consent.

Table 1. Patient characteristics

	TURD-Bt n=56	TUR-Bt n=32
Age (years)	72.88 ± 11.29 (49-92 years)	71.84 ± 13.65 (36-92 years)
Male	41 (73.21%)	27 (84.37%)
Female	15 (26.79%)	5 (15.63%)
Smoker	17 (30.36%)	20 (62.50%)
Co-existing systemic diseases		
Without disease	8 (14.29%)	9 (28.12%)
1 disease	10 (17.86%)	7 (21.88%)
2 diseases	18 (32.14%)	7 (21.88%)
3 diseases	9 (16.07%)	2 (6.25%)
4 or more diseases	11 (19.64)	7 (21.88%)
Comorbidities		
Hypertension	25 (44.62%)	14 (43.75%)
Benign prostatic hyperplasia	20 (35.71%)	8 (25.00%)
Other tumours	12 (21.43%)	2 (6.25%)
Cerebral infarction	11 (19.64%)	2 (6.25%)
Diabetes mellitus	10 (17.86%)	6 (18.75%)
Coronary heart disease	8 (14.29%)	5 (15.63%)
Urinary stone	7 (12.50%)	0
Ureteral obstruction or renal insufficiency	6 (10.71%)	3 (9.38%)
Other diseases	25 (44.64%)	18 (56.25%)
Total	124 (221.43%)	58 (181.25%)
ASA grade		
Grade I	22 (39.29%)	13 (40.63%)
Grade II	20 (35.71%)	10 (31.25%)
Grade III	13 (23.21%)	9 (28.12%)
Grade IV	1 (1.79%)	0
pT Stage		
Stage Ta	8 (14.29%)	5 (15.63%)
Stage T1	37 (66.07%)	22 (68.75%)
Stage T2	11 (19.64%)	5 (15.63%)
CIS	15 (26.79%)	8 (25.00%)
Tumour grade		
Grade 1	26 (46.43%)	15 (46.87%)
Grade 2	24 (42.86%)	11 (34.38%)
Grade 3	6 (10.71%)	6 (18.75%)

TURD-Bt: transurethral resection and degeneration of bladder tumour; TUR-Bt: transurethral resection of bladder tumour. The difference of smoker was significant between the 2 groups ($p < 0.01$).

Operative technique

Surgery was performed using spinal anesthesia. During the surgery, we used a standard 26 Fr continuous-flow Storz resectoscope and an electrosurgical generator (Bircher Type-4400, Conmed, Utica, NY) with a maximum output power of 330 W and current frequency of 494 kHz.

In the TURD-Bt group, a wing loop or grooved roller electrode was used. Electrosurgical generator was set to a pure cutting current of 230 to 250 W for resection and vaporization, and 70 to 80 W for coagulation. For the big tumour, which was projecting into the bladder cavity, the projecting portion was resected by a wing loop first, the base was vaporized to the muscular layer by a grooved roller electrode, and then the tumour bed was repeatedly coagulated by a grooved roller electrode. Finally, 1 to 2 cm of normal mucosa in the periphery of the lesion and all suspicious lesions on the bladder mucosa were coagulated by a grooved roller electrode (Fig. 1). For the small tumour or carcinoma in situ (CIS), the tumour was directly vaporized and coagulated by a grooved roller electrode.

TUR-Bt was performed as usual. All procedures were performed by 1 urologist. In the 2 groups, patients had immediate postoperative pirarubicin instillation and then regular postoperative intravesical pirarubicin therapy was administered for 2 years in all patients.

One urological pathologist performed all the histopathological analyses. Postoperatively, follow-up was performed in 1 month, urinary cytology and cystoscopy were performed every 3 months, and computed tomography (CT) or ultrasonography was performed every 6 months for 2 years to examine the upper urinary tract and look for recurrence and metastasis; this was done every year by the outpatient department and then by telephone and regular mail after the 2-year mark.

Statistical analysis

Differences of measurement data were evaluated using a Student's t-test. Pre- and postoperative outcomes for each patient were compared using a paired t-test. Enumeration data were compared using X^2 test. P values <0.05 were considered significant. Values were reported as the mean ± standard deviation (SD).

Results

The TURD-Bt group included 56 patients and the TUR-Bt group 32 patients. No significant difference was observed in patient age, gender, coexistent systemic diseases, comorbidities, American Society of Anesthesiologists (ASA) grade, pathological stage, and tumour grade between the 2 groups. Of the total 88 patients, 87 were pathologically diagnosed

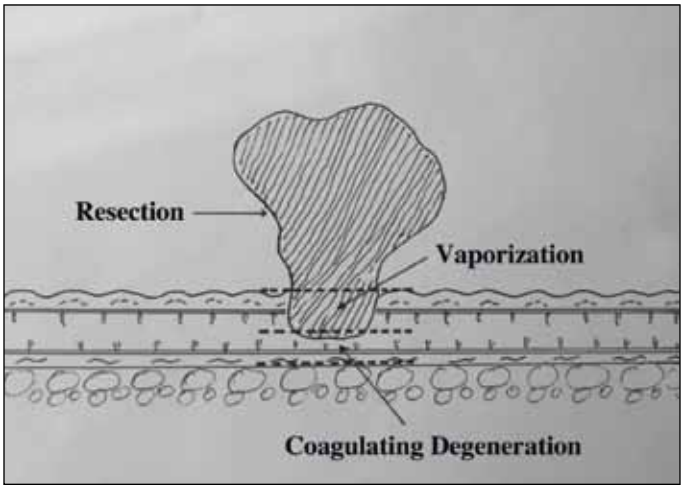

Fig. 1. The surgical management to the bladder tumour in different anatomical layers.

with bladder transitional cell carcinoma and 1 patient from the TURD-Bt group had adenocarcinoma. The follow-up time was 48.55 ± 23.74 months (21-96 months) in TURD-Bt group and 56.28 ± 17.61 months (24-82 months) in TUR-Bt group ($p > 0.05$). The characteristics in patients with progressive factors are shown in Table 2.

Compared with preoperative hemoglobin level, postoperative hemoglobin level was decreased by 5.28 g/L in the TURD-Bt group ($p < 0.001$) and by 4.35 g/L in the TUR-Bt group ($p > 0.001$). There were no significant complications during surgery in the TURD-Bt group (Table 3). We tallied the surgical outcomes in patients with or without progressive factors in the two groups (Table 4, Table 5).

In patients with postoperative recurrent tumours (that is, after the reoperation), in the TURD-Bt group, 4 continued with TURD-Bt and 1 patient therapy was changed to radical cystectomy for advanced stage disease, In the TUR-Bt group, 2 patients continued with TUR-Bt, other 5 patients were changed to radical cystectomy for advanced stage disease and 3 patients to TURD-Bt.

Among the 10 patients who died in the TURD-Bt group, 1 died of bladder tumour, 2 of tumour metastases without bladder tumour recurrence, and 7 of causes unrelated to bladder tumour. In the 12 patients who died from the TUR-Bt group, 6 died of bladder tumour, 2 of tumour metastases without bladder tumour recurrence, and 4 of causes unrelated to bladder tumour.

Discussion

Radical TUR-Bt alone may represent a bladder-sparing option in patients with solitary tumours at the trigone, posterior, or lateral walls with focal invasion into muscularis propria; it has been associated with long-term bladder survival of 60% to 70% in appropriately selected patients.[1,3,13,14]

Table 2. Characteristics in patients with progressive factors

	TURD-Bt n=42	TUR-Bt n=24
Age (year)	72.79 ± 12.46	73.38 ± 13.92
Recurrent tumour	11 (26.19%)	8 (33.33%)
Multiple tumours	26 (61.90%)	15 (62.50%)
Tumour >3 cm	21 (50.00%)	11 (45.83%)
Stage T2	11 (26.19%)	5 (20.83%)
Grade 3	6 (14.29%)	6 (25.00%)
Adenocarcinoma	1 (2.39%)	0
Ureteral obstruction	4 (9.52%)	1 (4.17%)

TURD-Bt: transurethral resection and degeneration of bladder tumour;
TUR-Bt: transurethral resection of bladder tumour. No significant difference was observed between the 2 groups.

The major advantage of TUR-Bt is bladder preservation. Several points need to be made about radical TUR-Bt. The tumour may be present beyond the limits of the resection, and the established risk of understaging is 30% to 50%. Kolozsy reported a series of patients undergoing "differential" TUR-BT, in which additional tissue was resected[15] as the base and periphery of the lesion after all visible tumour had been resected. About one-third of the lesions had residual tumour at the base and periphery even after resection of all visible tumour. These patients would have still had an inadequate resection if only the visible tumour had been resected. Therefore, complete endoscopic removal of the bladder tumour may be needed.[1,14]

In 2001, Li and colleagues evaluated the effects of high-frequency current on renal, prostatic, muscular, dermal, and adipose tissue from human, pig, and rabbit in vitro and in vivo.[16-20] Under the electromicroscope, vaporization through simple coagulating current had obvious damage to renal, prostatic, muscular, and dermal tissue under the burned surface. The damaging effects were gradually decreased from the burned surface to the tissues 6 mm away. At about 0 to 2 mm under the burned surface, the microstructure of the tissues close to the burned surface disappeared and the distal end had severe damage. There were disrupted cell nuclei, mitochondria, endoplasmic reticulum and other organs were fused as sheets with microstructure; moreover, thin filaments and collagen fibers had coagulating necrosis. About 3 to 4 mm under the burned surface, blistering occurred in the cytoplasm of tissues, the mitochondria crests were fused or disappeared, the endoplasmic reticulum was swollen, and the basilar membrane, thin filament, and collagen fibre were damaged. The significant histological changes could even be seen at 5 to 6 mm under the burned surface. Electric resistance is complicated; it can be affected by tissue density and its moisture content, elements in the body fluid, and the presence of positive or negative ions. The muscle tissue is composed of muscle fibres with plenty of water and inorganic salts in the sarcoplasm. The electrical resistance

Table 3. Operative complications

	TURD-Bt n=56	TUR-Bt n=32
Surgical time (min)	32. 23 ± 10.09	37.33 ± 8.98
Preoperative hemoglobin (g/L)	128.80 ± 18.81	123.94 ± 16.13
Postoperative hemoglobin (g/L)	123.52 ± 16.78	119.59 ± 17.98
Obturator nerve reflex	7 (12.50%)	7 (21.87%)
Transfusion	0	1 (3.13%)
Bladder perforation	0	1 (3.13%)
Open surgical repair	0	1 (3.13%)

The difference of surgical time was significant between the two groups, $p < 0.05$.

Table 4. Surgical outcomes in patients without progressive factors

	TURD-Bt n=14	TUR-Bt n=8
Age (year)	70. 71 ± 11.10	67.25 ± 12.53
Overall survival	14 (100%)	5 (62.50%)
Tumour recurrence	0	3 (37.50%)
Change in surgical method	0	2 (25.00%)
Cancer death	0	1 (12.50%)
Non-cancer death	0	2 (25.00%)
Follow-up (months)	48.50 ± 23.70	55.50 ± 18.48

No significant difference in age and follow-up time was observed between the 2 groups.

rate of muscle tissue is 90.0 with direct current, which is a good conductor; the electrical resistance rate of adipose tissue is 10.8×10^2, which is not a good conductor. The findings further suggested that the effect of high-frequency current on adipose tissue was minimal and damaging effects only could be seen 1 mm under the burned surface.

According to the change in bladder volume, bladder wall thickness is between 1.1 and 4.5 mm.[21,22] Procedures to effectively remove the tumorous thickness on the bladder wall include resecting the tumour, vaporizing the tumor and bladder wall, and degenerating the bladder wall and periphery tissue around the tumour bed. This can be summed up as follows: effective removing thickness = resection + vaporization + degeneration (Fig 2). As a result, tissue structure of the residual tumour in deep layer under the tumour bed is further degenerated by the damaging effect of electric current. Preoperative staging to the bladder tumour has been very inaccurate and has not improved much over the past years. This is of particular concern when one is deciding on less aggressive forms of therapy for muscle-invasive disease.[12,23-25] However, the purpose of complete or radical resection and degeneration of bladder tumour could easily be more achieved by TURD-Bt. Meanwhile, 1 to 2 cm normal mucosa in the periphery around the lesion and all suspicious lesions on bladder mucosa were coagulated by a grooved roller electrode, which could effectively remove and degenerate residual CIS and other invisible tumour – crucial to decrease the incidence of tumour recurrence.

During surgery, the tumor bed is repeatedly coagulated with a grooved roller electrode, decreasing the moisture content in the tissue and increasing the electrical resistance rate. As a result, electric intensity in the circuit and the electric decreases and the tumour bed is not easily vaporized by the electric current.[15-19] Furthermore, the periphery around the bladder has adipose tissue and it is not easily damaged by the electric current. TURD-Bt is more safe than TUR-Bt and can completely degenerate tumor cells through the bladder wall, while keeping the bladder wall intact. In TURD-Bt, the obturator nerve reflex is less than it is in TUR-Bt and the risk of obturator nerve reflex is easily controlled. When obturator nerve reflex occurs, the wing loop is exchanged to a grooved roller electrode, and then the tissue is further vaporized with coagulating current until the obturator nerve reflex disappears.

The resected depth of the bladder tumour and wall could be evaluated by CT or ultrasonography preoperatively. After the tumor is resected, the tumour bed could be further vaporized and degenerated by the coagulating current.[20,21] Therefore, the surgical procedure for complete resection and degeneration of the bladder tumour will be predictable and controllable. Surgery time in the TURD-Bt group was shorter than in the TUR-Bt group. In our study, all patients with or without progressive factors did well after TURD-Bt surgery. There were no significant complications during surgery in the TURD-Bt group. Overall survival rate, tumour recurrence and cancer death in the TURD-Bt group were much better than in the TUR-Bt group.

Table 5. Surgical outcomes in patients with progressive factors

	TURD-Bt n=42	TUR-Bt n=24	*p* value
Age (year)	72. 79 ± 12.46	73.38 ± 13.92	>0.05
Overall survival	32 (76.19%)	12 (50.00%)	<0.05
Tumour recurrence	8 (19.05%)	18 (75.00%)	<0.01
First relapse time	18.40 ± 15.18	19.82 ± 15.00	>0.05
Advanced stage	1 (2.38%)	5 (20.83%)	<0.05
Reoperation	5 (11.90%)	10 (41.67%)	<0.01
Change surgical method	1 (2.38%)	8 (33.33%)	<0.01
Continue former endosurgery	4 (9.52%)	2 (8.33%)	>0.05
Cancer death	3 (7.14%)	8 (33.33%)	<0.05
Survival time	29.33 ±16.17	32.43 ± 17.96	>0.05
Non-cancer death	7 (16.67%)	4 (16.67%)	>0.05
Survival time	22.79 ± 24.46	18.00 ± 8.49	>0.05
Follow-up time	48.57 ± 24.03	56.54 ± 17.71	>0.05
Total death (cancer and non-cancer)	10	12	

No significant difference in age and follow-up time was observed between the 2 groups.

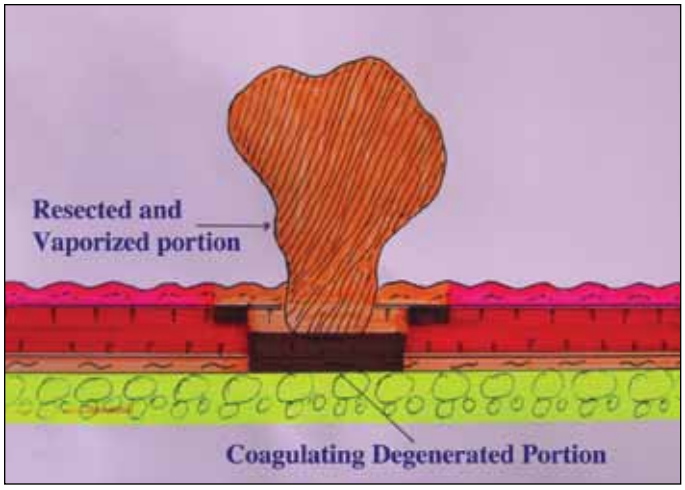

Fig. 2. The anatomical layers of resected, vaporized and coagulating degenerated portion were located in bladder wall.

Conclusions

Our study showed that complete resection and degeneration of the bladder tumour can be expected and that the bladder wall can be preserved during a TURD-Bt. The incidence of tumour recurrence is decreased by degenerating the invisible residual tumour in the deep tissue and suspicious lesions. The surgery is safe and effective and could be predictable and controllable before and during surgery. For bladder cancers without lymph node metastasis, distal metastasis and with favourable bladder compliance, TURD-Bt could be performed to replace radical TUR-Bt and preserve the bladder. Longer follow-up is needed to evaluate long-term results. Moreover, additional randomized trials comparing other transurethral surgeries are warranted to delineate the best transurethral surgery to manage bladder tumour.

Competing interests: Dr. A. Li, Dr. Fang, Dr. Zhang, Dr. W. Li, Dr. H. Li, Dr. S. Liu, Dr. Wang and Dr. Zhang declare no competing financial or personal interests.

This paper has been peer-reviewed.

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