

# Frequency of Residual Tumor on Redo Transurethral Resection of Bladder (TURB) and Its Impact on Management of Non Muscle Invasive Bladder Cancer

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## ABSTRACT

**Objective:** In this study, we have searched the frequency of residual tumor and its stage in cases found to have Non Muscle Invasive Bladder Cancer (NMIBC) on first procedure and underwent Redo-TURB. More so the impact of Redo-TURB on the management was studied.

**Study design:** Cross sectional study.

**Place and Duration of Study:** This study was conducted at the Urology Department of Nishtar Medical University/Hospital Multan from July 2017 to August 2019.

**Materials and Methods:** Based upon the Inclusion and exclusion criteria, using non-probability consecutive sampling technique, we selected a total of 144 patients. These cases were diagnosed with NMIBC on first TURB but due to certain reasons underwent Redo-TURB.

**Results:** There were 144 patients in total. Males were 108/144 (75%) while females were 36/144 (25%). Mean age of the patients was 53.18+ 5.82 years. Mean duration of symptoms before the diagnosis was found to be 6.20 + 2.30 months. Residual tumor was found to be present in 96/144 (66.7%) while no tumor was identified in 48/144 (33.3%). Histopathology of Redo-TURB case having residual tumor came out as Non-muscle invasive bladder cancer(NMIBC) 77/96 (80.21%) and muscle invasive bladder cancer (MIBC) 19/96 (19.79%). There was no significant effect of gender, age and duration of symptoms on the frequency of residual tumor.

**Conclusion:** Redo-TURB should be advised in particular situations in patients who are diagnosed to have NMIBC on first resection. The aim is to achieve more complete tumor resection, proper staging and management of NMIBC. Redo-TURB also helps to identify cases having invasive disease that need aggressive treatment but were under staged due to incomplete resection

**Key Words:** Non Muscle Invasive Bladder Tumor, Redo Transurethral Resection of bladder tumor, Residual Tumor

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## INTRODUCTION

Bladder cancer is one of the most common urinary tract tumors; being the 9<sup>th</sup> most common tumors worldwide<sup>1</sup>. Non-muscle invasive bladder cancer (NMIBC) accounts for 70% of all new cases; this is known as 'superficial bladder cancer'<sup>2,3</sup>. Muscle-invasive disease and flat non-invasive carcinoma in situ (CIS) account for 25 % and 5% respectively. Superficial urothelial tumors are usually papillary in nature that grow in an exophytic fashion into the bladder lumen<sup>2,4,5</sup>.

NMIBC can appear as single but can arise as multiple de novo being field change of transitional epithelium. Tumor can be narrow based on single stalk or can be broad based in cases of less well differentiated type. Surrounding mucosa also develops changes like edema and dilated, tortuous dark colored vessels. The most common sites for superficial tumors are the trigon and lateral walls of the urinary bladder<sup>2</sup>.

Transurethral resection of bladder tumor (TURB) is the gold standard treatment option for NMIBC<sup>6,7</sup>. However, after initial complete treatment by endoscopic transurethral resection (TURB), there is high incidence of recurrence and progression of disease and about 15% patients develop MIBC<sup>2,8</sup>. The risk of such progression is high with high grade disease, pT1, multiple primary tumors and concomitant CIS<sup>2</sup>. The behavior of bladder tumor provides a rationale for check cystoscopies<sup>9</sup>. Follow up check cystoscopies are advised at regular intervals to all patients. Findings of first check cystoscopy after 3 months of TURB have great prognostic value regarding recurrence and progression of disease<sup>10</sup>. There are certain indications wherein the

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first TURB is thought to be incomplete so Redo TURB is advised after two to four weeks in patients with pT1, high grade, incomplete resection of bladder tumor and cases in which muscle not included in biopsy.

Ali MH and co-workers from Egypt conducted an analytical prospective study on 91 patients with pathological stage T1 and Ta bladder tumor in which all the patients underwent Redo TURB within 2 to 6 weeks of the initial resection. They recorded histopathological findings of the second TURB and compared them with the initial ones. Their study brought to light that on second-look TURB, 38 (41.7%) patients had no tumor at all, 22 (24.2%) patients had residual cancer of the same stage, 9 (14.8%) patients of pT1 had lower stage and 22 (24.2%) had higher stage tumor<sup>11</sup>. Therefore, upstaging led to change the treatment strategy in 22 (24.2%) patients. In another study carried out in USA, Herr<sup>12</sup> reported 49% patients with upstaged tumor on re-TURB in the patients with T1G3/T1HG whose muscularis propria was not present in the specimen. Also, he observed that only 14% patients found upstaged on re-TURB in the patients whose initial TURB reflected benign muscularis propria. Moreover, 17% of the patients showed histological evidence of cancer on TURB despite of a normal cystoscopic examination<sup>13</sup>.

**MATERIALS AND METHODS**

Across sectional study was done in Urology department of Nishtar Hospital Multan (NHM) from 01-07- 2017 to 31-08- 2019. There were total 144 patients and sampling technique was non-probability consecutive sampling.

**Inclusion Criteria:**

- Patients of age 40-60 years of either sex
- The patients who had pT1, G3 on histology.
- Muscle if not identified in biopsy specimen.
- Incomplete resection of bladder tumor.
- Tumor operated in non-specialized centers

**Exclusion Criteria:**

- The patients with known advanced bladder carcinoma.
- Patients who had undergone any kind of previous treatment.
- Co-morbid conditions e.g. ischemic heart disease
- MIBC on first TURB

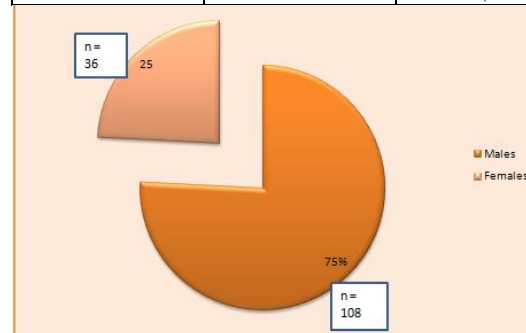
A proforma was specifically designed to record findings of this study. We collected samples and data from the patients with diagnosed cases of non-muscle invasive bladder cancer on biopsy after primary TURB, admitted to the urology ward of Nishtar Hospital Multan after an informed consent and assurance of confidentiality. Patients were followed for redo TURB 2 to 4 weeks after the initial resection. Frequency of residual tumor and muscle invasive disease at redo TURB of non-muscle invasive bladder tumor was documented on the proforma.

**RESULTS**

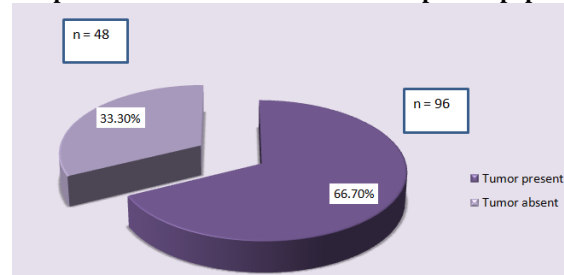
There were 144 patients in total. Males were 108/144 (75%) while females were 36/144 (25%). Mean age of the patients was 53.18+ 5.82 years. Mean duration of symptoms before the diagnosis was found to be 6.20 + 2.30 months. Residual tumor was found to be present in 96/144 (66.7%) while no tumor was identified in 48/144 (33.3%). Among those who were found to have residual tumor. It was found to be muscle non-invasive in 77/96 (80.21%) and muscle invasive in 19/96 (19.79%) (Table 1, Graph 1,2,3).

**Table No.1: Characteristics of the study population**

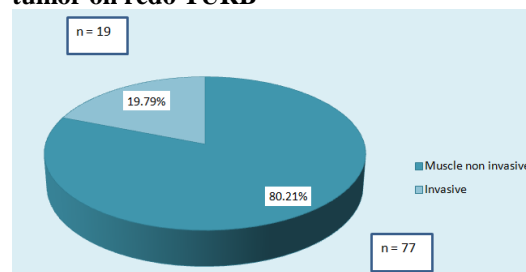
Total patients	144	
Males	108/144 (75%)	
Females	36/144 (25%)	
Mean age	53.18+ 5.82	
Mean duration of symptoms	6.20 + 2.30	
Residual tumor	Yes	96/144 (66.7%)
	No	48/144 (33.3%)
Stage of residual tumor	Muscle non invasive	77/96 (80.21%)
	Invasive	19/96 (19.79%)



**Graph No.1: Gender distribution in the patient population**



**Graph No.2: Frequency of patients with residual tumor on redo TURB**



**Graph No.3: Frequencies of muscle noninvasive and invasive tumors on redo TURB biopsy**

When the effect of gender was noted, it was found that among 108 male patients, the mean age was 52.89 + 5.89 years, mean duration since diagnosis was 6.18 + 2.30 months. There was no residual tumor found in 35/108 (32.4%) patients while it was found in 73/108 (67.6%) patients. Among those who had residual tumor it was found to be muscle non-invasive in 59/73 (80.82%) while it was invasive in 14/73 (19.17%). Among 36 females mean age was 54.06 + 5.59 years, mean duration was 6.28 + 2.32 months. No residual tumor was found in 13/36 (36.1%) while tumor was found to be present in 23/36 (63.9%) (p-value > 0.05). Among those with residual tumor present on redo-TURBT, 18/23 (78.26%) had muscle non-invasive tumor while 5/23 (21.7%) had invasive tumor (Table 2).

**Table No.2: Comparison of various characteristics among males and females.**

		Males (n = 108)	Females (n = 36)	p-value
Mean age		52.89 + 5.89	54.06 + 5.59	
Mean duration of symptoms		6.18 + 2.30	6.28 + 2.32	
Residual tumor	Present	73/108 (67.6%)	23/36 (63.9%)	> 0.05
	Absent	35/108 (32.4%)	13/36 (36.1%)	
Stage of residual tumor	Non-invasive	59/73 (80.82%)	18/23 (78.26%)	> 0.05
	Invasive	14/73 (19.17%)	5/23 (21.7%)	

**Table No.3: Comparison of various characteristics among patients with different age groups.**

		Age 40-50 (n = 40)	Age 51-60 (n = 104)	p-value
Males		31/40 (77.5%)	77/104 (74%)	
Females		9/40 (22.5%)	27/104 (26%)	
Mean duration of symptoms		6.20+ 2.47	6.20+ 2.24	
Residual tumor	Present	24/40 (60%)	72/104 (69.2%)	0.664
	Absent	16/40 (40%)	32/104 (30.8%)	
Stage of residual tumor	Non-invasive	18/24 (75%)	59/72 (81.94%)	0.785
	Invasive	6/24 (25%)	13/72 (18.05%)	

When the effect of age was noted, it was found that there were 40 patients in age group 40-50 years. Mean duration of symptoms was found to be 6.20+ 2.47 months. Males were 31/40 (77.5%) while females were 9/40 (22.5%). Residual tumor was present in

24/40(60%) while it was not present in 16/40 (40%). Among those who had residual tumor, it was found to be muscle non invasive in 18/24 (75%) and invasive in 6/24 (25%). Among 104 patients with age > 50 years, mean duration was found to be 6.20+ 2.24 months. Residual tumor was not present in 32/104 (30.8%) while it was present in 72/104 (69.2%). Among those who had residual tumor on redo TURBT, the tumor was found to be muscle non-invasive in 59/72 (81.94%) while it was found to be invasive in 13/72 (18.05%) (Table 3).

When the effect of duration of symptoms was noted it was found that among 83 patients with duration < 6months, mean age of the patients was 52.98 + 5.77 years, males were 63/83 (75.9%) while females were 20/83 (24.1%). Residual tumor was found to be absent in 32/83 (38.6%) and present in 51/83 (61.4%). Among those who were found to have residual tumor, upon staging of the tumor it turned out to be muscle non invasive in 41/51 (80.39%) and invasive in 10/51 (19.6%). Among those with duration of symptoms more than 6 months there were 61 patients in total with mean age of 53.46+ 5.93 months. Males were 45/61 (73.8%) while females were 16/61 (26.2%). Residual tumor was present on redo TURB in 45/61 (73.8%) while it was absent in 16/61 (26.2%). Among those who had residual tumor found 36/45 (80%) were found to be muscle non invasive while 9/45 (20%) were found out to be invasive (Table 4)

**Table No.4: Comparison of various characteristics among patients with different duration of symptoms.**

		Duration < 6months (n = 83)	Duration > 6months (n = 61)	p-value
Males		63/83 (75.9%)	45/61 (73.8%)	
Females		20/83 (24.1%)	16/61 (26.2%)	
Mean age		52.98 + 5.77	53.13 + 5.85	
Residual tumor	Present	51/83 (61.4%)	45/61 (73.8%)	0.081
	Absent	32/83 (38.6%)	16/61 (26.2%)	
Stage of residual tumor	Non-invasive	41/51 (80.39%)	36/45 (80%)	0.563
	Invasive	10/51 (19.6%)	9/45 (20%)	

**DISCUSSION**

For Non-muscle invasive bladder cancer, Transurethral resection of bladder tumor is considered Gold standard surgical procedure. Recent data suggests that Primary TURB can remove bulk of tumor , but still in some of

the situations, complete resection of tumor is not possible that leads to under staging of the disease and mis-management. Some of Histopathology reports describe the fact that Redo TURB performed within eight weeks after initial TURB has higher incidence of residual tumor of about 18-77 %<sup>14,15</sup>, meanwhile, tumor stage changed in about 40% of patients<sup>16</sup>. Following are factors causing Re-TURB positive: Grade and stage of tumor, size of tumor, Recurrence history of Tumor, interval between two TURBs, operation by surgeon, etc<sup>17,18</sup>. Various studies show that positive rate is comparatively high in Re-TURB, hence, most analysts believe that under the condition of TURB, tumor features itself are the key factor of residual tumor, and higher incidence of tumor recurrence or progression in those patients who are showing positive rates in TURB<sup>19</sup>. This research shows that a high rate of residual tumor can be found in the repeated TURB performed 4-6 weeks after initial TURB in patients with non-muscle invasive bladder urothelial carcinoma.

In terms of surgical complications, there was no bladder perforation or rupture upon Redo-TURB, and relevant documents at home and abroad<sup>14,15,20</sup> also confirm that the complications of Re-TURB are basically the same as those of routine TURB. Therefore, we believe that it is safe to perform Re-TURB 4-6 weeks after the initial TURB.

In our study there were 144 patients in total. There was a male predominance as males were 108/144 (75%) while females were 36/144 (25%). This was because bladder cancer is more frequent among males as compared to females with a male to female ratio of 3:1 to 5:1<sup>23,8</sup>. Mean age of the patients was 53.18+ 5.82 years which was reflective of our inclusion criteria and the age group in which bladder cancer is more frequently encountered. Mean duration of symptoms before the diagnosis was found to be 6.20 + 2.30 months. Residual tumor was found to be present in 96/144 (66.7%) while no tumor was identified in 48/144 (33.3%). Among those who were found to have residual tumor, the tumor was found to be muscle non-invasive in 77/96 (80.21%) while it was found to be invasive in 19/96 (19.79%). There was no significant effect of age, gender or duration of symptoms on the frequency of tumor on 2<sup>nd</sup> look TURB. These results were similar to those reported in other studies. In an analytic prospective cohort study conducted by Ali et al.<sup>11</sup> included 91 patients with stage T(1) and T(a) bladder cancer. All patients underwent Redo TURB during 2 to 6 weeks after the first resection. Histopathologic findings of the second TUR of bladder tumor (TURB) were compared with those of the initial one. Specimens of resection obtained during the Redo TURB showed no tumor in 38 (41.7%) patients; 22 (24.2%) patients had residual cancer of the same stage, 9 (14.8%) patients of pT(1) had a lower stage, and 22 (24.2%) had a higher stage. Treatment plan needed revision in 22 (24.2%) cases as a result of upstaging of histopathology report of Redo TURB. Appearance, size, grade, and stage of the tumor at the initial resection are all considered independent risk factors for upstaging detected at Redo TURB.

In another study conducted by Schwaibold et al. the initial result and histopathological diagnosis of TURB in the series of 136 patients was T1 transitional cell carcinoma (TCC). Of the 136 patients, 101 underwent TURB for first time and 35 had recurrent tumors. The second TURB was done 4-6 weeks after first procedure. The evaluation included the presence of previously undetected residual tumor, inclusion of muscularis propria in specimen, changes to histopathological staging/grading, and tumor location. In all, 71 patients (52%) had residual disease according to findings from specimens obtained during RedoTURB. The staging was: no tumor, 65 (48%); Ta, 11 (8%); T1, 32 (24%); Tis, 15 (11%); and > or = T2, 13 (10%). Histopathological changes that worsened the prognosis (>T1 and or concomitant Tis) were found in 21% of patients. Residual malignant tissue was found in the same location as the first TUR in 86% of the patients, and at different locations in 14%. Overall, 28 patients (21% of the original 136) had a radical cystectomy as a consequence of the second TUR B findings.

In a study conducted by Grimm et al, residual tumor was found in 33% of all Re TURB cases including 27% of Ta and 53 % of T1 disease and 81% at the initial resection site. Progression to muscle invasive disease was observed in only 2 patients (3%) after a mean observation of 61 months<sup>21</sup>. Repeat Transurethral resection (Redo TURB) is advocated as a fundamental step towards complete clearance and appropriate staging of T1 bladder cancer tumors<sup>22</sup>.

In another study conducted by Katsuyoshi Hashine, Takhiro Ide et al, no cancer was found in 33 patients(41.8%), CIS in 18 (22.9%), Ta in 15 (19.0%), T1 in 12(15.2%), and muscle invasive T2 bladder cancer in 1 patient (1.3%)<sup>23</sup>. Study conducted by Cumberbatch MGK, residual tumor at re TUR was found in 17-67% of patients following Ta and in 20-71% following T1 cancer. Most residual tumors (36-86%) were found at the original resection site. Upstaging occurred in 0-8%(Ta to > T1) and 0-32% (T1 to > T2) of cases<sup>24</sup>. Compared to patients without second TUR, patients with second TUR had significantly higher 5-year, 7-year and 10-year rates for Recurrence free survival(59.4%, 57.9%, 54.8% respectively) and progression free survival (93.3%, 91.9%, 90.4% respectively) and 10-year overall survival was significantly higher in patients with second TUR(59.1%). Second TUR should be routinely performed in all stages pT1 NMIBC patients with life expectancy of at least 10 years, given the positive contribution to all oncological outcomes.

It is clearly shown that second TUR, which is performed only after complete first TUR, has significantly decreased the recurrence and progression rates with newly diagnosed T1 disease compared to patients with T1 disease but with no second TUR<sup>25</sup>.

## CONCLUSION

Redo TURB should be advised in particular situations in patients who are diagnosed to have NMIBC on first resection. The aim is to achieve more complete tumor

resection ,proper staging and management of cases identified to have invasive disease that need aggressive treatment.

#### Author's Contribution:

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**Conflict of Interest:** The study has no conflict of interest to declare by any author.

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