Original Article

Rationale of restaging transurethral resection of bladder tumor in patients with nonmuscle invasive bladder cancer in the current era

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Abstract

Background: We present retrospective data of patients with nonmuscle invasive bladder cancer (NMIBC) who underwent restaging transurethral resection of bladder tumor (Re-TURBT) at a tertiary care center.

Materials and Methods: Records of all NMIBC patients undergoing Re-TURBT between March 2021 and September 2023 were retrospectively analyzed. Patients were risk stratified based on TURBT pathology. Re-TURBT was performed between 4 and 6 weeks. Adverse features such as number, size, and appearance were noted. Patients with persistent disease at Re-TURBT were counseled for early cystectomy with urinary diversion or intravesical Bacillus Calmette–Guerin (BCG). In case of disease upstaging, patients were counseled for radical cystectomy.

Results: Thirty-eight NMIBC patients (30 males and 8 females) underwent Re-TURBT. Six patients had residual/persistent disease at 6 weeks, all high risk and high grade (HG, *P* value not significant, $P = 0.31$). There was no association with number and appearance of tumors with residual/persistence at 6 weeks. The mean lesion size on imaging in cases with and without residual disease was 3.32 ± 0.86 versus 3.39 ± 0.92 cm, respectively, *P* value not significant (0.868). There was no residual disease in the low-grade (LG) pT1 group, but HG pTa and pT1 ($n = 3$) had residual disease. Four HG pT1 patients opted for early cystectomy. Two patients each had pT0 and two pT2. At 3 months of follow-up, urethral strictures were seen both in high risk and intermediate risk. Among four patients who had stricture, meatal stenosis was common (50%, $n = 2$). Two patients had long-segment stricture requiring perineal urethrostomy with stage I Johannsen repair. All HG pT1 lesion patients eventually underwent cystectomy (3 were under staged and two treated completely with TURBT, one with TURBT + BCG and one patient progressed to metastasis).

Conclusion: Re-TURBT is essential for the management of HG pTa and HG pT1 lesions for accurate staging and treatment of residual disease. However, LG pT1 patients can safely be excluded from Re-TURBT.

Keywords: Bladder cancer, nonmuscle invasive, restaging, transurethral resection of bladder tumor

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INTRODUCTION

Bladder cancer (BC) is one of the most common cancers in the world.[1,2] As per the histopathology, the majority of BC cases are papillary cancers, while, according to the disease clinical stage, they are nonmuscle invasive BC (NMIBC), i.e., stages Ta and T1. Even after some treatment, about

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50% of such patients suffer recurrence, and in about 20% of these patients, there is progression to higher clinical stages.[1,2]

NMIBC constitutes a very heterogeneous group of cancers with different disease courses.[3] For example, low-grade (LG) changes are characterized by a low recurrence rate and by low progression. On the other hand, high-grade (HG) tumors have a quite considerable recurrence rate, high progression and worse outcomes, and even metastasis. Hence, staging, grading, and risk stratification are essential for determining the most appropriate management strategies for NMIBC based on recurrence and progression.[1]

Restaging transurethral resection of bladder tumor (Re-TURBT) is indicated in pT1 BC patients as there are increased chances of persistence (58%) and understaging (11%) as per the European Association of Urology (EAU) guidelines.[1,4] Furthermore, patients with HG pTa BC have increased chances of residual disease.[1,4]

There are, however, some disadvantages of Re-TURBT-increased chances of urethral stricture, rendering further follow-up with cystoscopy with added morbidity to patients.[1,4] Re-TURBT has also been called into question owing to frequent negative results. Hence, there is a need to identify patients and tumor characters to better stratify the outcome of NMIBC.

We present retrospective data of patients with NMIBC who underwent Re-TURBT (based on TURBT pathology) at a tertiary care center.

MATERIALS AND METHODS

A retrospective study was conducted from the Department of Urology database, AIIMS, Raipur, between the period of March 2021 and September 2023. All NMIBC patients who underwent Re-TURBT in the department were included in this study.

All patients were managed and monitored as per the NCCN (National Comprehensive Cancer Network) guidelines. After initial TURBT, the patients were risk stratified based on TURBT pathology. Re-TURBT was performed between 4 and 6 weeks as per protocol. Patients with tumor persistence and upstaging at Re-TURBT were analyzed. Adverse features such as number, size, and appearance (solid/papillary) were noted. Patients with persistent disease at Re-TURBT were counseled for either early cystectomy with urinary diversion or intravesical Bacillus Calmette–Guerin (BCG). In case of disease upstaging, patients were counseled for radical cystectomy.

Descriptive and comparative analyses would be performed. All data would be analyzed for normality; those with a normal distribution would be reported as mean with standard deviation, and those with a skewed distribution would be reported as median with range. The data would be compared using Fisher's exact test to calculate *P* value. A *P* value of 0.05 or lower would be considered statistically significant.

RESULTS

A total of 38 NMIBC patients were included in this study; 30 were males and 8 females. Smoking was the most common risk factor seen in 78% of them.

At Re-TURBT, six patients had residual/persistent disease at 6 weeks, and all were seen in the high-risk group and were of HG only (*P* value not significant, $P = 0.31$). This is depicted in Table 1. On analyzing tumor characters, there was no association with number and appearance of tumors with residual/persistence at 6 weeks.

The mean lesion size on imaging in cases with and without residual disease was 3.32 ± 0.86 versus 3.39 ± 0.92 cm, respectively, and revealed no significant association with recurrence at 6 weeks ($P = 0.868$).

In subgroup analysis of HG and LG NMIBC, i.e., HG pTa, HG pT1, and LG pT1, no evidence of residual disease was noted in the LG pT1 group, but HG pTa and pT1 had three patients with residual disease each. The rest four HG pT1 patients opted for early cystectomy. Two patients had pT0 and two had pT2.

The outcome (residual/upstaging) of the disease at 3 months of follow-up is depicted in Table 2. Of the six patients who had persistent/residual disease, one patient with HG pT1 opted for early cystectomy, and his final stage was pT0. The rest five opted for induction BCG, two were free of tumor at 3-month follow-up, two had persistent HG tumor at 3 months who underwent early cystectomy, and one progressed to metastasis. Of the three patients who underwent laparoscopic-assisted radical cystectomy, two patients had pT2, and one had pT0.

At 3 months of follow-up, urethral strictures were seen both in high risk and intermediate risk but was significantly higher in the latter group (33% versus 3%, $P = 0.035$). Among four patients who had stricture, meatal stenosis was common (50%, $n = 2$). Two patients had long-segment stricture requiring perineal urethrostomy with stage I Johanssen repair. The association of urethral stricture and intermediate- and high-risk NMIBC patients is depicted in Table 3.

Table 1: Association of tumor characters and residual tumor at 6 weeks

Tumor characters/recurrences	No, *n* (%)	Yes (high grade), *n* (%)	Total, *n* (%)	*P*
HPE grade				
LG	9 (28.12)	0	9 (23.68)	0.307*
HG	23 (71.87)	6 (100)	29 (76.31)	
HPE stage				
pT1	13 (40.63)	3 (50)	16 (39.47)	1*
pTa	19 (59.38)	3 (50)	22 (57.89)	
Lesion size on imaging (cm)				
≤3	12 (37.50)	3 (50)	15 (36.84)	1*
>3	20 (62.50)	3 (50)	23 (60.52)	
Mean±SD	3.39±0.92	3.32±0.86	3.38±0.9	0.868‡
Number (imaging)				
Single	19 (59.38)	56 (100)	25 (65.79)	0.14*
Multiple	13 (40.63)	0	13 (34.21)	
Intraoperative appearance				
Papillary	27 (84.38)	3 (50)	30 (78.9)	0.233*
Solid	5 (15.63)	3 (50)	8 (21.1)	
Risk stratification based on EAU guidelines				
Intermediate risk	9 (28.13)	0	9 (24.32)	0.307*
High risk	23 (71.88)	6 (100)	29 (75.68)	

SD: Standard deviation, HG: High grade, LG: Low grade, EAU: European Association of Urology, HPE: Histopathology Examination, ‡No Significant Association, *Slight Significance

Table 2: Residual, upstaging of disease at 3 months of follow-up

Tumor character (*n*=38)	Number of patients (%)	Residual/persistence at 6 weeks, *n* (%)
Grade		
HG	29 (76.31)	6 (20.68)
LG	9 (23.67)	0
Subgroups		
HG pT1	7 (18.42)	3 (42)
LG pT1	9 (23.62)	0
HG pTa	22 (57.89)	3 (13.63)

HG: High grade, LG: Low grade

All HG pT1 lesion patients eventually underwent cystectomy, of which three were under staged and two were treated completely with TURBT, one with TURBT + BCG and one patient progressed to metastasis.

DISCUSSION

Recurrence, progression to higher clinical stages, and metastases are the major problems related to cancers, and these hold true for NMIBC as well.[1] At present, the decision for management of a malignancy patient solely relies on the results of histopathological tests.[1] According to the current NCCN guidelines, Re-TURBT is indicated in absent detrusor muscle in the specimen (staging and incomplete resection), all pT1 lesions (residual and downstaging), and all HG lesions (residual disease).[1,4,5]

In a review by Rhijn *et al*., they stated that in NMIBC, 70% of patients present as pTa, 20% as pT1, and 10% with carcinoma *in situ* (CIS) lesions. Recurrence (in ≤80% of patients) is the main problem for pTa NMIBC patients, whereas progression (in ≤45% of patients) is the main threat in pT1 and CIS NMIBC.[6] Thomas *et al*. in their study on high-risk NMIBC patients at their institution have concluded that by conservative management, high-risk NMIBC is associated with a poor prognosis, and surveillance and BCG were ineffective in altering the natural history of this disease.[7]

Re-TURBT helps to detect disease progression and residual disease as well as upstaging of NMIBC. However, it increases the time to intravesical BCG and, as shown in our study, also causes increased chances of urethral stricture. These hinder the surveillance program and result in additional morbidity. Hence, a complete TURBT to stage the disease can never be substituted with Re-TURBT and at the same time carefully selection of patients is of immense importance as missing such patients can upstage the disease (can even metastasize).

According to risk stratification by EAU, size, grade,and number are considered poor prognosis for recurrence and progression. However, in our study, we observed that these factors did not significantly affect the rate of residual or persistent disease. As compared to LG, HG tumors have increased chances of recurrences and residual disease, so Re-TURBT cannot be neglected in them, as observed in our study that three patients (8%) had upstaging, two patients had progression to MIBC, and one even progressed to metastasis. As none of the LG pT1 patients had residual or upstaging of disease at 6 weeks, a complete TURBT can be curative in such a setting. These patients can be safely excluded from Re-TURBT, thereby reducing stricture rates in these patients.

Table 3: Association of urethral stricture with intermediate and high risk

Urethral stricture	Intermediate risk (*n*=9), *n* (%)	High risk (*n*=29), *n* (%)	Total, *n* (%)	*P*
No	6 (66.67)	28 (96.55)	34 (89.47)	0.035*
Yes	3 (33.33)	1 (3.45)	4 (10.53)	
Total	9 (100)	29 (100)	38 (100)	

*Fisher's exact test

HG pT1 lesions are best offered early cystectomy, but TURBT and BCG still can still be offered as a part of bladder preservation. For HG pTa, residual disease can be treated with intravesical BCG, but BCG refractory cases usually have poor prognosis and should be offered early cystectomy as early as possible.

Thus, risk stratification of NMIBC is important as well as Re-TURBT to monitor for progress of NMIBC. However, a large population is required to conclude our findings. Better trials in population-based studies would help to generate guidelines for management of NMIBC.

We emphasize that despite the complications of urethral stricture, Re-TURBT is an essential step for detecting residual and persistent NMIBC and its management.

CONCLUSION

Re-TURBT is an essential step of BC management, particularly in HG pTa and HG pT1 lesions for accurate staging and treatment of residual disease. However, LG pT1 patients can safely be excluded from Re-TURBT.

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Conflicts of interest

There are no conflicts of interest.

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