

The Impact of Re-Transurethral Resection for Non-Muscle Invasive Bladder Tumour

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ABSTRACT

Urinary bladder cancer is a disease from indolent low-grade non-muscle invasive disease to muscle-invasive disease which has poor outcomes despite the treatment. There is an increasing trend of this disease in the developing countries like Nepal. Non-muscle invasive bladder carcinoma occupies almost seventy per cent of the cases. Re-transurethral resection of bladder tumour has been recommended by all the guidelines for Ta high-grade and T1 non-muscle invasive tumors for accurate staging and from the therapeutic aspect. However, the second procedure has difficulty like the patients' concern about the completeness of the procedure, perioperative morbidity, and the financial burden involved in a major surgery which puts a strain on the already overburdened healthcare systems in developing countries. Several publications have raised the question and have advocated for the avoidance of a second procedure in today's era.

Aims and Objectives: To evaluate the potential impact of re-TURBT with comparison to the standard TURBT in high-grade NMIBC.

Method: The study was a retrospective analysis of a prospectively maintained database in which the first 98 patients were selected for the study. The criteria were set for those patients with a follow-up of a minimum of 6 months after the initial TUR to be included in the study. Patients who underwent an early resection (Group A) had 37 patients and those who did not (Group B) had 61 patients. Early resection was performed after two weeks of initial TUR and within six weeks of initial TUR.

Results: Detrusor muscle was present in 78.30% ($n = 29$) of patients in Group A and 83.60% ($n = 51$) of patients in Group B. Residual tumor was present in 48.64% ($n = 18$) of re-resected cases. Among these residual tumour cases, 4 cases were found to be upgraded. The overall incidence of tumour recurrence was 38.23% and 83.60% in Groups A and B, respectively. Similarly, there was no tumour progression at the end of follow-up in group A, while in group B progression was seen in 10 patients (16.40%) concluding P-value significant $P < 0.001$.

Conclusion: re-TURBT aids accurate staging and clearance of residual burden of the disease. Early resection is beneficial in decreasing the tumor recurrence and hence decreases the rate of tumour stage progression.

Keywords: Bladder Cancer; re-TURBT; re-resection; non-muscle invasive bladder cancer; recurrence; restaging; progression; upgrading.

INTRODUCTION

Urinary bladder cancer is the 10th most common cancer worldwide and its incidence is on the rise especially in developed countries [1] accounting for 3% of global cancer diagnoses. In the U.S., bladder cancer is at sixth among all the neoplasms. Around 90% of bladder cancer are found at the age of 55 years and above with the male-to-female ratio of 1:4 [2]. In India, it is ranked 17th in incidence and 19th in mortality, with a varying incidence across the Indian population. Significant variation in incidence rates of different regions in India was seen [3]. The highest incidence of bladder carcinoma is seen in Delhi with equal predilection for both genders. The strongest risk factor for bladder cancer is tobacco smoking, which accounts for 50-65% of all cases and occupational exposures to carcinogens in developed countries, and chronic bladder urothelial irritation from *Schistosoma hematobium* infection in Africa and the Middle East [4]. Chemicals associated with bladder cancer include arylamine dye, aniline dye, phenacetin (an analgesic), cyclophosphamide (a cytostatic drug), and arsenic [5].

The superficial tumors restricted to the bladder mucosa are defined as Ta or T1, with 20% of cases being classified as Ta, 70% as T1, and 10% as CIS. Disease progression has been demonstrated to correlate with tumor size, multi-focality, tumor stage, grade, and early recurrence. On initial diagnosis urothelial carcinoma of the bladder presents as non-muscle invasive papillary tumors in approximately 70 to 85% of cases [6] with variable recurrence rate from 0 to 80%. Progression to the muscle invasive disease can be seen in 10% of pTa tumors and 35% of pT1 tumors [7, 8].

Transurethral resection (TUR) of tumor along with intra-vesical chemotherapy or immunotherapy remains the “gold standard” in the management of non-muscle invasive bladder cancer (NMIBC). The initial resection of the tumor may be insufficient at completely removing and staging the tumor

which means an increase in tumor recurrence as well as progression of the disease. With the initial TUR the prevalence of residual tumour with high-grade non-muscle invasive bladder cancers (HG-NMIBC) is high and can be above 50% [6, 9]. Hence, it's recommended that early resection aids in accurate staging and also clears the residual disease. Subsequent rates of tumor stage progression are significantly improved [10].

However, re-TUR is not only invasive and costly but also associated with an increased risk of complications. Prolonged hospitalization (longer than two days) due to hematuria after an operation or repeated hospitalization within two weeks (6.71%), surgical treatment due to severe hematuria occurred within two weeks after the operation (0.01%), postoperative fever (8.21%), and retaining urethral catheter for more than one week (15.67%). The purpose of this study was to compare the results of early resection compared to the regular TURBT [11].

MATERIALS & METHODS

The study was a retrospective analysis of a prospectively maintained database including NMIBC patients from 2019 May to 2023 May, first, 98 patients diagnosed with pT1 HG-NMIBC were selected for the study. The criteria were set for those patients with a follow-up of a minimum of 6 months after the initial TUR to be included in the study after approval from the local ethical committee.

All patients signed an informed consent before enrollment. At enrollment, a detailed clinical history, physical examination including digital rectal examination, laboratory investigations including complete hemogram, blood urea, serum creatinine, random blood sugar, serum electrolytes, coagulation profile, microscopic examination, and urine routine, urine culture and sensitivity, chest X-ray, and electrocardiogram were carried out. All patients had undergone upper tract imaging with an ultrasound and a CT urogram at

initial diagnosis. None of the patients had evidence of upper tract malignancy at the workup.

According to the hospital data patients total of 98 patients were qualified for enrolment in the study, those who underwent an early resection (Group A) had 37 patients and those who did not (Group B) had 61 patients. Early resection was performed after two weeks of initial TUR and within six weeks of initial TUR.

STATISTICAL ANALYSIS

Data were collected retrospectively which included patient demographics, histological parameters at initial TUR and re-resection, and recurrence and progression rates. Statistical analysis was performed using SPSS version 18.0 statistical analysis software. The quantitative variables i.e. age (years), tumor size (mm), and number of tumours was presented as mean ± standard deviation. The qualitative variables i.e., gender, recurrence or progression of tumor was analyzed and frequencies were calculated. Comparison among groups was done by using the chi-square test. Statistical significance was assessed by P-value. Data was stratified for age, gender and tumor size. The Chi square test was again performed post-stratification.

OBJECTIVE

To evaluate the potential impact of re-TURBT with comparison to the standard TURBT, those patients who underwent an early re-resection and those who did not in terms of tumor recurrence and progression.

LIMITATIONS

This study was a retrospective review of a prospectively maintained database from a single institution. Additionally, there was selection bias in patient selection for re-TURBT based upon the patient's choice due to financial load.

RESULT

In group A 65.82 years was the mean age and similarly, in group B 66.82 years was the mean age. In group A, there were 34 (94.63%) males and 2 (5.40%) were females. In group B, there were 54 (88.50%) males and 7 (11.50%) were females. In group A there were 27(73%) who had single tumor and 10 (27%) who had multiple tumours. Similarly in group B, there was 39 (63.93%) had single tumor while 22 (36.06%) with multiple tumors. The detrusor muscle involvement in the first specimen in group A was 29 (78.3%) while in group B it was 51 (83.6%).

Table 1: Demographic Profile of Patients

Variable	Early re-TURBT	Standard	Total	
Age in years (mean)	65.82	66.82		
Gender	Male	35 (94.63%)	54 (88.50%)	89 (90.81%)
	Female	2(5.40%)	7 (11.5%)	9 (9.19%)
Number of Tumor	Single	27(73%)	39 (63.93%)	66 (67.34%)
	Multiple	10 (63.93%)	22 (36.06%)	32 (32.65%)
Size of tumor	<3 cm	24 (64.86%)	38 (62.30%)	62 (63.26%)
	>3cm	13 (35.14%)	23 (37.70%)	36 (36.74%)

During the re-TURBT in group A residual tumour was seen in 18 cases (48.64%). Among these cases 4 (22.23%) were found to be upgraded compared to the original histopathology at initial TURBT, i.e., three (3) T1 tumors were found to be T2a and One Cis tumour was upstaged to T1. These 3 upgraded to the T2 stage and underwent radical cystectomy. The mean follow-up

period in group A was 24.86 months while in group B it was 26.13 months. At the end of follow-up in group A, 13/34 (38.23%) had tumor reoccurrence while in group B it was 51/61 (83.60%). The P-value was extremely significant P<0.001. Similarly, there was no progression at the end of follow-up in group A, while in group B progression was seen in 10 patients

(16.40%) concluding P-value significant P<0.001.

Table 2: Comparison: re-TURBT and Standard method

Variable	Group			
		Re-TURBT	Standard Method	
Tumor Reoccurrence	Yes	13/34 (38.23%)	51/61 (83.60%)	64 (67.37%)
	No	21/34 (61.76%)	10/61 (16.40%)	31 (32.63%)
Tumor Progression	Yes	0	10/61 (16.40%)	10 (10.53%)
	No	34 (100%)	51/61 (83.60%)	85 (89.47%)

DISCUSSION

TURBT is the gold standard treatment for the management of NMIBC. According to the guidelines, re-TURBT should be done to confirm the recurrence, residual disease, or proliferation. EUA mentions in cases for which initial resection is incomplete, no muscle is involved in the resected specimen or a T1 tumour is detected, a second TURB should be performed within 2-6 weeks [12, 13]. In our study, we have compared selected parameters useful for predicting recurrence/residual disease and the upstaging. We also evaluated the impact of conventional restage TURBT in T1 tumours, especially non-muscle invasive high-grade tumours in the primary specimen. In our study, we found that in 18 out of 37 cases (48.64%) in group A there was a residual tumor and on re-TURBT, the tumour upstaging was in 4 cases among the 18 cases (22.23%). In a milestone study on second look TURB, 76% of the recruited patients had the residual disease and among the residual disease cases, almost one-third were upstaged to muscle-invasive disease [14]. Even when an expert urologist feels that he has achieved a macroscopically complete resection of the disease, upstaging to muscle-invasive disease remains common to overlook the second look [15]. Engelhardt et al also mention the residual disease of 52% in their study [16]. Vasdev et al concluded that tumor recurrence was 35% and 42% with and without re-resection. On follow up there was significant tumor progression 3.3% vs 14.4% [10]. In our study group A, there was no tumor

progression after the re-TURBT while in group B the tumour progression was in 10 cases (16.40%) at the end of follow-up. The prime goal of re-TURBT is to enhance the accuracy of residual disease and upstaging detection. Re-TURBT also improves recurrence and progression-free survival [17].

Various studies advocate a delay of two to six weeks to allow post-resection inflammatory changes to heal so that better visualization and demarcation of tissues can be done. The timing of re-TUR differed across studies. Calò et al. demonstrated that re-TUR in 6 to 12 weeks after initial TURBT provided better progression-free survival rates than re-TUR later than 12 weeks. In addition, Krajewski et al. demonstrated that recurrence-free and progression-free survival rates were worse in patients who underwent re-TUR after 6 weeks. Despite some studies reporting contradicting data on the impact of time from initial TURBT to re-TUR on residual tumor rates, delayed re-TUR seems to harm subsequent oncologic outcomes [18]. Keeping this in mind we performed our re-TURBT from 2 weeks to 6 weeks after the initial TURBT.

Mariappan et al. demonstrated that the likelihood of obtaining detrusor muscle and early recurrence were both associated with the surgeon's experience. Further, the presence of detrusor muscle has been established as one of the quality indicators of TURBT, impacting the oncologic outcomes of NMIBC patients [19,20]. In our study in group A, we had detrusor muscle in

resected tissue in 29 cases (78.30%) and in group B it was in 51 cases (83.60%). We hope to obtain local proof that re-TURBT is a more useful and effective strategy through this study. This will aid in the improvement of our practice, and in the future, we will use early resection as a therapy plan for patients with bladder cancer rather than a single TURBT.

CONCLUSION

Re-TURBT improves the staging of bladder cancer and despite the low upstaging risk, we cannot neglect the role of re-TURBT as its role is not only diagnosing the risk of upstaging but also has a vital role in the diagnosis of residual as well as recurrent growth so that proper staging and treatment can be done accordingly.

Declaration by Authors

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