

## Comparison of Early Re-Resection Versus Standard Surgical Method for Transurethral Resection of Urinary Bladder Tumor: A Randomized Controlled Trial

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### Abstract

**Objective:** To compare results of early re-resection versus the standard surgical approach for bladder tumour transurethral resection.

**Method:** This 6-month randomized controlled at Urology ward Jinnah Hospital was conducted on 160 sample size calculated through WINPEPI software. Patients of bladder cancer were randomized into two groups, Group A had an early resection, within 6 weeks of the initial transurethral resection. Group B was without early re-resection. Patients were re-evaluated for tumour progression and recurrence at the resected site during follow-up. Data was entered and analyzed using SPSS version 20.0.

**Results:** In Group A 81% were males with 57.24±8.55 years mean age. In group B there were 90% males with mean age 54.39±8.26 years. In early re-resection group, 3 (3.8%) had tumor progression and 77 (96.3%) did not have tumor progression. In standard method group, 10 (12.5%) had tumor progression and 70 (87.5%) did not have tumor progression. Significant difference among two groups was observed. ( $p < 0.05$ ). In early re-resection group, 35 (43.8%) had recurrence of tumor and in standard method group, 55 (68.8%) had recurrence of tumor. The difference in both groups was significant ( $p < 0.05$ ).

**Conclusion:** Thus early re-resection (at 6 weeks) is beneficial in suppression of tumor progression and its recurrence as compared to standard method of resection which is done at three months.

**Keywords:** Re-resection, standard surgical method, transurethral resection, bladder tumor, tumor progression, recurrence

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### Introduction

Urinary bladder cancer is 10th most common cancer worldwide and its incidence is rising especially in developed countries.<sup>1</sup> Most incidence occurs in between 40 -70 age group, with a men to women ratio of 3:1. More developed countries account for about 59 percent of bladder cancer cases. Southern, Western Europe and Northern America are with highest rates of

bladder cancer, whereas middle Africa, central Asia, Latin America, and west Africa have the lowest rates.<sup>2</sup> Urinary increased frequency, urgency and lower urinary tract features are the commonly presented symptoms.<sup>3</sup> According to Karachi Cancer Registry (KCR), bladder cancer was the 4<sup>th</sup> most common cancer in males and 5<sup>th</sup> in Females.<sup>4</sup> Bladder cancer known risk factors in addition to smoking cigarette are exposure to a number of industrial chemicals such as aniline dyes, painkiller (phenacetin) misuse, benzidine chemicals and catheters causing chronic irritation.<sup>5</sup>

The superficial tumors restricted to the bladder mucosa are classified as Ta or T1, with 20% of cases being classified as Ta, 70% as T1, and 10% as CIS.<sup>4,5</sup> The size of the tumor, multifocality, stage of the tumor, grade of the tumor, and early recurrence all influence disease progression.<sup>6</sup>

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With its varied behaviour, T1 grade 3 (T1G3) bladder carcinoma is one of the most difficult surgeries for urologists and patients alike.<sup>7</sup> Transurethral resection of bladder (TURBT) is considered as the gold standard treatment for these patients with bladder carcinoma (non-muscle invasive). Because the initial TURBT may not be enough to completely remove and stage the tumour, the risk of recurrence and advancement is raised. Non-muscle invasive bladder cancer (MNIBC) is widely known for having a high recurrence rate of >50 percent following initial resection. Reasons for this are incomplete resection and implantation of floating tumor cells.<sup>8</sup>

In usual practice, first TURBT is performed, and the patient is re-evaluated three months later for the second TURBT. However, according to European and American guidelines, the re-resection after initial TURBT should be performed within 2-6 weeks. The goal of early resection is to assure precise tumor staging, halt the cancer from progressing further, and thereby improve the prognosis.<sup>9</sup> According to one study, tumour recurrence rates were 35 percent and 42 percent, respectively, with and without re-resection. Patients who did not have early re-resection had significantly greater occurrence of progressive tumor stage during follow-up (late re-resection 14.4% vs. early re-resection 3.3%) ( $P < 0.05$ ).<sup>10</sup> The purpose of this research is to compare the results of early re-resection vs regular TURBT surgery. In comparison to normal protocol, literature has shown that re-resection within 6 weeks after initial resection had a superior outcome and prognosis for cancer patients. However, due to a lack of local evidence, it is not used in public sector settings. Furthermore, there is a scarcity of data in this area. We hope to obtain local proof that early re-resection of TURBT is a more useful and effective strategy for TURBT through this study. This will aid in the improvement of our practice, and in the future, we will use early resection as a therapy plan for patients with bladder cancer rather than a single TURBT.

## Material and Methods

This is a randomized controlled trial conducted at Urology ward of Jinnah Hospital Lahore. A sample size of 160 cases was calculated, with 80 cases in each group, using a 5% threshold of significance, an 80 percent power of study, and the projected percentage of tumour advancement, which was 3.3 percent with early re-resection and 14.4% with the standard procedure. After approval from Ethical Review board of JHL/AIMC Candidates were chosen using a non-probability, purposive sampling

method. Patients with bladder cancer who were 30-70 years old and of either gender were included. Bladder Carcinoma patients were randomly assigned two groups by using two folded cards (A & B) pickup method. Group A patients had an early resection, within 6 weeks of the initial transurethral resection. The conventional procedure was used in group B without re-resection. All of the procedures were carried out by a single surgical team with the help of the researcher. All of the procedures were carried out under spinal anaesthesia. Patients were then transferred to post-surgical wards and monitored there until discharge, as well as in the OPD. Patients were re-evaluated for tumour progression and recurrence at the resected site during follow-up. All of this data was entered into a proforma. SPSS version 20.0 was used to enter and analyse all of the data. The quantitative variables i.e. age (years), duration of diagnosis (months), tumor size (mm) were presented as mean  $\pm$  standard deviation. The qualitative variables i.e. gender, recurrence or progression of tumor were analyzed and frequencies were calculated. Comparison among groups was done by using chi-square test. To assess statistical significance  $P$ -value  $\leq 0.05$  was decided. Data was stratified for age, gender, duration of symptoms and tumor size. Chi square test was again performed post stratification.

## Results

In group A 57.24 $\pm$ 8.55 years was the mean age. In group B 54.39 $\pm$ 8.26 years was the mean age. In group A, there were 65 (81.3%) males and 15 (18.8%) were females. In group B, there were 72 (90%) males and 8 (10%) were females. In early re-resection group A, the mean duration of tumor was 20.35 $\pm$ 9.90 days. In standard method group B, the mean duration of tumor was 31.70 $\pm$ 16.28 days. There were 80 (50%) who had tumor size <3cm and 80 (50%) had tumor size >3cm. (Table I) In early re-resection group A, there were 40 (50%) who had tumor size <3cm and 40 (50%) who had tumor size >3cm. In early re-resection group, 3(3.8%) had tumor progression and 77 (96.3%) did not have tumor progression. In standard method group B, 10(12.5%) had tumor progression and 70 (87.5%) did not have tumor progression. The difference in both groups was significant ( $p < 0.05$ ). In early re-resection group, 35 (43.8%) had recurrence of tumor and 45 (56.3%) did not have recurrence of tumor. In standard method group, 55 (68.8%) had recurrence of tumor and 25(31.3%) did not have recurrence of tumor. The difference in both groups was significant ( $p < 0.05$ ). (Table II) Data was stratified

for age of patients. On stratification, the difference regarding recurrence of tumor with respect to two operative procedures is significantly different in younger age group (35-50 years) as compared to old age group (51-70 years). Thus age has an effect on outcome of these procedures. Data was also stratified for duration and Size of Tumor. Results were statistically significant among those with less duration and smaller sized tumors. (Table-III)

**Table 1:** Demographic and Disease Profile of Patients recruited in Standard (Group B) and Early Re-resection group (Group A). N= 180

Variable		Group		Total
		Early Re-resection N= 80	Standard N=80	
Age	Mean	57.24 yrs	54.39 yrs	55.81 yrs
	Standard Deviation	8.55	8.26	8.50
Gender	Male	65 81.3%	72 90.0%	137 85.6%
	Female	15 18.8%	8 10.0%	23 14.4%
Duration of Symptoms	Mean	20.35 months	31.70 months	26.03 months
	Standard Deviation	9.90	16.28	14.59
Size of Tumor	< 3 cm	40 50.0%	40 50.0%	80 50.0%
	> 3 cm	40 50.0%	40 50.0%	80 50.0%

**Table 2:** Comparison of Early Re-resection and Standard Method in terms of Tumor Progression and Recurrence

Variable		Group		
		Early Re-resection N= 80	Standard method N= 80	
Tumor Progression	Yes	3 3.8%	10 12.5%	13 8.1%
	No	77 96.3%	70 87.5%	147 91.9%
	P Value = 0.043 (Statistically Significant)			
Recurrence of Tumor	Yes	35 43.8%	55 68.8%	90 56.3%
	No	45 56.3%	25 31.3%	70 43.8%
	P value = 0.001 (Statistically Significant)			

### Discussion

TURBT is the first and most important step in the management of bladder tumors. This procedure has two pronged objectives. First is to determine histological diagnosis, and then to determine tumor stage and grade, and to achieve complete removal of non-muscle-invasive bladder tumors.<sup>11</sup> The point of concern is that results of transurethral resection are far from optimum, and the diagnosis and therapeutic purposes are not always achieved. The guidelines of European Association of Urology, recommend a second transurethral resection if there is suspicion that the initial resection was incomplete.<sup>12</sup> If patient has high grade bladder tumor with no involvement of muscle, second transurethral resection plays a vital role.<sup>12</sup> In our study, we observed that 3(3.8%)

**Table 3:** Stratification Analysis to Control for Confounding by Age, Gender and Size of Tumor on Progression and Recurrence of Tumor among Early re-resection and Standard Method.

Variable	Tumor Recurrence	Groups		P-Value	
		Early Re-resection (Group A)	Standard Method (Group B)		
Age (years)	35-50	Yes 4 20.0%	20 80.0%	0.000	Statistically significant in younger age group
	51-70	Yes 2 3.3%	4 7.3%	0.195	
Duration of Tumor (months)	10-30	Yes 34 44.2%	40 70.2%	0.003	Statistically significant in less duration group
	31-60	Yes 1 33%	15 65%	0.286	
Tumor Size	<3 cm	Yes 15 37.5%	31 77.5%	0.000	Statistically significant in smaller sized tumors
	>3 cm	Yes 20 50.0%	24 60.0%	0.369	

had tumor progression in early re-resection group while 10(12.5%) had tumor progression in standard method group. Also 35 (43.8%) who had recurrence of tumor in early re-resection group while in 55 (68.8%) who had recurrence of tumor in standard method group. The difference in both groups was significant ( $p < 0.05$ ) for both outcome variables. Vasdev et al conducted a trial and found that tumor recurrence was, respectively, 35% and 42% with and without re-resection. When follow-up was done, there was a statistically significant trend of tumor stage progression in patients who did not undergo early re-resection (Group B 14.4% vs. Group A 3.3%,  $P < 0.05$ ).<sup>10</sup> Our study has demonstrated slightly better results than Vasdev trial and both studies are demonstrating beneficial effect of early re-resection. This rate of residual disease is quite similar to the findings reported by Engelhardt et al to be 52% within an interval of eight weeks.<sup>13</sup> The major query to decide is regarding suitable interval to perform re-resection. Klan et al, has reported a rate of residual tumour of 43%. This study did not find any benefit to wait for two weeks or more from initial transurethral resection. Many studies on the other hand have advocated a delay of two to six weeks, to allow post-resection inflammatory change to settle facilitating better visualization and demarcation of tissues. Benefits of early re resection has also been documented by Lawrence Kim in 2020 and has also stated the effects of staging and size of tumor on outcome as mentioned in our study.<sup>9</sup> Our study results are in accordance with other published researches employing shorter re-resection intervals of four to six weeks and reporting residual tumour rates ranging from 33% to 62%.<sup>9</sup> In this study, the percentage of high grade tumors were only 10%. A recently published research advocates a re-resection at a gap of up to eight weeks and residual cancer was found in 66.7% of cases of pT1 tumors as mentioned by Han et al.<sup>14</sup> Upon stratification the outcome of both procedures was different with reference to tumor size. This finding is also supported by J C Chen as they showed a difference. But in our study cut off size was 3 cm and in Chen study it was 4 cm.<sup>15</sup>

## Conclusion

Thus early re-resection (at 6 weeks) is beneficial in suppression of tumor progression and its recurrence as compared to standard method (resection done at three months). This will help in improving prognosis of patients and improve quality and longevity of life of patients.

**Conflict of Interest:** *None*

**Funding Source:** *None*

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### Authors Contribution

**MA, SKB:** Conceptualization of Project

**SKB, AA:** Data Collection

**AA, MA:** Literature Search

**SKB:** Statistical Analysis

**NI, MY:** Drafting, Revision

**AA, SKB:** Writing of Manuscript