

# Is a second look necessary in multiple and/or large Ta tumors?

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**Summary** *Introduction: Most of the bladder cancers are tumors without muscle invasion at the time of diagnosis. Transurethral resection is the standard treatment in bladder tumors without muscle invasion. Proper review of transurethral resection is important for correct risk classification. In this study, our main objective was to show that a “second look” in patients with multiple and/or > 3 cm tumors regardless of T stage during the early term can be helpful in detection of possible residues and determining risk classification.*

*Materials and methods: 156 patients with primary, multiple and/or > 3 cm tumors were included in the study. Patients were divided into 3 groups as Group 1 (Ta), Group 2 (T1 without second TUR) and Group 3 (T1 with second TUR). Macroscopic tumor occurrence rates were compared in their 3<sup>rd</sup> month control cystoscopy.*

*Results: Macroscopic tumor detection rates in patients' 3<sup>rd</sup> month control cystoscopy were 21 (46.7%) in Group 1, 18 (30%) in Group 2 and 4 (7.8%) in Group 3. When compared with Group 3 patients, Group 1 and Group 2 had higher statistically significant macroscopic tumor detection rates ( $p = 0.001$ )*

*Conclusion: A second look in patients with multiple and/or > 3 cm tumors during early term will enable the surgeons to detect possible tumors and do a better job in risk classification.*

**KEY WORDS:** Bladder cancer; Multiple; Large; Second look.

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## INTRODUCTION

About 80% of bladder cancers are seen without muscle invasion at the time of diagnosis. The “golden standard” in treatment of bladder tumors without muscle invasion is transurethral resection (TUR) (1). Proper review of transurethral resection is important for correct diagnosis and treatment as well as risk classification (2).

In this study, our main objective was to show that a “second look” in patients with multiple and/or > 3 cm tumors regardless of T stage during the early term can be helpful in detection of possible residues and determining risk classification.

## MATERIALS AND METHODS

Data of 1406 bladder cancer patients who were diagnosed in our clinic between 2000 and 2014 was retrospectively reviewed; 156 patients with primary, multiple and/or > 3 cm tumors were included in the study.

Patients with secondary tumors, without complete resection, without muscularis propria tissue in pathology samples and microscopic tumors detected in second TUR were excluded. Patients were divided into 3 groups as Group 1 (Ta), Group 2 (T1 without second TUR) and Group 3 (T1 with second TUR). Patients in Group 2 consist of T1 patients before second TUR diagnosis. Groups were compared in demographic and clinical parameters. Macroscopic tumor occurrence rates were compared in their 3<sup>rd</sup> month control cystoscopy. Our main aim was to review the hypothesis “According to TNM staging, patients with Ta (multiple and/or large) tumors warrant a second-look”. In order to retrospectively review this hypothesis, we tried to show the relationship between patients with T1 stage tumors who went under second TUR and patients who did not receive further surgery. Considering that the residual tumor existence can also be seen in patients with Ta-stage tumors, we chose this methodology.

Except intracavitary therapy, no additional local adjuvant therapies were used in that patient group. Since the main focus of the study is to prove that a second look is necessary following TUR surgery, other patients who received additional local adjuvant therapies were excluded from the study. All patients received a 6-week standard intracavitary therapy protocol. The assessments were made on the 3<sup>rd</sup> month of treatment using cystoscopy findings.

Statistical analysis was made using computer software. Chi-square test was used in categorical variables and Student-t test was used in continuous variables. Values under  $p < 0.05$  were considered statistically significant.

## RESULTS

Out of 156 patients, 45 patients were put into Group 1, 60 into Group 2 and 51 into Group 3. Patients were reviewed in terms of sex, age, pathological grade and adjuvant intracavitary treatments (Table 1). Group 1

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patients had lower statistically significant high-grade tumor rates compared to other groups. There were no statistically significant differences between the groups when other parameters were reviewed. Since all patients included in the study required intracavitary therapy, all patients received this treatment. No statistically significant differences were seen between the groups in terms of intracavitary therapy during statistical analysis. Macroscopic tumor detection rates at 3<sup>rd</sup> month control cystoscopy were 21 (46.7%) in Group 1, 18 (30%) in Group 2 and 4 (7.8%) in Group 3. Nineteen patients in Group 3 were diagnosed with macroscopic tumors during their second TUR. When compared with Group 3 patients, Group 1 and Group 2 had higher statistically significant macroscopic tumor detection rates ( $p = 0.001$ ) (Table 2A). When macroscopic tumor detection during re-TUR rates in Group 3 patients were compared to control cystoscopy results of the other 2 groups, there was a correlation (Table 2B).

**Table 1.**  
Comparison of groups in terms of age, sex, grade and adjuvant therapy.

	Group 1	Group 2	Group 3	p
N	Y	Z	W	
Age (mean $\pm$ SD)	66.7 $\pm$ 10.9	64.1 $\pm$ 12.2	68.0 $\pm$ 9.1	0.158
Sex				
Male	40 (88.8%)	57 (95%)	48 (94.1%)	0.444
Female	5 (11.2%)	3 (5%)	3 (5.9%)	
Grade				
Low	34 (75.5%)	41 (68.3%)	28 (54.9%)	<b>0.009</b>
High	11 (14.5%)	19 (31.7%)	23 (45.1%)	
Adjuvant therapy				
IC Chemotherapy	40 (88.9%)	50 (83.4%)	40 (78.5%)	0.390
IC Immunotherapy	5 (11.1%)	10 (16.6%)	11 (21.5%)	

**Table 2A.**  
Group comparison of macroscopic tumor presence detected on 3<sup>rd</sup> month control cystoscopy.

Macroscopic tumor	Group 1	Group 2	Group 3	p
Yes	21 (46.7%)	18 (30%)	4 (7.8%)	<b>0.001</b>
No	24 (53.3%)	42 (70%)	47 (92.7%)	

**Table 2B.**  
Comparison of macroscopic tumors detected on second TUR in Group 3 patients with Group 1 and Group 2.

Macroscopic tumor	Group 1	Group 2	Group 3	p
Yes	21 (46.7%)	18 (30%)	19 (37.3%)	0.216
No	24 (53.3%)	42 (70%)	32 (62.7%)	

## DISCUSSION

TUR is accepted as the basic surgical procedure in diagnosis and treatment of bladder cancers without muscle invasion. However, many studies suggest a second TUR after the initial TUR for resection of residual tumors

(3, 4). Tumors detected during initial control cystoscopy on 3<sup>rd</sup> month of surgery in multiple and/or > 3 cm tumors were known to be mainly residual tumors (5). A residual tumor from a previously incomplete TUR detected in first control cystoscopy on 3<sup>rd</sup> month will be labeled as early recurrence which will change the patient's risk classification. Residual tumors are important in the treatment of multiple and/or tumors larger than 3 cm. Literature reports residual tumor rates as 33-78% (6). *Divrik et al.* prospective and randomized study reports this rate as 33.8% in T1 patients. In *Grimm et al.* prospective study, the authors suggested a second TUR to patients that received the initial TUR in their clinic and reported a residual tumor detection rate of 33.7% (8). Similarly in our study, 19 (37.2%) out of 51 T1 stage patients who underwent re-TUR were diagnosed with residual tumors. *Herr et al.* performed a secondary TUR in 150 patients who underwent the initial TUR in different clinics and reported 70.4% residual tumor rate (2). The initial TUR quality of those patients is unknown as well as the presence of muscle tissue in pathological samples and if the tumor was completely finished or not. In the other 2 studies mentioned above and our study, the initial TUR was done in their respective clinics, complete removal of tumor was reported by the surgeon and muscle tissue was found in pathological samples. Even after a proper and complete TUR, 1 out of 3 patients is diagnosed with residual tumors. This rate is deemed as significant.

A significant drop in recurrence and progression rates in high-risk Ta/T1 patients was reported with secondary TUR (7-9). Yet in most of the studies, second TUR is only recommended to T1 patients (10-12) There are also studies that recommend second TUR in high grade Ta patients (13, 14). In a study done by *Lazica et al.*, high-risk Ta patients who underwent a second TUR were reviewed and 41.4% of those patients were diagnosed with residual tumors (14). In this study, there was a significantly higher rate of tumors in multifocal tumor cases diagnosed in second TUR. There was a similar increase in tumor detection rates in patients with tumors > 3 cm, but this was not deemed as statistically significant (14). Residual tumor presence following TUR is connected with the stage, degree, size and number of the initial tumor (7). Multiple tumors increase recurrence risk (15-18). In addition, tumor size is also found to be in connection with recurrence risk (16, 19). These results were compatible with the meta-analysis reports done by EORTC (20).

In our study, 19 (37.3%) patients were diagnosed with macroscopic tumors during re-TUR and only 4 (7.8%) patients were diagnosed with macroscopic tumors during 3<sup>rd</sup> month control cystoscopy. It was seen that most of the macroscopic tumors detected during re-TUR were residual tumors which were missed during initial TUR. 21 (46.7%) patients in Group 1 and 18 (30%) patients in Group 2 were diagnosed with macroscopic tumors in their 3<sup>rd</sup> month control cystoscopy. Those rates were consistent with macroscopic tumors diagnosed during re-TUR rates seen in Group 3 patients. We think that a second look done in 4-6 weeks after the initial TUR in Group 1 patients will decrease those rates similar to

Group 3 patients. As a result, risk classification and treatment strategies of the patients will be more realistic. The main limitation in our study was the small number of patients. More widespread and prospective studies are necessary on this subject.

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