

ORIGINAL ARTICLE

A prospective evaluation of second transurethral resection in non-muscle invasive bladder tumors

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Summary

Purpose: In this prospective study we evaluated the benefit of a second transurethral bladder resection (TURB) for Ta-T1 bladder carcinomas.

Methods: One hundred consecutive patients with superficial bladder tumor (Ta-T1) undergoing TURB and routine repeat TURB (Re-TURB) 4-6 weeks after the initial resection were included in the study. Re-TURB was applied to the scar of the first resection and other suspicious lesions in the bladder.

Results: From January 2003 to December 2008 100 patients were enrolled onto the study (mean age 60 years). At the first TURB, 56 (56%) patients had multiple lesions and

44 (44%) had a solitary tumor. Re-TURB revealed histological residual tumors in 40 (40%) patients. Residual tumor was found in 40% of Ta and 40% of T1 disease and 29% of the tumors were found at initial site of resection. Re-TURB revealed residual tumor in 55% of patients with multiple tumors and only 20% of patients with a solitary bladder tumor.

Conclusion: These data suggest that tumor stage is not a good indicator to determine the necessity of Re-TURB in superficial bladder carcinomas. Routine Re-TURB is beneficial in Ta-T1 multiple bladder tumors.

Key words: bladder neoplasm, non-muscle invasive, second transurethral resection, staging

Introduction

Superficial bladder cancer accounts for 75-85% of patients with this kind of malignancy and the standard treatment is TURB of all visible tumor(s). Two important criteria should be met for a satisfactory resection; first, sufficient tissue resection for correct pathological evaluation and diagnosis, and second complete resection of the tumor(s) for treatment. Unfortunately TURB does not meet these criteria at all times [1,2]. Moreover, incorrectly estimated prognosis is a result of incorrect staging due to incomplete initial resection [3,4].

It has been recommended to perform a repeat resection to correct the staging errors and detect residual tumors [1,2]. The value of this approach has been also shown in a retrospective study conducted by Herr et al. diagnosing residual tumors in 75% of cases after the repeat resection of primary Ta-T1 tumors [4].

Our policy is to perform a second TURB in patients with a Ta-T1 tumor, except for solitary, low grade Ta tumors. In this prospective study we evaluated the benefit of Re-TURB for Ta-T1 tumors. We hope that the information contained in this study will help resolve the debate between urologists about the necessity of a Re-TURB.

Methods

First resection

From January 2003 to July 2008, 100 patients with a mean age of 60 years (range 29-87) underwent TURB for superficial bladder tumor (Ta: 60, T1: 40). The resection for all patients was standardized; first a thorough cystoscopy was performed. The tumor location and size were recorded. All tumors were resect-

ed and a separate deep resection was performed from the tumor base. After the resection was completed the border of the tumor was cauterised and no other cauterisation was performed except for bleeding control. The tumor size (> or <3 cm), location, multiplicity, grade and stage were recorded.

Inclusion & exclusion criteria for Re-TURB

Patients with a solitary, small, Ta G1 tumor and patients with high risk of complications related to anaesthesia due to comorbidities were excluded from the study. Incomplete resections in the first TURB were not included into the Re-TURB protocol until complete resection was achieved on consecutive resections. Re-TURB was performed in all the remaining patients 4-6 weeks after the initial complete resection.

Second resection

A thorough cystoscopy was performed and all visible tumors and suspicious areas were recorded and were resected. Finally a deep muscle specimen was taken from the initial site. All specimens were evaluated separately and the final treatment and staging was decided after the second resection.

Table 1. Primary tumor characteristics

Characteristics	Number of patients	%
Stage		
Ta	60	60
T1	40	40
Grade		
1	53	53
2	24	24
3	23	23
Number of lesions		
1	44	44
Multiple	56	56
Tumor size (cm)		
<3	29	29
>3	71	71

Table 2. Residual tumor rate according to stage and grade on Re-TURB

Stage	G1	G2	G3	Residual tumor n (%)
Ta (n=60)	44	12	4	24 (40)
T1 (n=40)	9	12	19	16 (40)
Residual tumor n (%)	22 (42)	6 (25)	12 (52)	40 (40)

Statistical analysis

The association of residual tumors with the primary tumor characteristics was analysed using the Mann Whitney U test with a 95% confidence level.

Results

Histopathologically-proven residual tumors after Re-TURB were diagnosed in 40 (40%) patients. Fifty-six patients (56%) had more than one disease foci at the initial diagnosis (Table 1). The residual tumor detection rate was significantly correlated with initial multifocal disease ($p < 0.05$) and tumor size > 3 cm ($p < 0.05$). There was no correlation with tumor stage and grade ($p > 0.05$; Tables 2-4). In 46% of tumors > 3 cm and 24% of tumors < 3 cm a residual tumor was detected ($p < 0.05$; Table 4). Thirty-one (77%) of newly diagnosed tumors during Re-TURB were detected in areas either having macroscopic characteristics of a tumor or suspicion of a tumor (Table 5, Figure 1). Residual tumors during Re-TURB were found at the initial resection site in 29% of the patients and at other locations in 71% of the patients.

Tumor stage progression in the residual tumors was seen in 5 (12.5%) patients. Upstaging to muscle

Table 3. Initial tumor lesion number and relationship with residual tumor rates on Re-TURB

	Number of lesions	
	1	>1
Number of patients	44	56
Tumor after Re-TURB, n (%)	9 (20)	31 (55)

Table 4. Residual tumor rates according to tumor size on initial resection

	Tumor size (cm)	
	<3	>3
Number of patients	29	71
Residual tumor, n (%)	7 (24)	33 (46)

Table 5. Macroscopic properties of residual tumors during Re-TURB. In patients with no suspicious area or visible tumor, resection was performed from the initial resection site which is represented by (-). Areas which resembled a tumor due to its visible properties are represented with (+)

	Suspicious (%)		
	+	Suspicious	-
Number of patients	33	13	54
Residual tumor			
Histology (+) n:40	26 (78)	5 (38)	9 (16)
Histology (-) n:60	7 (22)	8 (62)	45 (84)



Figure 1. Macroscopic properties of histopathologically proven tumors during Re-TURB.

invasive disease was seen in 3 patients who were treated with either radical cystectomy or radiotherapy.

Discussion

The standard treatment for superficial bladder tumors is TURB. However, cystoscopies after the initial resection reveal a high rate of recurrence [3-7]. On the other hand, the presence of recurrence is an important parameter in determining the control cystoscopy intervals and intravesical cytotoxic treatment regimens. The rate of recurrence after TURB varies between 4 and 78% [4,8-10]. Taking into consideration the short interval between the initial resection and the first control cystoscopy the most likely reason of recurrence may be incomplete initial resection.

TURB technique should be performed according to two specified rules. First, the tumor bulk should be completely eliminated by resection of all visible tumors. Second, deep resections from the tumor base and borders should be performed after the complete resection of all tumours within the bladder. However, literature reveals that not all resections are carried out within these specified rules. On the other hand, even when the termed "correct resection" rules are followed, recurrence and progression may be seen due to the residual tumors. Klan et al. performed Re-TURB in 46 patients following strictly the previously mentioned rules (fractional TURB) in 30 (65%) of them; nevertheless a 43% residual tumor rate was reported [1]. Similarly, Kolosz et al. [11] performed resection with the mentioned rules to T1 patients and found a 36% residual disease.

Factors influencing the recurrence of a newly diagnosed bladder tumor have been analyzed. In the study of Pamar et al. the presence of tumor and its number at the first control cystoscopy following the initial TURB were found to be more important than the initial tumor stage and grade in predicting the recurrence

speed [12]. Similarly, Fitzpatrick et al. [13] and the EORTC studies [8] found that third-month control cystoscopy recurrences were the most important prognostic parameters for time until progression and progression free interval. When these data are taken into consideration, it is important to know whether the detected tumor on the first control cystoscopy is either a residual tumour or a recurrent tumor. This information will in turn help to determine the treatment and follow up protocols of patients with superficial bladder tumors.

Another aim of Re-TURB is to correct the staging errors. Herr [4] showed that 19.8% of 96 tumors initially staged as superficial in fact proved to be muscle – invading. Mersdorf et al. [2] obtained similar results. In their study, 14% of Ta and 49% of T1 tumors were upstaged after Re-TURB. Moreover, the study of Herr showed that absence of muscle in the primary resection is an important source of staging errors. In the absence of muscle the staging error was 49%, whereas in its presence it was only 14%. Recently, Hartwig et al. [14] reported an increase in stage, grade or extent of disease in 21% of patients, and led to radical cystectomy in 18% of patients after a repeat TURB. These findings underline the importance of optimal resection and repeat TURB in specimens including muscle.

Factors affecting the rate of tumor detection in the Re-TURB is the solid component proportion of the primary tumor, grade and multiplicity [2,15]. The rate of residual tumors in single stage Ta and T1 tumors after Re-TURB was found to be 7% [16]. Brausi et al. [8] reported that the rate of early recurrence and residual tumor increased from 7% for patients with a solitary tumor to 27-40% for patients with more than 5 tumors.

The surgeon's learning curve may be another factor affecting the residual tumor rate. In the study of Brausi et al., the impact of the surgeon's skills has been emphasized. The recurrence rate has decreased from 9.1% to 6.3% in two different studies conducted in the periods of 1979-1983 and 1987-1989 [8]. On the other hand in the series of Zurkirchen et al. [17] no significant difference in residual cancer rates was found between the experienced surgeons and the trainee group.

The residual tumors detected in our patients were mostly macroscopically visible tumors (64%). Whether the findings of residual tumors on the Re-TURB are due to overlooked multifocal disease or incomplete primary TUR remains unclear. Tumors detected in the Re-TURB in different locations suggest an overlooked multifocal disease in our study and the rate of such tumors was found to be 71%. According to the data published by Grimm et al. and Dalbagni et al. more than 50% of the residual tumors were at the initial resection site [18,19]. In another study where the cystoscopy information was

correlated with the histopathological information, 40% of the residual tumors were detected at the initial resection site where no macroscopic visible tumor was seen. In our study the rate of macroscopically invisible tumors was 29% [1]. On the other hand in our study 22% (9/40) of tumors detected in the second resection had no macroscopic visible tumors and most of the residual tumors detected were macroscopically visible lesions in different locations rather than in the initial resection site.

Recent studies show that in addition to being a part of follow up protocols and determining prognosis, Re-TURB actually may be a beneficial treatment procedure. In the study of Grimm et al. Re-TURB patients were compared with TURB-only patients [15]. Even though the study follow up period was rather short, it revealed a statistically significant advantage of recurrence free survival rate and lowered progression rate. Another study revealed the increased effectiveness of intravesical instillation of BCG in Re-TURB patients when compared to patients who did not undergo a Re-TURB [20].

An important question awaiting an answer is to whom should we perform Re-TURB? Fifty percent of the superficial bladder tumors are Ta G1. The recurrence rate of these tumors is low and even if recurrence occurs the recurrent tumor usually is a low grade lesion. Either missing out or insufficient treatment of these tumors do not cause any risk for the patient [21,22]. On the other hand T1 tumors are potentially lethal. For this reason precise staging and treatment is essential. Reaching this goal can only be achieved by performing a good quality resection both from the tumor base and border. When these criteria are not met Re-TURB should be indispensable. Different studies have shown that after a second pathologists opinion 50% of Ta tumors are restaged as T1. When this information is kept in mind it seems logical to evaluate high grade Ta tumors in the same context as T1 tumors are. Further information obtained by Re-TURB in these patients would increase the therapeutic and prognostic reliability. It does not appear possible to implicitly decide about the necessity of Re-TURB without the accurate definition of good quality TURB and Re-TURB and also without prospective, long-term studies.

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