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Surgery Section

Role of Repeat Transurethral Resection of Bladder Tumours after Primary Resection: A Retrospective Cross-sectional Study

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ABSTRACT

Introduction: Bladder Cancer (BC) is the second most common cancer of the urinary tract. Initial treatment by Transurethral Resection of Bladder Tumour (TURBT) helps guide treatment. In High Grade (HG) and invasive cancers, improved staging is achieved by performing a repeat (rTURBT).

Aim: To examine the outcome, residual disease, complications, outcomes and quality of procedure of repeat TURBTs at the study tertiary center.

Materials and Methods: This was a retrospective study conducted at the Department of Urology in Government Medical College, Srinagar, Jammu and Kashmir, India between October 2018 and December 2019. A total of 123 TURBT's were performed during the study period, of which 34 were repeat TURBT's. Case records were examined for each of these patients. Student t-test and Chi-square tests were used to compare data sets.

Results: Data was complete for 30 out of 34 patients. There was residual disease in 12 (40%) patients. Upstaging was seen in 2/12 (17%) of patients, down-staging in 0/12, and same stage in 10/12 patients (83%). No disease was seen in 18/30 (60%) of patients. No major surgical complications occurred. In 12 patients of non-invasive, High Grade (HG) tumours, who underwent rTURBTs, 6 (50%) were found to have residual disease.

Conclusion: rTURBTs should be performed in all patients with high-grade or T1 tumours. Further studies are required to analyse risk-factors for residual disease which may narrow the indications of rTURBT, thus saving time and costs, and reducing need for an additional procedure.

Keywords: Bladder cancer, Muscle-invasive bladder cancer, Nonmuscle invasive bladder cancer

INTRODUCTION

Bladder Cancer (BC) is the second most common malignancy of the genito-urinary tract and represents a significant cause of cancer morbidity and mortality [1]. Its incidence and prevalence have been rising, although the mortality has decreased [2]. BC is heterogeneous in behaviour, with a spectrum ranging from the benign behaviour of low-grade Ta BC to the aggressive metastatic potential of a high-grade invasive cancer. At presentation, 80-85% of BC are restricted to the bladder and of these, 85% are urothelial Non-Muscle-Invasive Bladder Cancer (NMIBC).

Initial management of BC is complete Transurethral Resection of the Bladder Tumour (TURBT) which provides accurate primary staging (tumour type, grade, and depth of invasion) and guides further management. The histopathological analysis of TURBT specimens differs from other histological evaluation of tumours, due to the presence of multiple fragments, lack of orientation of specimens, and cautery artefacts [1]. The most important information from histopathology is the presence or absence of invasion of the lamina propria or Detrusor Muscle (DM). On occasion, it may be difficult for the pathologist to distinguish between (MM) and Muscularis Propria (MP) muscle bundles in specimens [3]. Dalbagni G et al., revealed the absence of MP in 40% of T1 tumours, while Maruniak NA et al., showed that 51% of the histological specimens had no MP [3,4].

Therefore, the staging may be inconclusive, or incomplete-adversely impacting the outcome. Major uro-oncological guidelines recommend a second-look or repeat TURBT (rTURBT) after primary TURBT in all T1 tumours, as there is a risk of residual disease and upstaging of tumour [5-7].

A rTURBT poses the risk of complications, which may delay treatment, and impact outcome; rTURBT also increases costs. Recently, studies have focused on identifying risk factors for rTURBT at the time of first TURBT. Identification of risk factors for patients most likely to require a rTURBT may narrow the indications of rTURBT to a smaller number and reduce the burden of an additional procedure on patients least likely to benefit from it [8]. This study aimed to study the outcome, residual disease, complications, and quality of the rTURBT among patients undergoing this procedure.

MATERIALS AND METHODS

This retrospective study was conducted at the Department of Urology in Government Medical College, Srinagar, Jammu and Kashmir, India between October 2018 and December 2019. Data was collected from the case files of patients that underwent TURBT at the Department during the study period. Institutional Ethics Committee approval was given vide letter 125/ETH/GMC dated 20.10.2018. Patients that had known muscle invasive disease, with suspected upper tract malignancy, or those who had an incomplete primary TURBT were excluded from the study. As per Hospital protocol and as per established guidelines, those patients with incomplete primary resection, absence of DM in the specimen, HG tumour or T1 stage on histopathology were advised repeat TURBT.

Surgical Technique

Both TURBT and rTURBT are performed as per major international guidelines. General anaesthesia is preferred unless there is a contraindication. Monopolar electrocautery was used, using settings of 80W for coagulation and 120W for cutting. The resectoscope sheath used is Karl Storz 24F (Karl Storz, Germany). rTURBT's include deep resection of the scar and the edges of the initial resection site.

All patients are left with indwelling catheters with continuous 0.9% saline irrigation until the next morning. Immediate postoperative Mitomycin C (MMC) instillation is done if there is any visible disease prior to TURBT, and if the patient has no perforation or haematuria.

Residual disease is defined as the presence of cancer in the rTURBT specimen on pathological evaluation. The European Organisation for Research and Treatment in Cancer (EORTC) calculator was used to calculate the probability of progression and recurrence [5].

STATISTICAL ANALYSIS

Statistical analysis was done using Google Drive (drive.google.com, Accessed on 29.5.2020) and Microsoft Excel 2016 (Microsoft Corp, Seattle, USA). Student t-test and Chi-square test was used to compare data sets. Statistical difference was accepted when p-value was <0.05.

RESULTS

A total of 124 TURBT's were performed in the institution during the study period, of which 34 were rTURBT's. Often more than one indication was present in patients. Among the 34 patients who underwent rTURBT, pathological data was available for 30 patients. Indications for rTURBT were T1 in 13 patients, High Grade (HG) histology in 22 patients, and Tx (no staging possible) in 10% patients. Mean age was 58 years (SD 10.7) [Table/Fig-1]. Among the 90 patients that underwent initial TURBT, 48 (53%) had DM in the pathological specimen.

Variables	Categories	N (%)
Age	Range: 40-80 years	30
	Mean (SD): 58 (10.7)	
Sex	Female	2 (7%)
	Male	28 (93%)
Grade[1]	LG	8 (27%)
	HG	22 (73%)
Muscularis propria on initial resection	Present	19 (63%)
	Absent	11 (37%)
Stage[1]	Ta	12 (40%)
	T1	15 (50%)
	Cis	3 (10%)
Stage and grade (ISUP 2004)[1]	Ta-HG	12 (40%)
	T1-LG	5 (17%)
	T1-HG	10 (33%)
	Tx	3 (10%)
Tumour size	<3 cm	18 (60%)
	>3 cm	12 (40%)
Number of tumours	Single	16 (53%)
	Multiple	14 (47%)
Bladder cancer setting	Primary	24 (80%)
	Recurrent	6 (20%)
Probability of recurrence[2]	1 year	33%
	5 years	55%
Probability of progression[2]	1 year	4.14%
	5 years	14.12%

[Table/Fig-1]: Demographic and pathological data of patients selected for rTURBT.
[1]EAU Guidelines on non-muscle invasive bladder cancer [5]
[2]Based on EORTC risk calculator for predicting recurrence and progression in the EAU guidelines of non-muscle invasive bladder cancer [5]

Tumour free status on rTURBT was confirmed in 18 patients (60%). Residual tumour was detected in 12 patients (40%). Tumour at rTURBT was detected in the scar area of initial TURBT in all 12 patients (100%)- 6 had Ta tumours, 4 had T1 tumours, and 2 had T2 tumours. Ten patients had HG tumours as opposed to 2 who had low grade tumour [Table/Fig-2].

Out of 12 patients who had residual tumour, 2 patients (17%) had their disease upstaged from T1HG to T2 after which they were offered radical cystectomy. The remaining 10 patients had same disease stage at rTURBT as the primary resection. No patients from the Tx subgroup (where neither sub-epithelial connective tissue nor muscle was present) at initial TURBT had disease on rTURBT. Mean length of hospital stay for primary TURBT was 2.8 days and 2.2 days for rTURBT. All patients received post-TURBT intra-vesical instillation as per guidelines. No patient had any recurrence after rTURBT after a mean follow-up of six months.

Primary TURBT finding	rTURBT negative for BC	rTURBT positive for BC	rTURBT upstaged (to T2)	Likelihood of recurrence	p-value
TaHG	6 (50%)	6 (50%)		50%	
T1LG	3 (60%)	2 (40%)		40%	
T1HG	6 (60%)	2 (20%)	2 (20%)	40%	
Tx	3 (100%)	0		0	
Results of rTURBT	18 (60%)	10 (33%)	2 (7%)		
Comparing, T1LG v T1HG	3/5 6/10	2/5 4/10			>0.05

[Table/Fig-2]: Results of rTURBT according to histopathology at primary TURBT. There were more than one indications of rTURBT in many patients.
Comparing T1LG vs T1HG it was found that the likelihood was similar

Safety of rTURBT

The overall postoperative complication in the series on rTURBT was 2/30 (6.6%). Grade 1 Clavien-Dindo complication (urinary retention) was noted in both the patients. Bladder perforation requiring exploratory laparotomy post-rTURBT, or blood transfusion, was not needed in any patient.

DISCUSSION

Recurrence and Progression Rates

The aim of this study was to assess the role of rTURBT. The reason for performing a rTURBT is to restage the disease and rule out residual disease. Residual disease rates (40%), upstaging rates (7%), and upstaging rates among T1HG cases (20%) in this study are within the ranges mentioned in a recent systematic review and another study [9,10]. Divrik T et al., found residual disease in in 34%, Zappala P et al., reported residual disease in 40% [11,12]. All recurrences were detected at the primary site of resection.

As the Department has a teaching programme for Urology residents, and some procedures were performed by trainees, Surgeon's experience was not included in this study. In rTURBT, the DM was present in the specimen in 29 patients (97%). The single case where DM was not present, showed no residual disease in the specimen. All patients received MMC postoperatively as per protocol, hence postoperative MMC as a comparator could not be analysed.

Primary Versus Recurrent Bladder Tumours

In this series, 24 patients (80%) had primary BC. Interestingly, in this series, all the patients with residual disease on rTURBT were primary BC patients. None of the six patients with recurrent BC (who had already undergone TURBT) had residual disease on rTURBT. This is a small number, but the hypothesis is that this may be due to the application of postoperative intra-vesical instillation of Bacille-Calmette Guerin (BCG) in all intermediate and high-risk BC cases in the centre as per guidelines, thus probably reducing the progression seen in recurrent cases [5]. Duration between primary BC and recurrence in this paper was not studied.

Time till rTURBT

All patients in this study underwent resection within the time frame of six weeks after primary resection as recommended by major guidelines [5-7]. This is because there is a dedicated weekly outpatient clinic for uro-oncological cases, and BC cases are posted in the operation theatre on priority basis.

Role of rTURBT in Ta HG Tumours

Recent studies have questioned TaHG stage as an indication for rTURBT [5,8,13,14]. In this study, 50% (6/12 patients) of TaHG subset had presence of residual disease on rTURBT, leading to the questioning of the exclusion of TaHG as an indication for rTURBT. Among the subgroup of T1 stage on comparing grades (T1HG vs T1LG, p-value >0.05), residual cancer was just as likely in the HG subgroup and in the LG subgroup. In the T1HG group, there was an upstaging to T2 of 20% (2/10), and these patients were offered radical cystectomy.

Location of Recurrent Tumour

All of the recurrences in the case series were found at the base of the crater of the previous resection. The findings are similar to that of Kolozsy Z that found that the common area of residual tumour is at the base of crater remaining at the resected tumour site [15].

Quality of rTURBT

Herr HW and Donat SM suggested that quality control might be measured in TURBT using the presence of DM in the specimen [16]. In terms of the presence of DM on initial TURBT, a total of 53% of patients in the subset of patients selected for rTURBT had DM on initial TURBT, which is lower than reported elsewhere and may be reflective of the teaching programme in the department. Herr HW and Donat SM also advocate about the importance of rTURBT in achieving two goals [16], namely, distinguishing MIBC from T1 tumours and identifying patients who may benefit from early cystectomy. Two patients (6.6%) in this study who had diagnosis of T1HG at first resection, were upstaged to T2 in line with findings from a recent Systematic Review (0-26%) [9].

Analysis of the factors predicting presence of disease on rTURBT, revealed that TaHG, T1LG, T1HG, and primary BC setting were predictive of residual disease. This is in line with recent studies on the subject [8,17].

Limitation(s)

This was a single-centre study that was retrospective in design. The sample size is small since the inception of the study institution took place in 2014.

CONCLUSION(S)

The results of this study add further evidence regarding the importance of rTURBT; rTURBT improves the staging of BC and may change the plan of management in certain patients. In future, it may be recommended that risk factors be analysed that further narrow the indications for rTURBT, for which larger, multi-centre studies will be required. A large, multi-centre study is recommended to analyse further the role of rTURBT specifically with regard to the TaHG subtype.

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