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ROLE OF RESTAGING TRANSURETHRAL RESECTION OF BLADDER TUMOR IN PATHOLOGICAL UPSTAGING OF NON-MUSCLE INVASIVE HIGH-GRADE UROTHELIAL BLADDER TUMORS. OUR INSTITUTE EXPERIENCE

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ABSTRACT **Background:** Transurethral resection of superficial bladder tumours is well known to be gold standard management. It is evident from the literature that initial TURBT is not enough for accurate pathological staging in non-muscle invasive bladder cancer.

Aim: Our study is aimed at role of restaging TURBT in detection of residual disease for pathological upstaging in these high-risk patients to plan appropriate treatment.

Methods: This is a prospective study of 32 patients with initially diagnosed Ta/T1 high-grade bladder cancer who had restaging TURBT in a study by Department of urology, NIMS, Hyderabad between January 2016 and December 2018 were included. Low-grade tumors, carcinoma in situ and muscle invasive bladder tumors were excluded. Data elements collected on patient demographics, presence of residual disease, disease progression and recurrence in the follow-up period. The data was statistically analyzed using descriptive statistics by SPSS version 17. P value <=0.05 is considered as statistically significant.

Results: The mean age for patients included in the study was 60.5 years. In our study, we found that 15 out of 32 cases (47%) has been detected with residual disease ensuring that single TURBT may not been efficient with complete removal of tumor. Six out of 32 cases (19%) had upstaging and 5 out of 32 cases had concurrent carcinoma in situ leading to change in treatment. Therefore, 11 out of 32 cases (34%) has been under staged by initial TURBT were adequately staged by restaging TURBT and subjected to radical cystoprostatectomy or chemo radiotherapy, This mandates the need for restaging TURBT at 6-8 weeks interval for adequate staging and management. Upstaging on restaging TURBT was seen in 19%. The progression-free survival rate at 16 months was 25 % in patients with residual tumour and 94% in cases without residual disease.

Conclusion: We conclude that restaging TURBT effectively detects residual disease, helping pathological upstaging and planning definitive treatment in non-muscle invasive high-grade bladder tumour.

KEYWORDS : TURBT, Transurethral resection, High grade non muscle invasive bladder tumour, Pathological upstaging, Progression free survival.

INTRODUCTION

Non-muscle invasive high-grade bladder tumors are known to have high predilection for the developing muscle invasion, metastasis and eventual mortality.[1] The crucial step in the diagnosis and treatment of any bladder cancer is the initial TURBT. There are reports supporting that this procedure is often not performed to adequate standards.[2] This has led to suggestions by experts for restaging TURBT within 90 days for better staging and management of residual cancers.[3] This study is intended to know the rationale whether restaging TURBT helps in pathological upstaging to optimize the management of high-risk superficial bladder cancers.

Aim

To study the role of restaging TURBT in pathological upstaging of patients with non-muscle invasive, high-grade urothelial bladder tumors and selecting appropriate treatment strategies for better patient outcomes.

MATERIALS AND METHODS

This is a prospective study conducted by Department of urology, at Nizam's Institute Of Medical Sciences, Hyderabad between January 2016 and December 2018. A total of 32 patients with initially diagnosed Ta/T1 high-grade bladder cancer who underwent a restaging TURBT were included in the study. Low-grade tumors, carcinoma in situ and muscle invasive bladder tumors were excluded. Data on age, sex, presence of remnant lesions/residual disease, progression and the pertinence of the disease in relation to initial pathologic evaluation of tissue samples obtained from the first TURBT.

The bladder examination with cystoscope was performed under anaesthesia documenting the number, location, and size of the bladder tumors. TURBT of visible tumors was performed with including adequate depth of muscle.

Restaging TURBT procedure was conducted in Ta/T1 high-grade tumours within 6 to 8 weeks of initial TURBT before intravesical instillation of immune/chemotherapeutic agent where indicated. The previously resected sites and the peripheral area around them including deep muscle were resected. In cases where residual disease was found, complete resection with deep muscle biopsy was obtained followed by intravesical B.C.G treatment (Swog / Lamm Protocol). Subsequent radical cystoprostatectomy was performed in muscle invasive disease. Recurrence was defined in this study as development and detection of urothelial carcinoma on the bladder with Ta or T1 stage regardless of grade, and progression was defined as any worsening of T stage during follow-up.

The data was statistically analyzed using descriptive statistics by SPSS version 17. Continuous variables were expressed as either Mean +_ Standard deviation or Median. All statistical outcomes were presented at 95% confidence intervals based on a two-sided test. We regarded p-values <=0.05 as statistically significant. Ethical Board approval has been obtained from the institute prior to study commencement.

RESULTS

The mean age of patients in the study group was 60.5 years and four out of 32 patients were women. Among the 32 patients with T1 high-grade bladder cancer on initial TURBT, 11 patients(34%) had a solitary tumor with diameter of less than or equal to 3 cm and 21 patients (66%) had multiple tumors or greater than 3 cm in diameter.

Out of 32 cases who undergone restaging TURBT, 8 cases had muscularis propria in the initial TURBT resection specimen with no microscopic invasion and 24 cases had no muscularis propria in the specimen and found to have lamina propria invasion by tumour. All these specimens were reported as high-grade urothelial tumors and restaging TURBT was performed for adequate staging.

Cystoscopy was performed at 6 to 8 weeks after the initial TURBT during restaging revealed, 3 patients (9%) had visible papillary tumors, 6 patients (19%) had erythematous lesions / mucosal changes suspicious of malignant lesion without visible tumors, and 23 patients (72%) had no macroscopic abnormalities.

On restaging TURBT, a total of 15 patients were detected with residual tumor pathologically. Among them, 3 patients had visible tumor and 4 patients with suspicious lesions and 8 patients had no macroscopic abnormality.

Table 1 illustrates the proportion of macroscopic changes in residual and non-residual disease groups. This difference is statistically significant with p-value of .028427.

	Residual Disease	**Non residual Disease**	***Marginal Row Totals***
Macroscopic changes	7 (4.22) [1.83]	2 (4.78) [1.62]	9
No Macroscopic changes	8 (10.78) [0.72]	15 (12.22) [0.63]	23
Marginal Column Totals	15	17	32 (Grand Total)

Out of 15 patients with residual tumor, 6 patients had upstaging of tumor, among this 2 patients were subjected to radical cystoprostatectomy and 2 patient was deferred treatment and lost follow up, 1 patients died of unrelated cause and 1 patient is subjected to chemo-radiotherapy and follow up. Five out of 15 patients in residual group had Tis in conjunction with T1, While, rest of 4 patients had no change in there pathological staging. Therefore, 11 out of 32 cases (34%) was under staged by initial TURBT resulted in change of treatment plan after restaging TURBT. Of the HPE on restaging TURBT of residual, there are 6 patients with up staging, 5 patients with conjunction with T1/Ta and 4 patients with no change in pathological stage.

Seventeen patients of no residual disease along with 4 patients with residual disease found to have no change in their pathological stage of disease were subjected to follow up. Among 21 cases under follow up, 12 out of 21 patients remained disease free during the course of study period. 7 of 21 patients (33%) had recurrences beyond the study period. Five patients with in the first year and 2 patients between 14 months to 16 months had recurrence. Median time to recurrence was 9 months. Three of 4 patients (75%) with residual disease had recurrence, whereas 4 of 17 patients (23%) in the no residual disease group had recurrence.

Table 2 illustrates recurrence rates in residual and non residual disease group.

Group	**Recurrence**	**No recurrence**	***Marginal Row Totals***
Residual disease group	3 (1.33) [2.08]	1 (2.67) [1.04]	4
Non residual disease group	4 (5.67) [0.49]	13 (11.33) [0.25]	17
Marginal Column Totals	7	14	21 (Grand Total)

In the residual disease group, the recurrence-free survival rate at 16 months was 1 out of 4 cases (25%) and no residual disease group was 76% (13 out of 17 cases). This difference between the two groups was statistically significant with P-value of .049442.

In non residual disease group, there are 13 patients with no recurrence during follow up and 4 patients with recurrence during follow up after restaging TURBIT. However, in residual disease group there is 1 patient with no recurrence during follow up and 3 patients with follow up after restaging TURBIT. Progression occurred in 4 patients out of 21 cases under follow up (19%) within 16 months after injection of BCG treatment after restaging TURBT. Median time to progression was 9 months.

Out of 7 patients in whom recurrence was noted during follow up, 4 patients progressed from T1 high-grade to pT2 disease and there were multiple metastases in two patients; Three of these patients had residual disease and one had no residual disease at restaging TURBT.

Table 3 illustrates the difference in progression free survival between residual tumour and non residual tumour groups

Group	**Progression**	**Non progression**	**Marginal Row Totals**
Residual disease	3 (0.76) [6.57]	1 (3.24) [1.55]	4
Non residual disease	1 (3.24) [1.55]	16 (13.76) [0.36]	17
Marginal Column Totals	4	17	21 (Grand Total)

For the residual tumor group, the progression-free survival rate at 16 months was 25 %, whereas the value for without residual tumors was 94%. This difference is statistically significant with P- value of .001538.

DISCUSSION

Naselli et al.[4] in their meta-analysis concluded that clinically and pathologically complete previous TURBT should undergo restaging TURBT for their disease to know the rate of residual disease and of upstaging.

When restaging TUR is performed within few weeks of the original resection, residual tumor is identified at the site of the initial resection at least 40% of the time[5]. In our study, residual tumor was detected in 15 out of 32 cases (47%) and 8 out of 23 patients (35%) with no macroscopically visible tumors by cystoscopy were found have residual disease on restaging TURBT. This finding supports the evidence that cystoscopy is not sufficient on its own to find residual lesions. Nordic study suggested that 40% of their patients with T1 bladder tumors had remnant disease after an initial resection[6]. But in our study, it is 47% (15 out of 32 cases). Upstaging on restaging TURBT was well reported in the literature. Grimm et al.[7] reported 14% and Schwaibold et al[8] as 10% in their studies, respectively. Our study data revealed upstaging of 19%.

This study analysis reinforces the importance of restaging TURBT in the management of high- grade lesions and its potential role in pathological upstaging. The limitations of this study is small numbers and short follow-up.

CONCLUSION

Despite small numbers, our study data supports good survival outcomes with restaging TURBT for adequate pathological staging in Non muscle invasive high-grade bladder cancer to accomplish adequate tumor resection and need for prompt radical cystectomy in selected cases.

Conflict of Interest

Authors declare no conflict of interest.

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