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Routine Second Transurethral Resection of Bladder Tumor in T1 and High Grade Urothelial Carcinoma with Muscle Present In Biopsy – Is It Necessary in All Cases?

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Abstract: Second transurethral resection of bladder tumour (TURBT) after primary TURBT is recommended after incomplete initial TURBT, when detrusor is not present in specimen. Routine restage – TURBT from the base of revious tumour bed is indicated in all T1 or high grade tumours. We assessed incidence of residual tumour, upgradation of tumour and the need of second transurethral resection (TUR) and who can be benefited from second procedure. All the patients with pathologically proven T1 or high grade urinary bladder urothelial carcinoma (UC) diagnosed from August 2013 to July 2017 were included in this study. Repeat TUR was performed in all patients within four weeks. Patients with visible residual tumour or specimen with no detrusor muscle as per histo-pathological examination (HPE) were excluded from study. Specimen from second resection was examined for any residual tumour, stage and grade of residual tumour. Total 75 patients underwent second transurethral resection from August 2013 to July 2017. Only 8 (10.66%) patient had residual tumour in repeat resection. Only 3 (4%) patients had stage up gradation. Rates of residual tumour and upgradation of stage were less than previous study. In the subset of patients with single papillary or single sessile <3cm tumour chance of detection of residual tumour and up staging of tumour is very less. Second TURBT is standard care for all high grade or pT1 urothelial carcinoma. There is a question about additional benefit of second TUR in a small subset of patients where there is nonvisible tumour after primary resection and detrusor muscle is present in the specimen with single, < 3 cm initial tumor.
Keywords: Second transurethral resection, Urothelial cell carcinoma of urinary bladder, High grade, T1 stage

INTRODUCTION

Urinary bladder urothelial carcinoma incidence is rising in East Coast of India. UC (urothelial carcinoma) is broadly classified as non-muscle invasive bladder cancer (NMIBC) and muscle invasive (MIBC). NMIBC comprises of pathologically Ta and T1 tumour stage. According to WHO, UC is categorised into high and low grade. Transurethral resection of bladder tumour (TURBT) is the first treatment modality for bladder tumour –for histopathological diagnosis, staging and grading of the disease. Second transurethral resection of bladder tumour (TURBT) after primary TURBT is recommended after incomplete initial TURBT, when detrusor is not present in specimen. Routine restage – TURBT from the base of previous tumour bed is indicated in all T1 or high grade tumours [1]. The rationality behind this recommendation is that the presence of residual tumour and up staging of cancer by up to 30% in second TUR, which may change the management radically. However, this second resection is associated with double admission, complication and delay in adjuvant therapy. This group of patients require some form of adjuvant therapy as there is high chance of recurrence and progression of disease. Delay in adjuvant therapy can lead to poor outcome.

With this background, we conducted a study to evaluate the need of a second resection in selected group of patients after a quality resection, with muscle present in all resected specimen and no visible lesion after initial TURBT.

MATERIALS AND METHODS

A prospective analytical study was performed in our institute from August 2013 to July 2017. Ethical committee approval was taken for this study. Among the patients of urinary bladder tumour those diagnosed

with high grade or pT1 urothelial carcinoma following TURBT were included in this study. Patients with more than two urinary bladder tumours or visible residual tumour after initial TURBT or specimen without detrusor muscle in histopathology report were excluded from the study. All visible tumours were completely resected at initial TURBT. All specimens were sent for HPE. Absence of detrusor muscle in HPE was an exclusion criterion. Re-resection was planned within four weeks. Second resection was done from the previous resected site and also from any other suspicious site. Specimen of second resection was also sent for HPE. Further management was planned according to histopathology report of re – resected specimen. Statistical Analysis: All data were analysed using Microsoft excel 2010 and SPSS software.

RESULT

Total 239 patients underwent TURBT during the study period. Out of them, 105 patients had high grade urothelial carcinoma. Among those 105 patients, 34 had more than 2 bladder tumours and were excluded from study. 71 patients with high grade disease were included in the study. 64 of them had high grade and lamina propriety invasive (T1) disease. Out of 134 patients with low grade tumour, 4 had pathologically T1 disease and were also included in the study. Keeping the inclusion and exclusion criteria in mind, total 75 patients were selected for second resection. Out of 75 patients, 59 were male and 16 were female. The median age of male was 68 years (47 – 84 years) and of female was 66 years (59 – 74 years) (Table-1).

Table-2 and Table 3show the characteristics of the urinary bladder lesions of all the patients who underwent routine second resection. Tumours were grouped as papillary or sessile, single or multiple (=2) tumours, size <3cm or > 3cm. Out of 75 patients, 49 had papillary tumours and 26 had sessile tumours. Out of 26 sessile tumours one was low grade but T1 UC in primary resection. Out of 49 papillary tumours 19 were multiple (=2) and out of 75 patients four patients had low grade disease. Three patients also had pathologically Ta disease but high grade UC. In this study multiple means two tumours in urinary bladder at initial TURBT not more than that. Patients having more than two urinary bladder tumours at initial TURBT were excluded from this study.

Out of 75 patients who underwent second resection only 8 patients had residual tumour in repeat resection. It accounts for only 10.66%. Out of these eight patients, 2 patients had multiple papillary tumour, 2 patients had sessile tumours > 3cm and 4 patients had sessile multiple tumours. Pathologically 3 patients (4%) went to higher stage from their primary tumour stage. 1 patient of Ta group upgraded to T1, this patient also had multiple papillary lesions. 2 patients of T1 upgraded to T2; these patients also had multiple sessile tumours macroscopically. The T2 tumour patient was managed with radical cystectomy. Rate of residual tumour and upstaging of tumour was far less than in a previously described study (Table-4).

Subgroup analysis showed that residual tumour in papillary tumour group was 4.08% and in the sessile tumour group was 23.07% (6 out of 26) (Relative risk 5.65 with 95% CI 1.22 to 26.06). That means there is 5.65 time higher chance of residual tumour in the sessile tumour group than the papillary tumour group. Residual tumour for the single tumour group was 4.44% and for the multiple tumour group was 20% (RR: 5.37 with 95% CI 1.17 to 24.58). According to size criteria residual tumour in the <3cm tumour group is 0% and in the >3cm tumour group is 10.52%.

Regarding upstaging, the papillary tumour group had one (2.04%) and the sessile tumour group had two patients (7.69%) (RR: 3.77 with 95% CI 0.36 to 39.63).

If the tumour characteristics are combined it shows that in the group with single papillary tumour, and single sessile tumour <3cm there is no residual tumour, but in both the groups with multiple tumours, there is a higher chance of residual tumour and upstaging.

Table-1: Demographic profile of patients

SEX	Number	AGE (Years)
Male	59	47 – 84(Median : 68 years)
Female	16	59 – 74(Median : 66 years)

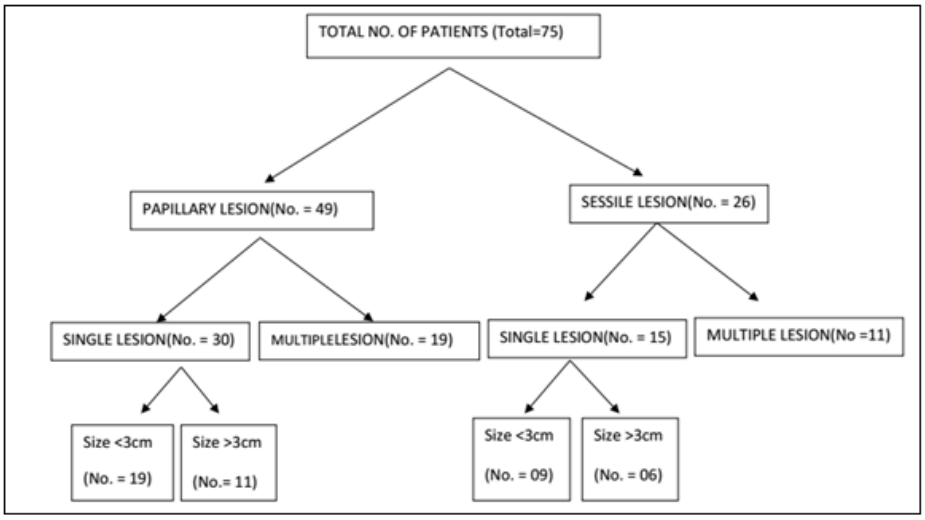

Fig-2: Distribution of patients according to macroscopic character of tumour

Table−3: Histopathological tumour characteristics at primary TURBT

Stage of tumour	Papillary		Sessile	
	Single	Multiple	Single	Multiple
pTa, High grade	02	01	00	00
pT1, Low grade	03	00	01	00
pT1, High grade	25	18	14	11
Total	30	19	15	11

Table−4: Distribution of patient according tumour characteristics, residual tumour and upstaging

	No. of patients with residual tumour	Upstaging of tumour
Papillary, Single, <3cm (19)	00(0%)	00(0%)
Papillary, Single, >3cm (11)	00 (0%)	00(0%)
Papillary, multiple, (19)	02(10.52%)	1(5.26%)(Ta to T1)
Sessile, single, <3cm (9)	00(0%)	00(0%)
Sessile, single, >3cm (06)	02(33.33%)	00(0%)
Sessile, multiple, (11)	04(36.36%)	02(18.18%)

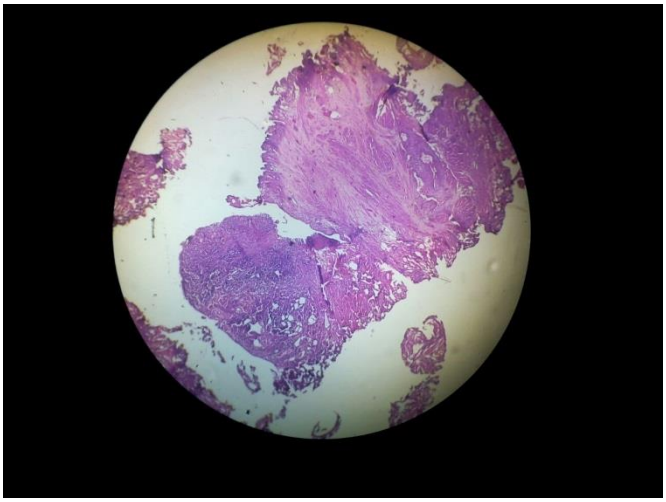

Fig-**3: Restage TURBT chips showing inflamatory cells in muscle, without tumor cell (Scanner view, X 4)**

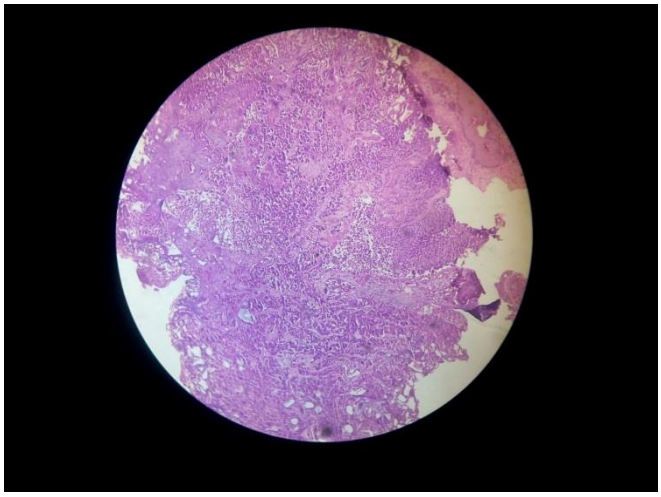

Fig-**4: Urothelial carcinoma invading lamina propria (T1) - Low power (X40)**

DISCUSSION

Transurethral resection of bladder tumour (TURBT) is the initial management of urinary bladder UC. Complete TURBT with detrusor muscle is the primary requisite for pathological staging and grading of tumours. But literature shows that there are chances of residual tumour and under staging of the disease after initial resection. For this reason, routine second transurethral resection of any T1 or high grade urothelial carcinoma of urinary bladder is the standard practice and is recommended by many guidelines. But is it worthy nowadays? With advancement of optics, better scope available and surgical expertise does it really needed?

Grimm MO *et al.* [2] in an observational study showed that residual tumours were found in 33% of patients in second TUR, including 27% of Ta and 53% of T1 disease, and in 81% at the initial resection site. 5/83 patients underwent radical cystectomy due to second TUR findings. The estimated risk of recurrence after years one to three was 18%, 29% and 32%, respectively.

Herr *et al.* [3] reported a recurrence rate of 45% in 67 patients and 80% in 30 patients who underwent restaging/second TUR before BCG treatment and who received BCG treatment respectively after initial TUR for the 12-month follow-up. The conclusion of this study was that second TUR of high-risk NMIBC improved the initial response rate to BCG therapy and reduced the frequency of subsequent tumour recurrence.

Divrik [4] *et al.* in a RCT shows that second TUR has been shown to affect the recurrence and progression rates favourably. Previously the studies included all the patients with macroscopic residual tumour, all stages and grades. But recently they clearly showed that second TUR, which is performed only after complete first TUR, has significantly decreased the recurrence and progression rates in patients who had pathologically T1 disease compared to those patients with pT1 disease who have not undergone second TUR. Although second TUR proved effective in decreasing both recurrence and progression overall in pT1 patients, but the study could not definitively document the role of second TUR in the subgroup of patients with single, low-grade, and small pT1 tumours, because of the limited amount of patients with these characteristics.

Giacomo Novara [5] in an editorial review said that in Divrik et al's RCT there are several methodological biases. The findings are likely to overestimate the effect on a second TUR on long-term tumour recurrence and progression. It is a poor quality RCT. The study has to be considered as a missed chance to fill a gap in our knowledge of bladder cancer prognosis.

Marko Babjuk [6] opines that a second TUR is the currently recommended procedure for treatment of NMIBC. In the future, we must endeavour to replace this rescue surgery with a more effective initial procedure. Second TUR is currently an unavoidable component of the treatment strategy for NMIBC.

Recently in a study Tim O'Brien [7] *et al.* showed that when initial resection was performed by their specialist bladder cancer team, routine second TUR rarely changed management. Under staging of muscle invasive disease has not occurred for 4 years. The results of adjuvant BCG in patients managed by single resection have been excellent. Early re-resection may be best reserved for second opinions, after incomplete resection and for fit patients with multifocal or large high grade tumours who opt for bladder conservation.

Another study by Rasha Gendy *et al.* [8] also revealed that when muscle was present in the specimen, 0/17 (0%) high-grade Ta and 1/22 (5%) T1 specimens were upstaged and if muscularis propria was absent, 2/18 (11%) high-grade Ta and 6/24 (25%) T1 specimens were upstaged. The very low rate of upstaging if muscularis propria is present in the specimen in this contemporary series reinforces the importance of achieving a good quality initial resection.

In our study all the patients who were included had muscle in initial TURBT specimen. Only 8 patients (10.66%) had residual tumour and three (4.00%) patients had upstaging. Those with papillary single tumours or sessile tumours<3cm in size had no residual tumour. Maximum chance of getting residual tumour is in the group of patients who had multiple papillary tumours, sessile tumours >3cm and multiple sessile tumours. Upstaging is also maximum in the sessile, multiple bladder tumour group. So it is reasonable to perform routine second TUR in patients who had multiple tumours in both groups and sessile tumour >3 cm. But in case of papillary tumour or <3cm sessile tumour it is questionable.

CONCLUSION

First TURBT with high quality resection (detrusor muscle present in first resection) can obviate the need of second routine transurethral resection in a selected group of patients –those with single, sessile<3cm or single papillary tumour. Though for recommendation, large, multi-centric trials are required.

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