



Genitourinary Cancers

Utility and Safety of Repeat Transurethral Resection of Bladder Tumor Performed at a Tertiary Center

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Abstract

Introduction Repeat transurethral resection of bladder tumor (ReTURBT) has become an integral part of the management of superficial bladder cancers at various urological centers around the world. Early detection of residual disease, leading to upstaging in some cases, leads to decrease in recurrence rates. Our study aimed to analyze the impact of ReTURBT in detecting residual tumor and tumor recurrences, hence validating the benefits of procedure as a routine.

Materials and Methods A total of 152 patients with superficial bladder cancer who were treated at Cancer Institute (WIA) between January 2005 and December 2013 were analyzed and followed up for 3 years.

Results Of the 152 cases who underwent ReTURBT, 47 patients had residue in the final histopathology of the resected specimen (31%). The overall rate of upstaging to muscle-invasive disease following ReTURBT was 3.3%. The mean follow-up period was 47.13 months, during which 25 (17%) out of 147 patients who underwent ReTURBT had disease recurrence. There was no additional morbidity due to ReTURBT as compared with the primary procedure.

Conclusion ReTURBT is an effective procedure in treating recurrent tumors also as long as they remain superficial. The procedure when performed with utmost care in experienced hands remains a very safe procedure to be followed as a routine and standard.

Keywords

- ▶ nonmuscle-invasive bladder cancer
- ▶ recurrence
- ▶ transurethral resection of bladder tumor

Introduction

Transurethral resection followed by intravesical *Bacillus Calmette-Guerin* (BCG) therapy has been the standard of care for T1 bladder tumors. Historically, a single transurethral resection was performed followed by intravesical BCG therapy.¹ The residue left behind during the transurethral resection of bladder tumor (TURBT) was meant to be taken care by intravesical immunotherapy. Later, it was observed that the disease recurrence was very early in some set of patients (within 3 months). The reason behind the early recurrences was found out to be the status of residual tumor that was left behind after the

TURBT.² Patients with significant residual tumor following TURBT had early recurrence. In fact, those were actually due to persistence of the disease rather than a true recurrence. Hence, not having a residual disease was considered a prognostic factor for disease-free survival, thus evolved the need for improving the quality of initial TURBT and measures to assess its completeness. We conducted a study to analyze the impact of repeat TURBT (ReTURBT) in detecting residual disease and in restaging the disease following complete TURBT. We also evaluated the benefit of performing the procedure as a routine in a developing country scenario, considering its morbidity.

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Materials and Methods

It was a combined retrospective and prospective study that included a total of 152 patients with superficial bladder cancer who were treated at Cancer Institute (WIA) from January 2005 to December 2013. It included all patients with newly detected cancer and those diagnosed at an outside facility who may have undergone TURBT elsewhere. Patients treated at an outside facility for superficial bladder cancer and presenting to the institute with recurrence were also included.

All newly diagnosed patients were evaluated by computed tomography (CT) of the abdomen and pelvis with urographic reconstruction along with urine cytology from three consecutive early morning samples. Patients who had undergone TURBT elsewhere and presented to the institute for further management were evaluated by reviewing the upfront imaging. The TURBT operation notes were reviewed, and completeness of the resection was ensured. Cystoscopy was performed in all the patients presenting after undergoing TURBT at an outside facility to ensure that no gross residue was left behind. If there was an obvious residue, then a second-staged TURBT was performed.

TURBT was performed under spinal or general anesthesia. After adequately distending the bladder with saline, the bladder was completely visualized. Resectoscope fitted with 30-degree lens was then introduced, and resection was performed piecemeal using a loop with the aid of cutting current.

Ultrasound of the abdomen and pelvis was performed before ReTURBT. As in the TURBT, the entire bladder was visualized and thoroughly checked for any residue and resected appropriately. If no residue is found, then the tumor bed was re-resected, and the resection was performed especially at the margins of the previous resected sites also.

In our institute, only the carefully selected patients who had low-grade solitary lesion that had been completely resected in initial TURBT and no residual tumor/CIS was found in the ReTURBT specimen were not offered intravesical BCG therapy. ReTURBT was performed for all nonmuscle-invasive bladder cancers including Ta histology.

Intravesical BCG is administered to T1 bladder tumors, commencing 3 to 4 weeks following ReTURBT. The treatment schedule followed at our institute was administration of intravesical BCG once a week for 6 weeks followed by maintenance dose of once a month administration for 6 months. A check cystoscopy was performed once after completing the weekly regimen and again after completing the maintenance therapy.

Follow-Up

The follow-up protocol for nonmuscle-invasive bladder tumors included a 3 monthly follow-up for the first 3 years and then every 6 monthly for the next 2 years. Follow-up was annual after the completion of 5 years. Every follow-up visit included clinical history and physical examination and urine cytology and flexible cystoscopy under local anesthesia. Annual investigations included chest X-ray and ultrasound of the abdomen and pelvis apart from the routine follow-up investigations.

The study protocol was approved by the local Institution Review Board at the authors' affiliated institution and meets the standards of the Declaration of Helsinki.

Statistical Analysis

All data were analyzed using SPSS statistics software Version 15 (SPSS Inc., Chicago, Illinois, United States). Chi-square test and binary logistic model analysis were also used. Statistical significance was at $p < 0.01$.

Results

Initial TURBT was performed in our institute in 88 (57.9%) out of 152 cases, and 64 (42.1%) patients had undergone TURBT elsewhere and presented to our institute for further management.

The mean age at diagnosis was 57.7 years. The most elderly patient was 80 years old, and the youngest was 27 years old. Males were predominant in the group, occupying 86.1% (131 patients) of the total and females comprising only approximately 13.9% (21 cases). The mean age of presentation was almost similar among both sexes: 60 years among females and 57.4 years among the males.

Out of 152 patients, 83 (54.6%) had unifocal disease and the remaining 69 (45.4%) patients had multifocal disease. Complete resection of visible tumor was performed in 145 (95.4%) of 152 patients. Seven (4.6%) cases who had large volume tumor had incomplete resection and underwent a second-stage TURBT before ReTURBT. Of 152 patients, Ta histology was seen in 14 (9.3%) cases. These patients with Ta histology were also included because they all got reassigned to a higher T status in ReTURBT. T1 histology without deep muscle identification was seen in 74 cases (48.6%) and T1 with deep muscle identification was seen in 64 cases (42.1%).

Of 152 patients, 7 (5%) had low-grade/grade 1 tumors, 110 (71%) had intermediate/grade 2 tumors, and 35 (24%) patients had high-grade/grade 3 tumors.

Deep muscle was identified in 71 (46.7%) of 152 patients and was absent in the resected specimen in 81 (53.3%) patients. In the subgroup of patients who underwent TURBT at an outside facility, only 17% had deep muscle identified in the TURBT specimen, whereas 68% of patients had deep muscle identified in the TURBT performed in our institute.

Out of 152 patients, 100 (65%) underwent ReTURBT within 6 weeks of initial surgery and 52 (34.2%) patients underwent ReTURBT after 6 weeks. There was considerable delay in the patients who had undergone TURBT elsewhere due to delay in presenting to our institute and in completing the evaluations.

Of the 152 cases who underwent ReTURBT, 47 (31%) patients had residue in the final histopathology of the resected specimen. Of the 47 cases with histologically positive residue in ReTURBT, 42 (89.4%) patients had pT1 tumors. The rest of the five (10.6%) patients had pT2 tumor and underwent radical surgeries.

Deep muscle was identified in 144 (96%) out of 152 cases who underwent ReTURBT. Of that, five (3.3%) patients had involvement of the deep muscle by the tumor.

Eleven patients got assigned to a higher grade by ReTURBT, thereby leaving 7.2% of upgrading by ReTURBT. Ten of the 14 Ta tumors got restaged to T1, 1 of the Ta tumors got restaged to T2 (7.1%), and 3 of 64 T1 tumors were upstaged to T2 tumor following ReTURBT (4.7%). The overall rate of upstaging to muscle-invasive disease following ReTURBT was 3.3%.

Of the 152 patients, 147 patients were followed up for a median follow-up of 47.13 months, of which 25 (17%) who underwent ReTURBT had disease recurrence. Also, 17 out of 69 cases of multifocal tumor developed recurrence (24.6%), whereas only 8 out of 83 patients with upfront unifocal tumor developed recurrence (9.6%) ($p = 0.013$). The timing of ReTURBT, presence of residue at ReTURBT, and administration of BCG had no significant impact on recurrence rate.

The 3-year disease-free survival following ReTURBT was 73.7%, with 56% of the recurrences occurring within the first year.

Discussion

Accurate histological staging is essential for the management for bladder cancers. Following TURBT, deep muscle could not be identified in 81 (53.3%) patients, and accurate T status could not be exactly ascertained in 74 (48.6%). Deep muscle was identified in 144 (96%) out of 152 cases who underwent ReTURBT. Of those, five (3.3%) patients had involvement of the deep muscle by the tumor. As emphasized by Zurkirchen et al, resecting deep muscle is a technique of expertise and directly correlates with the learning curve.³ Rate of identifying deep muscle is higher in our study compared with the other study because all the ReTURBT was performed by experienced surgeons.

In our study, ReTURBT upstaged 5 out of 137 patients; 3% of the patients got upstaged from T1 to T2 stage as compared with 24 to 32% conversion rate in other studies. Similarly, 7% got upstaged from Ta to T2 compared with 5.5 to 14%, as found in other studies.^{4,5} Reason for low percentage of upstaging in our study may be that other studies did not have “complete” gross tumor resection as criteria in initial TURBT. The concept of leaving behind some residue for the intravesical therapy to take care was prevalent in the 1990s. It is, in fact, after these studies that the importance of complete resection in the disease recurrence and progression was understood, and the quality control for TURBT began to be emphasized and followed in various centers across the world.

ReTURBT has significant influence on tumor recurrence. Sfakianos et al retrospectively analyzed 894 patients who were treated in the same method as followed by our study and reported a recurrence rate of 57.5% over 5 years.⁶ They concluded that the recurrence rate following single TURBT is almost twofold at 5 years when compared with those who had undergone ReTURBT, and the greatest difference in the recurrence rate (4.5-fold) was during the initial 3 months, which is mainly due to tumor persistence. This surge can be excluded by performing a ReTURBT. In our study, in

152 patients who underwent ReTURBT, 16.4% had recurrence over a median follow-up of 47 months.

Patients having multifocal disease at the entry level had higher rates of residual tumor and higher rates of tumor recurrence following ReTURBT and intravesical therapy. Brausi et al, in their combined analysis for seven EORTC studies, inferred similar results with single TURBT and intravesical therapy. They have observed an 18.9% recurrence rate for multifocal tumors following single TURBT and intravesical therapy and 5% recurrence rate for unifocal tumors. However, they calculated the recurrence of the tumor when detected at the first follow-up by cystoscopy, thereby emphasizing that despite intravesical therapy, multifocal disease tends to recur and thereby a ReTURBT becomes mandatory.⁷

Similarly, tumor grade was also found to be an important predictor of recurrence; 25.7% of high-grade tumors had recurrence, whereas only 13.6% of low-grade tumor had recurrence. Divrik et al directly correlated the presence of residual disease with tumor grade. In their study, residual cancer was detected in 62% of high-risk tumors.⁸

Other parameters, namely administration of BCG or presence of residue in ReTURBT, did not reveal any statistical significance in the recurrence pattern.

Effect of timing of ReTURBT on picking up residual disease was studied. It was 16% as compared with 17.2% for patients in which ReTURBT got delayed by <6 weeks. Exact timing of ReTURBT is still not standardized. Klän et al did not observe any advantage in delaying the ReTURBT by <14 days. Most authors quote 4 to 8 weeks as the standard time interval following initial TURBT for performing ReTURBT.⁹

ReTURBT is relatively a safe procedure carrying less operative time and comparable morbidity rate as that of TURBT. ▶Table 1 depicts a comparison between the two procedures. Duration of the procedure is less compared with TURBT, which is statistically significant: 115.2 minutes versus 64 minutes ($p = 0.015$). The duration of postoperative bladder irrigation (2 vs. 1.2 days), duration of retaining Foley's catheter (2.9 vs. 1.6 days), and duration of hospital stay (3.2 vs. 2.1 days) were all shorter for ReTURBT compared with initial TURBT. Hence, it is a safe procedure to perform as a routine.

The study is limited by its retrospective-prospective nature, which restricts the analysis. Furthermore, at our

Table 1 Comparison of transurethral resection of bladder tumor with repeat transurethral resection of bladder tumor

	TURBT	ReTURBT
Mean duration of surgery (minutes)	115	64
Mean duration of hospital stay (days)	3.2	2.1
Mean duration of bladder irrigation (days)	2	1.2
Mean duration of retaining catheter (days)	2.9	1.6
Major complications	1	2
Minor complications	7	3

Abbreviations: ReTURBT, repeat transurethral resection of bladder tumor; TURBT, transurethral resection of bladder tumor.

institute, we perform ReTURBT for Ta histology as we believe that any upstaging/ upgrading will significantly affect management, especially when a considerable number of TURBT are referred from other centers.

Conclusion

The study reaffirms that in T1 bladder cancers, ReTURBT comprehensively confirms the completeness of initial resection, treats the residual tumor effectively, and picks up the missed muscle-invasive tumors that need radical treatment. Tumor characteristics such as multifocality and high grade were associated with higher recurrences. The complications in ReTURBT are not significantly high compared with TURBT. The procedure when performed with utmost care in experienced hands in selected patients remains a very safe procedure to be followed as a routine and standard even in developing countries.

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None.

Conflict of Interest

There are no conflicts of interest.

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