

## Second transurethral resection in T1G3 bladder tumors – Selectively avoidable?

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### ABSTRACT

**Aim:** To assess the need of a second transurethral resection (TUR) in select T1G3 bladder tumor patients.

**Materials and Methods:** All the pT1G3 bladder tumors diagnosed during the period between January 2005 and December 2008 were included. Second TUR was routinely performed in all the pT1G3 bladder tumors within 4–6 weeks. Fifty out of the 68 patients with T1G3 underwent a second TUR and were retrospectively reviewed. The primary bladder lesions were grouped as solitary papillary, multiple papillary and sessile lesions. Statistical analysis was performed using STATA version 11 (STATA Corp., Texas, USA).

**Results:** Forty percent ( $n = 20$ ) of the lesions were solitary papillary, 48% ( $n = 24$ ) were multiple papillary and 12% ( $n = 6$ ) were sessile lesions. All our resections had muscularis propria sampled at the end of the resection and separately sent for histopathological examination (HPE), which showed them to be tumor free. Thirty-six percent of patients had residual disease at the second resection and 4% were upstaged. Ninety-five percent of the patients ( $n = 19$ ) with solitary papillary lesions did not have any residual disease and 50% ( $n = 12$ ) of the multiple papillary and 83.3% ( $n = 5$ ) of the sessile group had residual disease at the second TUR.

**Conclusions:** Patients with T1G3 tumors do not represent a homogenous group. Second TUR is recommended in patients with high-grade T1 urothelial bladder carcinoma as it identifies residual disease and invasive disease. Solitary papillary lesions may be the only group where the need for the second TUR is questionable.

**Key words:** Bladder cancer, high grade, transurethral resection

### INTRODUCTION

T1G3 bladder cancer has a variable and unpredictable biologic potential.<sup>[1]</sup> Though noninvasive, the biological behavior of these tumors is similar to that of muscle invasive transitional cell carcinoma (TCC).<sup>[2]</sup> Factors predicting the poor prognosis of T1G3 tumors are multiplicity of tumors, high grade, size > 3 cm, sessile pattern, associated carcinoma insitu (CIS) and early recurrence after primary transurethral resection (TUR).<sup>[3-5]</sup> TUR of bladder tumors and intravesical

therapy is now accepted as the standard of care for T1G3 tumors. The primary TUR may leave residual disease, more so in multiple tumors, increasing the risk of early tumor recurrence and stage progression even after intravesical therapy.<sup>[5]</sup> A second-look TUR of T1G3 tumors has multiple benefits – to eradicate the residual disease, identify the early recurrence<sup>[6,7]</sup> and avoid potential understaging, resulting in inadequate treatment.<sup>[8]</sup>

A second TUR increases the cost, morbidity and delays intravesical therapy. After a satisfactory primary resection with adequate muscle in the specimen, is a second TUR necessary? The objective of this analysis was to assess the relevance of second TUR in T1G3 bladder tumors in the Indian scenario and to identify the subgroup where a second TUR may be avoided.

### MATERIALS AND METHODS

All the pT1G3 bladder tumors diagnosed primarily during the period between January 2005 and December 2008 were included. In all subjects, after complete resection of the tumor macroscopically during the primary resection,

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Quick Response Code:	Website:
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	DOI:
	10.4103/0970-1591.82833

deeper tissue with muscle was resected and sent separately for histopathological examination (HPE). All the patients had 40 mg of intravesical Mitomycin instilled at the end of the resection. The pathologist's report about the presence of uninvolved muscularis propria in the specimen was mandatory for inclusion in the study. Second TUR was routinely performed in all the pT1G3 bladder tumors within 4–6 weeks. All patients diagnosed to have T1G3 were planned for second TUR, except those with extensive disease involving almost the entire bladders, who were offered radical cystectomy. Resection was performed at the previous resection scar sites as documented by the earlier surgery records and also at the doubtful areas. The video-assisted resections were supervised or carried out by a consultant.

### Statistical analysis

Statistical analysis was performed using STATA version 11 (STATA Corp., TX, USA). Fisher exact confidence intervals were drawn for relative risk estimates and calculated with a 95% confidence interval.

## RESULTS

There were a total of 535 patients with TCC bladder, who underwent transurethral resection of bladder tumor (TURBT) during this period. Sixty-eight of them were detected to have pT1G3 bladder tumors and were planned for a second TUR. Five had extensive disease involving almost the whole of the bladder and were advised radical cystectomy. Thirteen patients were unwilling for another operative procedure. These 18 were excluded from the analysis. Fifty patients underwent a second TUR. The mean age was 57.5 years (range 31–76 years) and four were women.

Table 1 shows the demographics and the characteristics of the lesions of all the 50 patients who underwent second resection. The primary lesions were grouped as solitary papillary, multiple papillary and sessile lesions. Of the six sessile lesions, one was a multiple sessile tumor. At the second resection, 18 (36%) had residual disease. Of these, 10 (20%) had gross residual disease. More importantly, even in the absence of gross residual tumor, a second resection identified eight patients (44%) with a positive histopathology.

Solitary papillary lesions did not have any gross residual disease in the second TUR. Most of the gross residual disease was seen in patients with primary multiple papillary lesions and one patient from the sessile group had a gross residual disease [Table 2].

The characteristics of the primary lesion with the pathology found in the second resection were compared [Table 3]. Histopathologically, these were categorized as no residual disease, same stage tumors, lower stage tumors, CIS and higher staged lesions. Of the 20 patients with solitary papillary lesions, 19 (95%) did not have any residual disease

in the second TUR and one had a lower stage disease. Half of the patients with primary multiple papillary lesions were free of tumor at the second resection. One-third of the patients had the same stage tumor and two had upstaging of the disease. In the sessile group with residual disease, the same stage was seen in 84%.

Sessile tumors had 16.67 times greater risk of residual disease as compared to solitary papillary lesions (RR 16.67, 95% CI 2.39–116.37) and 1.66 times greater risk of residual disease as compared to multiple papillary tumors (RR 1.66, 95% CI 0.97–2.86). When multiple papillary lesions were compared to solitary papillary lesions, there was a 10-fold increase in risk of residual disease (RR 10, 95% CI 1.42–70.41). The residual disease in the sessile and multiple papillary lesions was statistically significant when compared to the solitary papillary lesions.

## DISCUSSION

TURBT is the initial step in the management of bladder cancer. A technically complete primary resection is warranted for accurate pathological staging and grading of the tumor. After complete resection of all the visible tumors, deep muscle is resected separately for histopathology. If the resected specimen has no muscle, there is a potential for understaging T1 tumors. In high grade tumors, second TUR plays a vital role. It is meant to detect and clear residual tumor, and in cases of upstaging, it helps to plan appropriate treatment. Detection of tumor at the second resection indicates poor prognosis. Gross residual tumors were seen in 20% of our study population. Ninety percent of the gross residual lesions were seen in those with primary multiple papillary lesions. Second TUR also proved reduction of early recurrence in high grade T1 tumors from 63 to 26%.<sup>[9]</sup> At the end of the first, third and fifth year, the recurrence free

**Table 1: Patient and tumor characteristics in primary TUR**

Characteristics	Value
Age in years	57.5 (31–76)
Median (range)	
Gender n (%)	
Male	46 (92)
Female	04 (08)
Primary lesion n (%)	
Solitary papillary	20 (40)
Multiple papillary	24 (48)
Sessile	06 (12)

n = Number of patients

**Table 2: Gross residual tumor and primary lesions**

Gross residual lesion	Solitary papillary	Multiple papillary	Sessile lesion
Solitary (n = 8)	0 (0)	7 (87.5)	1 (12.5)
Multiple (n = 2)	0 (0)	2 (100)	0 (0)

n = Number of patients; Percentage in parentheses

survival was 82%, 65% and 59%, respectively, in the patients who underwent a second TUR when compared to 57%, 37% and 32%, respectively, in the patients who did not undergo the second resection.<sup>[10]</sup>

Tumor architecture, papillary or sessile, and multifocality of these lesions are important prognostic factors for recurrence and progression of the disease. A solitary papillary lesion is considered to be a good prognostic factor as against multiple papillary and sessile lesions.<sup>[11]</sup> In our series, among those with solitary papillary lesions, one had a lower stage residual disease and 95% did not have any residual disease in the second resection. Perhaps this is the subgroup that is least likely to benefit from a second resection. Multiple papillary lesions and the sessile lesions had significant residual disease in the second resection. Fifty percent of the multiple papillary lesions and nearly 84% of the sessile lesions had residual disease. Both the patients who had upstaging of the disease had primary multiple papillary lesions.

The important factor here is the complete primary resection of the bladder tumor. Presence of the uninvolved muscularis propria in the resected specimen is the only identification for a complete resection.<sup>[12]</sup> Retrospective studies have shown that residual disease can be seen in up to 68% cases.<sup>[13]</sup> These high rates may also have been due to the fact that no muscle was present in many of the primary TUR specimens. Forty-nine percent of T1 lesions without muscle in the resected specimen were understaged when compared to only 14% with muscle in the resected specimen.<sup>[14]</sup> Understaging was reported in 64% of T1 tumors when muscle was absent in the specimen versus 30% when it was present.<sup>[15]</sup> All our resections had muscularis propria sampled at the end of the resection and separately sent for HPE, which showed

them to be tumor free. This can explain why only 4% of our patients were upstaged at the second resection.

Another factor is the invasion of lamina propria superficial to the muscularis mucosa (T1a) which is considered a good prognostic factor as against the lamina propria deeper to muscularis mucosa.<sup>[16]</sup> Questions have been raised whether a second resection is really necessary in a well-performed initial resection of high-grade T1 solitary papillary lesions with only superficial invasion of lamina propria (T1a) with negative deep muscle biopsy, especially when intravesical therapy is planned.<sup>[17]</sup>

A comparison of similar studies is shown in Table 4. Emphasis was not given to complete primary resection with curative intent in many of them. One series had muscle in only 63% of the primary TURBT specimens.<sup>[14]</sup> In another series, though the presence of muscularis propria was not mentioned in the primary TURBT, 72% of the solitary lesions were tumor free at re-resection.<sup>[6]</sup> None had muscle in the resected specimen in another series, where 42 T1G3 patients underwent primary TURBT.<sup>[7]</sup> The primary characteristic of the lesion, which is an important prognostic factor, was also not considered in many of these studies.

We recognize the limitations of this study, viz., a small study group and also not considering factors like the size of the lesion and depth of lamina propria involved.

### CONCLUSIONS

There is a need to improve the risk stratification to optimize the treatment of high-grade T1 disease. With the available present scientific data, second resection is recommended in all patients with high-grade T1 urothelial bladder carcinoma

**Table 3: Pathology of second resection**

Primary lesion	No tumor	Same stage	CIS	Lower stage	Higher stage
Solitary papillary (n = 20)	19 (95)	0 (0)	0 (0)	1 (5)	0 (0)
Multiple papillary (n = 24)	12 (50)	7 (29.1)	3 (12.5)	0 (0)	2 (8.3)
Sessile (n = 06)	1 (16.7)	5 (83.3)	0 (0)	0 (0)	0 (0)

n = Number of patients; Percentage in parentheses

**Table 4: Comparisons of similar studies**

Study	n	Primary lesion			Muscle in HPE Primary TURBT	HPE of second TUR			
		Solitary	Multiple	Sessile		No tumor	Same stage	Lower stage	Upstage
Dalbagni <i>et al.</i> 2002 <sup>[8]</sup>	15	NS	9	NS	6 (40)	1	14	0	0
Schips <i>et al.</i> <sup>[6]</sup>	52	25	14	13	NS	29	9	5	9
Herr <i>et al.</i> 1999 <sup>[14]</sup>	58	NS	NS	NS	35 (63)	13	14	15	16
Dalbagni <i>et al.</i> 2009 <sup>[18]</sup>	523	NS	NS	NS	242 (42)	NS	NS	NS	NS
Our study	50	20	24	6	50 (100)	32	15	1	2

n = Number of patients; Percentage in parentheses; NS, Not specified; HPE, Histopathological examination

and it does identify residual disease and invasive disease. Patients with T1G3 tumors do not represent a homogenous group. Isolated solitary papillary lesions may be the only group where the need for the second TUR can be avoided. Is a second TUR really necessary in a well-performed initial resection of high-grade T1 solitary papillary lesions with only superficial invasion of lamina propria (T1a) with negative deep muscle biopsy? A well-designed multicentric prospective study with a large cohort assessing various risk factors of high-grade T1 lesions is necessary to determine the subgroups, if any, where a second TUR can be avoided.

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**How to cite this article:** Katumalla FS, Devasia A, Kumar R, Kumar S, Chacko N, Kekre N. Second transurethral resection in T1G3 bladder tumors - Selectively avoidable?. *Indian J Urol* 2011;27:176-9.

**Source of Support:** Nil, **Conflict of Interest:** None declared.