

# Second Transurethral Resection of Bladder Tumour for the Treatment of Muscle-invasive Bladder Tumours

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## ABSTRACT

**Objective:** This work aims to evaluate the effectiveness of a second transurethral resection for muscle-invasive bladder tumours. The clinical literature of 15 cases of patients with muscle-invasive bladder cancer treated by second transurethral resection of bladder tumours (TURBT) was analysed.

**Methods:** The operation was based on the principle of TURBT down to the fatty layer outside the bladder wall. A second transurethral resection was performed four to six weeks after the initial resection. All patients received intravesical chemotherapy postoperation. Fifteen cases were followed-up for three to 26 months, with a mean period of 14 months.

**Results:** After the second transurethral resection, residual tumours were found in two patients. All patients underwent computed tomography scan and biopsy. No patient had a recurrence of the tumour. Eighty per cent of the patients had normal bladder function and 20% had mild-to-moderate lower urinary tract symptoms. All patients had a high quality of life.

**Conclusions:** A second TURBT is suitable for muscle-invasive bladder cancer when bladder preservation is planned as it prolongs the survival time and improves the patients' quality of life.

**Keywords:** Conservation treatment, muscle-invasive bladder tumour, transurethral resection, TURBT

# Segunda Resección Transuretral del Tumor de la Vejiga en el Tratamiento de los Tumores de Vejiga con Invasión Muscular

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## RESUMEN

**Objetivo:** Este trabajo tiene como objetivo evaluar la eficacia de una segunda resección transuretral de los tumores vesicales con invasión de la capa muscular. Se analizó la literatura clínica de 15 casos de pacientes con cáncer de la vejiga con invasión muscular, tratados con segunda resección transuretral de los tumores de la vejiga (TURBT).

**Métodos:** La operación se basó en el principio de TURBT hasta la capa de grasa fuera de la pared de la vejiga. De cuatro a seis semanas después de la resección inicial, se realizó una segunda resección transuretral. Todos los pacientes recibieron quimioterapia intravesical postoperatoria. Quince casos tuvieron seguimiento de tres a 26 meses, con un periodo promedio de 14 meses.

**Resultados:** Después de la segunda resección transuretral, se hallaron tumores residuales en dos pacientes. A todos los pacientes se les hizo una biopsia y una tomografía computarizada. Ningún paciente tuvo una recidiva del tumor. Ochenta por ciento de los pacientes tenían una función vesical normal, en tanto que un 20% presentaban síntomas de las vías urinarias de leves a moderadamente bajos. Todos los pacientes tenían un alto nivel de vida.

**Conclusiones:** Es conveniente una segunda TURBT para el cáncer de vejiga con invasión muscular cuando se planea la preservación vesical, ya que prolonga el tiempo de supervivencia y mejora la calidad de vida de los pacientes.

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**Palabras claves:** Tratamiento de conservación, tumor de la vejiga con invasión de la capa muscular, TURBT, resección transuretral

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## INTRODUCTION

Radical cystectomy for bladder cancer and orthotopic neobladder is a standard treatment for invasive bladder tumours (1). However, this procedure is accompanied by marked surgical trauma and various intra-operative and postoperative complications. The postoperative quality of life of patients was reduced, and some patients could not tolerate or would not accept surgery. In the past 20 years, the bladder preservation and survival rates have greatly improved for invasive bladder tumours with comprehensive bladder preservation. Patients with invasive bladder tumours were first treated with transurethral resection of the bladder tumour (TURBT), followed by radical cystectomy for bladder cancer. No residual tumour was observed in approximately 15% of radical bladder pathological specimens, and radical cystectomy for bladder cancer did little to control distant micrometastasis. Whether radical cystectomy for bladder cancer can be seen as excessive treatment for all patients is unknown. Although randomized control studies are lacking, current clinical trial data show that the overall five-year survival rate of bladder preservation is approximately 50%. Some single-centre studies with large homogeneous samples have shown that the overall five-year survival rate of radical cystectomy for bladder cancer in the T2 to T4 stage is 36% to 48% (2, 3). Therefore, compared with radical cystectomy for bladder cancer, the comprehensive treatment of invasive bladder tumours with bladder preservation offered similar results. A variety of methods are available for persons who do not want radical cystectomy for bladder cancer (4).

From October 2007 to December 2009, a second TURBT was given to patients with muscular-invasive bladder and various medical disorders, with poor condition for radical cystectomy, or those worried about their quality of life and who refused radical cystectomy.

## SUBJECTS AND METHODS

The 15 cases (13 males and two females) in this study were aged between 56 and 79 years. Co-morbidities included nine cases of hypertension, seven cases of diabetes, 10 cases of coronary artery disease, six cases of respiratory insufficiency, six cases of cerebrovascular diseases and eight cases who refused radical cystectomy for bladder cancer out of concern for their quality of life. All cases had incipient bladder tumours and were hospitalized because of repeated and painless gross haematuria. Multiple tumours were revealed by cystoscopy, parts of which were connected to clusters or substantial tumours. Carcinoma of the uroepithelium was revealed histopathologically, G2 to G3 cases. No local lymphadenopathy or local and distant metastases were found by enhanced computed tomography (CT) scanning, except for an enhanced local bladder wall in the T2 to T3 stage.

## Treatment method

All patients received bladder preservation treatment. They had signed the informed consent for therapy.

Patients were placed in the bladder lithotomic position, with lumbar anaesthesia or continual epidural anaesthesia, and given 5% mannitol as the flushing fluid. The electroexcision power ranged from 160–180 W, and the electrocoagulation power ranged from 60–80 W. Cystoscopy was carefully done before resection to identify the actual position and sizes of the bladder tumours. The perioperative bladder was kept moderately full. The tumours that could be easily removed were first resected, followed by the others. All patients were resected to the deep muscle layer, in which four cases reached the fat layer outside the bladder, 2 cm away from the tumours. Postoperatively, three-way catheters were retained. Continuous bladder irrigation was performed in case of excessive bleeding, and 50 mg epirubicin perfusion was administered if there was no significant bleeding and perforation.

Postoperative bladder perfusion was given once a week, and a second electroexcision of the bladder tumour was performed at four to six weeks. Postoperative bladder perfusion was given once a week for eight weeks, then once a month for 10 months. Cystoscopy and CT review were done once every three months. Lower urinary tract symptoms (LUTS) and quality of life were also investigated.

## RESULTS

### Postoperative pathologic stage

Fifteen cases of muscular-invasive bladder patients were all given complete resection of bladder tumours, with operation times of 60–120 minutes (average 80 minutes). No intra-operative massive haemorrhage, serious bladder perforation, and other complications were observed, except for two cases of mild bladder perforation. None of the patients suffered from electroexcision syndrome. The catheters were retained for seven to 12 days (average nine days). Postoperative pathology reports indicated G2 to G3 uroepithelial carcinoma. The postoperative pathologic stage included six cases of T<sub>2a</sub>, five cases of T<sub>2b</sub> and four cases of T<sub>3a</sub>.

A second electroexcision was conducted after five weeks of the first, on average. The incrustation or sphaelus was adherent to the centre of the cicatrix generated in the first electroexcision, with no overlying mucous membrane and only an inflammatory and swollen margin. Cicatrix, any inflammatory and swollen areas and suspicious neoplasm were completely resected, deep in the muscle layer of the bladder or the fat layer outside the bladder. There were three cases of bladder perforation during the operation and indwelling catheters were retained for seven to 12 days

(average nine days). Four cases of G2 to G3 uroepithelial carcinoma were observed in the postoperative pathology reports. Tumours were not seen in the 11 other cases.

### Postoperative follow-up

All patients were given postoperative follow-up for three to 26 months. There was no tumour recurrence or metastasis or ureterovesical stenosis, backflow and bladder contracture. Eighty per cent of the patients had normal bladder function and 20% had mild-to-moderate LUTS. All patients had a high quality of life.

### DISCUSSION

The comprehensive therapeutic schedule of bladder preservation is mainly divided into two kinds: TURBT combined with systemic chemotherapy and TURBT combined with systemic chemotherapy and local radiotherapy. However, no unified schedule exists in choosing cases, combining therapeutic schedules, and choosing chemotherapy drugs, courses, and radiation doses. In a recent meta-analysis of six randomized controlled trials of 491 patients, it was thought that the survival rate increased by 9% after three years of chemotherapy (HR 0.75; 95% CI 0.60, 0.96;  $p = 0.019$ ). However, recommending chemotherapy was previously considered because of smaller samples (5). Shipley *et al* reported 190 cases of T2 to T4a patients who were given radiation and chemotherapy after completing TURBT in the same period. The overall five- and 10-year survival rates were 54% and 36%, respectively, and the 10-year disease-specific survival rate of bladder preservation was 45%. These results indicate that in about half of the patients, a complete bladder could be preserved (6). However, it remains controversial whether large doses of radiation therapy in the treatment of bladder preservation would affect the normal bladder function, the intestinal tract and sexual function.

Solsona *et al* reported that patients with muscle-invasive bladder tumours were given bladder preservation, with a near curative effect of radical cystectomy (7). Theoretically, all patients with muscle-invasive bladder tumours (T2 to T4) could be given a comprehensive treatment of bladder preservation after ruling out distant metastasis, but with different survival rates and prognoses for different clinical and pathological features. Whether the complete resection of TURBT (no residual tumour macroscopically or microscopically) directly influenced the prognosis of patients was also considered. Dunst *et al* believed that the survival rates of T3 to T4 patients were similar to those of T2 patients given complete resection macroscopically and microscopically. Those patients who were not given complete resection had poor prognosis regardless of the stage of carcinoma, and the five-year survival rates of patients with macroscopic residual tumours were only 31% (8). Patients with muscle-invasive bladder tumours who did not want or

could not tolerate radical cystectomy for bladder cancer were afforded bladder preservation treatment. This approach, which was validated by clinical data, still showed a higher radical tumour recurrence rate after TURBT (9). A second radical electroexcision was done according to the experience in treatment of non-muscle-invasive bladder tumours (10–12). Some patients were given radical electroexcision by Rödel *et al*. They did not have pelvic lymph node metastasis, carcinoma *in situ* and urinary obstruction, and their tumour diameter was less than 3 cm away from the top of the bladder with optimistic clinical results (13). The indications of the second radical electroexcision were as follows: 1) a histological basis of muscle-invasion, 2) no hydronephrosis or distant metastasis in the early diagnosis, 3) normal kidney function and haemogram, 4) appropriate for radical bladder cancers, 5) no lymphatic metastasis in imaging (14) and 6) patients could not tolerate or would not accept radical cystectomy for bladder cancers. Patients with single and small tumours in the early invasive bladder cancer (stage T2) were also the best candidates for bladder preservation. Patients with tumours above stage T<sub>3b</sub> were contraindicated.

Radical TURBT was considered for the resection of tumours deep within the fat layer outside the bladder, specifically, the overall resection of the bladder wall with normal bladder mucous membrane 1 cm to 2 cm around the basal parts of the tumours. The bladder was carefully examined before TURBT to identify the numbers, sizes, sites and forms of tumours, as well as whether any lesion in the bladder neck and ureterostoma was present, to determine possible small focal cancer or carcinoma *in situ*. Generally, normal muscle fibre could be seen in the basal parts of the shallow muscle-invasive tumours. However, ambiguous basal structure or necrotic tissues suggested deeper invasion, which should be given additional electroexcision when necessary, until normal tissue is seen or bladder perforation to the fat layer outside the bladder occurs. The bladder tissue at 2 cm around the basal parts of the tumours after tumour resection was given electroexcision to the normal muscle fibre or the fat layer outside the bladder. All cases did not receive random biopsies because of the large number of tumours.

Transurethral resection of bladder tumour was again administered after TURBT for two to four weeks, which was similar to the first one. The bladder was observed carefully, especially the first surgical cicatrix and inflammatory and swollen area. The cicatrix, inflammatory and swollen area and suspicious neoplasm were completely resected to the deep muscle or the fat layer outside the bladder with the same range as the first electroexcision. The basilar part, which was obtained by electroexcision ring, was biopsied. Four cases (36.4%) of G2 to G3 uroepithelial carcinoma were noted in the postoperative pathology reports, but tumours were not observed in the 11 other cases. No residual tumours were observed in the basal biopsies. Schwaibold *et al* (15) applied

Re-TUR for the treatment of 136 T1 patients with bladder tumours, 52% of whom had residual tumours. These results might be related to the radical electroexcision in the deep muscle for the first treatment, of which four cases were to the fat layer outside the bladder.

The primary intra-operative problem of radical TURBT was bladder perforation. The tumours in the posterior and bilateral walls were resected first, followed by the top portion, so that the operation could be terminated at any time if a perforation occurred, because of the reduced absorption of flushing fluid that would take place. Postoperative complications were similar to those of conventional electroexcision, but with more bleeding because of the deeper resection, especially the tumours in the bladder neck, which could be related to the difference in neck contraction. Hamasaki *et al* (16) reported that 202 ml blood was transfused on average, but patients in this study were not transfused because no massive haemorrhage occurred. The bladder was flushed when necessary, depending on the bleeding conditions. The bladder perfusion was administered in case of less bleeding. Immediate postoperative infusion was given to maintain bladder irrigation chemotherapy.

Bladder preservation had a risk of bladder tumour recurrence, including non-muscle and muscle tumours. All patients were given regular postoperative bladder irrigation to reduce tumour recurrence rates. The tumour recurrence was related to the numbers and sizes of tumours. The tumour recurrence rates of multiple lesions were 43 times higher than those of single lesions, and the recurrence rates of patients with tumours > 3 cm diameters were six times higher than those with < 3 cm diameters (17). The most important index for predicting the survival rate of invasive bladder tumours was the occurrence of hydronephrosis; early diagnosis and status of resection (complete or not) directly affected the prognosis of patients (6, 8). To date, patients were followed up for three to 26 months (average 14 months). No tumour recurrence and metastasis were observed by regular cystoscopy and pelvic CT review. The follow-up results show that the patients had normal bladder function. Solsona *et al* (18) applied TURBT to patients with invasive bladder tumours. Consequently, the five- and 10-year survival rates without tumours were 80.5% and 74.5%, respectively, with no significant difference compared with the radical cystectomy control group. The five- and 10-year bladder function preservation was 82.7% and 79.6%, respectively. Zietman *et al* examined the bladder function of 32 patients treated by bladder preservation *via* urodynamics. Patients in the median were followed up for two years, 75% of whom had normal bladder function, and 20% of the males and 27% of the females had mild-to-moderate intestinal symptoms. No severe intestinal complication was observed (19). In a 10-year follow-up of 43 patients given local cystectomy for bladder cancer, Herr *et al* (9) reported that 58% of the patients retained normal bladder function (20). Chemo-

therapy and radiation were not given to the patients, and no intestinal complications were found. Further observation is still necessary because of the short follow-up time. In the present study, 80% of the patients had normal bladder function, and 20% had mild-to-moderate LUTS. All of them had a high quality of life.

A second radical TURBT in the treatment of muscular-invasive bladder tumour is not physically demanding on patients. From our cases, we believe that tumour resection and bladder preservation have enhanced the patients' quality of life. The proposed treatment is a better alternative for selected patients, and long-term outcome in a larger number of cases is required.

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