

The Role of Early Second Transurethral Resection of Bladder Tumor in Restaging of Non-Muscle Invasive Bladder Tumors

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Abstract

Objectives: This study analyzed the impact of early second transurethral resection of bladder tumor (TURBT) on the rate of residual tumor, and up-staging rates in patients had initial complete transurethral resection.

Patient and Methods: From January 2015 to August 2016, total 60 patients who were diagnosed with bladder cancer by initial transurethral resection of the bladder tumor they underwent second resection after 4-6 weeks. The results were analyzed for the presence of residual tumor, grade and stage accordingly.

Results: A 60 patients had initial TURB -T, non-muscle invasive bladder tumor stages found; T1 in 71.66% and Ta in 28%. In the second TURBT, the biopsy showed no tumor growth in 41 patients (68.3%) and tumor tissue identified in 19 patients (31.6%). Of the 19 patients with positive results, 12 (63.15%) patients showed the same tumor grade and stage as the first TURBT and in 7 (36.84%) patients the stage changed; 6 patients upstaged and 1 patient down staged.

Conclusion: Early Second TURBT is recommended in patients with newly diagnosed non-muscle invasive bladder tumor. Since it changes the diagnosis and treatment in a significant portion of patients.

Introduction

Cancer of the bladder is estimated to be the ninth most common cause of cancer worldwide (357000 cases in 2002) and the 13th most numerous cause of death from cancer (145000 deaths). Incidence rates are high in many southern and eastern European countries, in parts of Africa and the Middle East, and in North America. The highest estimated mortality is in Egypt, where rates are more than three times greater than the highest rates in Europe and eight times those in the USA [1]. The incidence of bladder cancer is three to four times greater in men than in women [2].

Costs associated with management of non-muscle invasive bladder cancer is enormous due to the indolent nature of the disease and its potential for recurrence and progression which mandates frequent investigations and interventions [3]. The current available evidence indicates that bladder cancer screening is not helpful in improving survival [4]. Cytology is useful for the detection of

high-grade tumors or Carcinoma in Situ (CIS). However, vaccine Bacillus Calmette Guren (BCG) therapy may give false positive results [5]. Cystoscopy is the gold standard for the diagnosis and surveillance of bladder cancer although it is invasive and costly [6]. White light cystoscopy although is able to visualize the resection of all gross tumor mass but the high recurrence rate associated with bladder cancer has led to the introduction of photosensitizing drugs allowing Photo Dynamic Diagnosis (PDD) during cystoscopy and TUR [7]. There are two main grading systems for bladder cancer. In 2004, WHO classification the intermediate grade had been removed so there is low grade and high grade.

The published data till now has shown controversial results of comparison one classification over another [8]. The most critical information gained from pathologic interpretation of TURBT specimens is information about invasion of the lamina propria or muscularis propria [9]. Approximately 75–85% of patients with

bladder cancer is confined to the mucosa (stage Ta), or submucosa (stage T1). These categories are grouped as non-muscle invasive bladder cancer (NMIBC). Also included in this group is the flat lesion (CIS) which are confined to the mucosa but are high-grade tumors. Of these, approximately 70% present as stage Ta, 20% as T1 and 10% as CIS. High-grade T1 tumors have a (50%) risk of progression and (80%) of recurrence within 3 years. While Ta lesions have a risk of recurrence of (50- 70%) and progression of (2-5%) [10] Residual tumor is the most important factor associated with early recurrence and although strategies such as extended TURBT has been utilized and attempts made at standardizing the TURBT procedure to decrease the residual tumor left behind at first TURBT but nevertheless residual tumor removed at the second TURBT are in the range of 38% for all specimens [11] Routine use of a restaging TUR (re-TUR), supported by the American Urological Association and European Association of Urology guidelines, detects residual tumor in a significant number of cases after initial TUR. It provides a more accurate staging of the disease and consequently, helps to guide its treatment [12]. Early second resection had been shown to reduce recurrence rates, and increase response to intravesical chemotherapy and/or immunotherapy. It should be considered in most high-risk non-muscle invasive cancers (T1; G3; multifocal) being managed by bladder conservation [13]. One of the important issues in second TURBT is the issue that the second resection may change the pathological staging and grading of the tumor because in many of these cases tumor invasion of the submucosa or muscle is found only during repeat resection and by this decrease the chances of upstaging or grading [14].

Patients and Methods

This is a prospective study after obtaining Iraqi Board Ethics and scientific committee approval. Sixty patients participated in the study from August 2015 to September 2016. 13 of the patients were female, 47 were male, and the average age was 54 years (range of 42-72 years). The study is conducted in the sulaimany teaching hospital. The patients included in the study were all newly diagnosed with non-muscle invasive bladder cancer and those with recurrence tumors, muscle invasion was excluded. Patients pre-operative demographic data were collected and recorded the second TURBT performed 4-6 weeks after the first resection. Consultant urologists and emphasis done to do a complete initial TURBT did resections. Photodynamic light cystoscopy not used. Even in the absence of grossly visible masses, the scar of the previous operation was biopsied again with a single deep cut. Information about the number, size, shape, location and the configuration of the bladder tumors were recorded. The size of tumors was collected in multifocal tumors and recorded. The patients received treatment according to EAU guide line (immune with or without chemotherapy) The pathological specimens were submitted to histopathological examination, which was done by expert pathologists. The pathological specimens were analyzed and the tumors

were classified as single or multiple and denoted as Ta papillary noninvasive tumors, T1 papillary lamina propria invasion, T2 papillary with muscle invasion and Tis Carcinoma in situ. The grading was done according to 2004 WHO grading as low grade and high grade. The final treatment decisions were made on the result of pathology and based on EAU guidelines for the management of non-muscle invasive bladder tumor. The post-operative data were recorded.

Results

Sixty patients with non-muscle invasive bladder cancer were included in the study the mean age was 54 years with a range of (42-72) years. Of which 47 patients were male and 13 were females. Initial TUR-BT showed Ta in 17(28.33%)patients and T1 in 43(71.66%) patients. The tumor was single in 31patients and multifocal (more than one lesion) in 29 patients. The tumor diameter estimated was less than 3 cm in 34 patients and more than 3 cm in 26 patients see (Table 1).

Number of patients	60		
Age	54(42-72)	Tumor No.	31
		Single	29
		Multifocal	
Sex		Tumor diameter	26
Male	47	<3 cm	34
Female	13	>3cm	

Table 1: Patient and tumor characteristics in second TURBT.

For multifocal tumors, the size of tumors was added all together and measured. After the second TURBT, the biopsy showed no tumor in 41 patients (68.3%) and tumor tissue identified in 19 patients (31.6%). Of the 19 patients with positive results 12 (63.15%) patients showed the same tumor grade and stage as the first TURBT and in 7 (36.84%) patients the stage changed (6 patients upstaged and 1 patient down staged) as shown in the (Table 2).

Biopsy of first TURBT		Biopsy of Second TURBT (%)				
		T0	Ta	T1	Tis	T2
Ta	17	10 (58.82%)	2 (11.76%)	4 (23.52%)	1 (5.8%)	
T1	43	31 (72.09%)	1 (2.3%)	10 (23.25%)		1 (2.3%)
Total	60	41 (68.3%)		19 (31.6%)		

Table 2: Showing the results of the first and second TURBT.

The effect of multi-focal on the residual tissue being was; of the 29 multifocal tumors (more than one lesion), 15 of them showed residual on the second TURBT and of the 31 single lesions ;4 showed residual tumor on the second TURBT see (Table 3).

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Lesions at the first TURBT		Residual tissue at the second TURBT
Single lesions	31	4
More than one lesion	29	15
	60	19

Table 3: The effect of tumor multiplicity on residual tissue identified at the time of the second resection (p value 0.0001).

Regarding the grade of the Ta tumors it was low grade in 4 patients and high grade in 13 patients according to 2004 WHO grading. The change in stage from Ta to T1 seen only in patients with high grade Ta (p value 0.041) highlighting the fact, that high grade Ta may have more risk to be upstaged on follow up TURBT (Table 4).

Stage at first TURBT	Number of patients	No treatment change (%)	Treatment change (%)
Ta low grade	4	4(100)	-
Ta high grade	13	8(61.5)	5(38.4)
T1 high grade	34	33(97)	1(3)
T1 low grade	9	8(88.8)	1(11.1)
Total	60	53(88.3)	7 (11.6)

Table 4: The change in treatment after the second TURBT.

Discussion

Superficial ‘no muscle-invasive’ bladder tumors represent a heterogeneous group of cancers, which include those that are papillary in nature and limited to the mucosa (Ta), high grade, flat and confined to the epithelium (Tis) and those that invade the sub-mucosa or lamina propria (T1). Recurrence and progression rates of superficial bladder cancer vary according to several tumor characteristics. The goal in the treatment of superficial bladder cancer is twofold: reducing tumor recurrence and the subsequent need for additional therapies [15]. The issues of residual tumor and staging errors have great impact on the recurrence and progression of the tumor, which cannot be compensated by intravesical immuno/chemotherapy [16]. The technique and the experience of the surgeon doing the procedure also has an impact on the amount of tissue removed in the first resection and the more experienced surgeons tend to have better results and less residual tissue being left [17]. In addition, the location of the primary tumor has effect on the outcome of the resection because some locations are difficult to do complete resection in them such as in the lateral wall, dome, anterior wall of the bladder and absence of detrusor muscle in the primary specimen are factors that lead to increasing rate of residual tissue [18].

In our study, the percentage of residual tissue was 31.6% and the staging correction was (11.66%). In a study done by Tariq Aziz Shahatha on the value of second transurethral resection of

bladder tumor he concluded that the residual tissue was identified in 20(31%) out of 64 cases with superficial (Ta, Tis, T1) bladder tumors and 13 (20%) were upstaged to muscle invasive tumor [14]. In the landmark study done by Klan et al they found that residual tumor was detected in (44%) of patients after the second transurethral resection [19].

In a randomized controlled trial done by Rauf T. Divrik et al, they found a rate of residual tumor of 33.3% and staging errors corrected by second resection of (7.6%) and after 5 years of follow up, they found recurrence free survival in the second TURBT group to be 59% and 32% in the group with no second TURBT [20]. In a study done by Herr et al on the value of second transurethral resection for high grade T1 tumors that was done after 2-6 weeks of the first resection they concluded that 75% of the patients with non-muscle invasive tumor had residual tumor on repeat resection and the tumor upstaged to invasive tumor in 29% of cases and this lead to change of management in 33% of patients [21]. In another study done by Hartwig E. Shwaibold et al they found that (52%) of patients enrolled in the study had residual disease and (21%) of patients were upstaged during the second transurethral resection done after 4-6 weeks [22]. A study performed by John P. Sfakianos et al on the effect of repeat resection on recurrence and progression rates in patients with non-muscle invasive bladder cancer treated with Bacillus Calmette Guerin (BCG) vaccine, they found that (55.5%) of their patients in the study to have residual tumor during second transurethral resection and on follow up after 5 years they found in patients with a single resection had shorter time to recurrence (22 months) than patients who underwent repeat resection (36 months) [23].

The second transurethral resection can be performed safely 4 weeks after the first procedure with no significant increase in complications and the complications are the same as those of routine transurethral resection [24]. The transurethral resection of bladder tumor is relatively safe [25]. The timing of the second transurethral resection is not strictly defined with various time frames being used across different studies [26]. Bladder cancer is the fifth most frequent type of cancer in western society and the most expensive cancer per patient. In a study done by Van Rhijn BW et al. in NMIBC, approximately 70% of patients present as pTa, 20% as pT1, and 10% with Carcinoma in Situ (CIS). While our study results of the first TURBT were T1 in 43 (71.66%) patients and Ta in 17(28.33%) patients, this may show different aggressive biological behavior in our locality [27]. In another study done by Gendy R et al. the residual cancer rates at the 3-6 month on one thousand and two hundred and nine transurethral resection specimens retrieved were analyzed. There were 162 (13.4%) T1 specimens and 631 (52.2%) Ta specimens, 218 (34.5%) of which were high grade [28]. Which show higher rate of Ta rather than T1 as in our study. In prospective study done by Vögeli TA et al. a 192 TUR, superficial TCC was found in 124 cases; 83 underwent Re-TUR

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according to the study protocol. Residual tumor was detected in 27% of pTa and 53% of pT1 tumors. Worsening of grading or T stage was found in 8%. Of the tumors detected by Re-TUR, 81% were localized at the site of the first TUR.; residual tumor formation was detected in a high percentage [29]. In our study, the changes in stages from Ta to T1 was seen only in high grade Ta and residual tumor in 19 patients and this made change in treatment in 7 (11.6%) patients. If the initial resection is incomplete, there is no muscle in the specimen, or a high-grade or T1 tumor is detected, a second TURB should be performed within 2-6 week, except solitary pTaGI lesions [30].

Conclusions

Re-TUR rates in high-risk non-muscle-invasive bladder cancer are low. However, in a contemporary series, the upstaging rates are low, but residual cancer rates high, supporting the need for re-TUR in this population. Our study shows that high-grade tumors are more likely to have residual tissue and staging change after transurethral resection than low-grade tumors. Early second look is useful for the clinician to be aware of early detection of residual tissue left and by this decrease recurrence and progression, to improve disease free survival outcomes.

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