

Is Second Resection Necessary for High Grade Bladder Carcinoma a Retrospective Analysis?Abhilekh Tripathi¹, Sachin Sharma², Tilala Yash Manharlal³, Jateen Anshuman⁴, Kishore Kumar Behera⁵, Sabyasachi Panda⁶, Amiya Sankar Paul⁷^{1,2,3,4,5,6,7}Department of Urology and renal Transplant SCB Medical College & Hospital Cuttack Odisha

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Conflict of interest: Nil

Abstract:

Introduction: Urinary bladder cancer is quite common in eastern part of India as people here are more addicted to tobacco and smoking cigarettes and present with total gross painless intermittent hematuria as initial presenting symptoms. After initial workup of the patient is posted for transurethral resection of bladder tumor as part of treatment and staging.

Method: In this retrospective analysis we studied 129 patients who were detected with UB mass were subjected to TURBT after initial work up and specimen sent for histopathological examination.

Result: 45 patients were having high grade bladder tumor, of which 40 were subjected to second TURBT within 2 to 6 weeks. Only 15 patients had recurrent tumor. Most of the recurrence i.e. 13 was in multiple papillary and sessile, > 3 cm tumors and only 2 recurrences in solitary, > 3cm group.

Conclusion: So the conclusion of our study is that 1. do secondary resection in patients with primary characteristic of tumor >3 cm, multiple papillary or sessile, with high grade should receive 2nd resection. 2. in some subset of patients with < 3 cm of bladder tumor, solitary with no deep muscle involved 2nd resection can be safely avoided but this group of patients should be kept in close followup as per the institutional protocol.

Keywords: UB mass, TURBT, Solitary Papillary, Multiple Papillary and Sessile.

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Introduction

TCC of the urinary bladder is the ninth most common cancer in worldwide cancer incidence. It is the 7th most common cancer in men and ranks 17th in women [1]. The incidence of bladder cancer varies significantly all over the world, with Egypt, Eastern Europe, and North America having the highest incidence rates, and Asian countries the lowest rates [2]. More than 90% of new cases occur in people in the 6th decade, but the disease may occur in younger population as well [3]. The mean age of the patients diagnosed with bladder cancer is 69 years for men and 71 for women and the estimated ratio between men and women is 3.8/1 [4].

Cigarette smoking and occupational exposure to urothelial carcinogens are the two most well-established risk factors for bladder tumors. Fifty percent of bladder cancer in men and 35% in women is due to cigarette smoking. Cigarette smokers have a 2 to 4 fold increased risk of bladder cancer compared to nonsmokers [7]. The incidence of urinary bladder cancer is directly related to the duration of smoking and the number of cigarettes smoked per day [8]. Sixteen to 24% of all the

bladder cancers are due to occupational exposure to urothelial carcinogens and is the second most important risk factor [9].

Aromatic amines used in the chemical, rubber, and dye industries (eg, benzidine, 2-naphthylamine, 4-aminobiphenyl, o-toluidine, and 4-chloro-o-toluidine) and polycyclic aromatic hydrocarbons (PAHs) used in the aluminum, coal, and roofing industries are all known to be associated with the development of bladder cancer. An increased risk of bladder cancer has also been reported in painters, varnishers, and hairdressers [2].

Chronic urinary tract infections, cyclophosphamide use, and exposure to radiotherapy are the other known causes which are associated with urinary bladder malignancy [10]. Long term irritation of the bladder by indwelling catheters or stones, is related to development of squamous cell carcinoma of the bladder. Schistosomiasis is endemic in Egypt and the Middle East and is considered to be a definite cause of bladder cancer [11].

Inadequate consumption of fruits, vegetables, and certain vitamins may also play a role in the

development of bladder cancer. There is an increased risk of bladder cancer in individuals with a family history of cancer. A population-based, family case control study found an almost 2-fold increased risk among first-degree relatives of patients with urothelial cell carcinoma [12].

Aim of the Study

Is second resection necessary for high grade bladder cancer.

Material and Methods

This is a retrospective study conducted in the Department of Urology, SCB Medical College Cuttack Odisha we retrospectively looked for all ub mass from October 2023 to January 2021. All the patients who were diagnosed to have a space occupying lesion in the bladder and were planned for a transurethral resection of bladder tumor were assessed.

Patients who were detected with UB mass were posted for operation after initial work up and patients who had > 3 cm UB mass were subjected to contrast enhanced CT scan before surgery, and all specimen of UB mass and deep muscle were send separately labelled for histopathological examina-

tion. And a second resection was planned after 2 to 6 weeks of initial procedure A total of 45 patients were diagnosed to have T1G3 disease and of which only 30 had a second resection done. Hence, these 30 patients were taken as the study group and the sample size.

All the T1G3 lesions were included in this study and different variables like the size, multifocality, characteristics of the lesions would be analysed. Descriptive statistics was calculated for all study variables. Prevalence of resection was calculated along with 95% CI. Chi square test was used to assess association between the categorical variables and the T2 upstaging.

Results

There were total 129 cases. There were 112 men (86.8%) and 17 women (13.2%) in this group. most of the patients were in 5th or 6th decade with smoking history or with history of tobacco chewing. (Fig 1). All of them underwent a transurethral resection of bladder tumor and the specimens sent for histopathological examination. Transitional cell carcinoma was diagnosed in 126 patients at different stages and grades (Table 1).

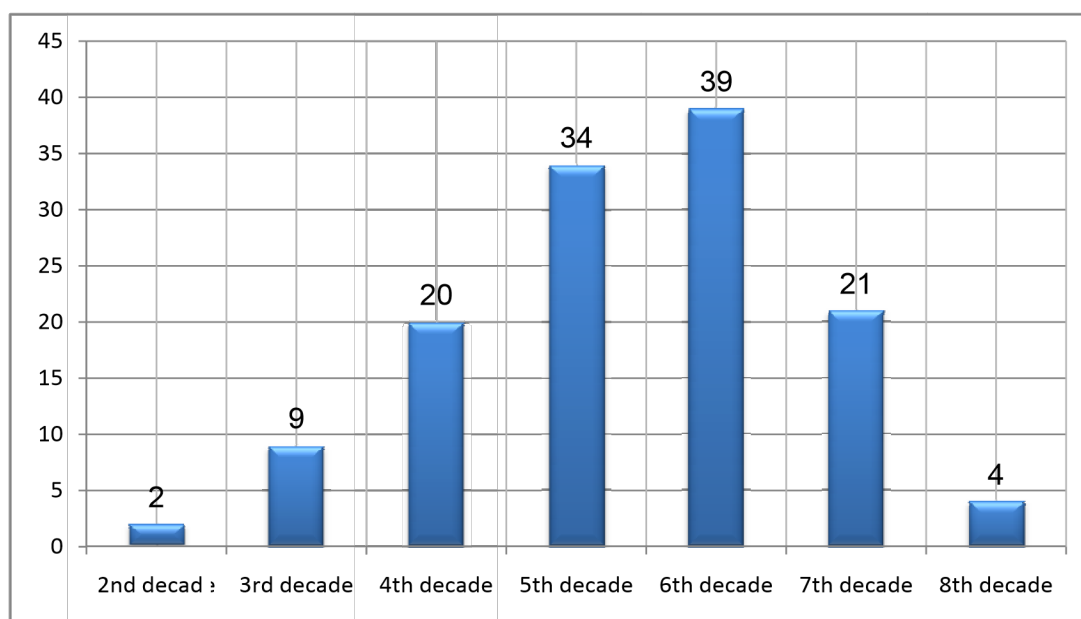


Figure 1: Age group of patients

Table 1: Stage & Grade of TCC

Stage & Grade	No. of patients (%)
TaG1	Nil
TaG2	24
TaG3	15
T1G1	04
T1G2	08
T1G3	45
CIS	03
T2 disease	30

Association of smoking was looked at in these patients with bladder lesions. None of the women had any association with tobacco. Out of the 129 patients with bladder lesions, 69 (53.48%) were regular smokers with variable cigarette pack years.

Of the 129 patients who underwent TURBT, 45 patients had T1G3 TCC bladder. Thirty eight of them were men and 7 were women. The mean age of the T1G3 patients was 57.6 years (37 – 75). Of these 45 patients with T1G3 lesions, 5 patients did not undergo a second resection. Two patients had multiple comorbidities for a second procedure, 3 were not willing for a second procedure. Out of 45, 40 patients had a second resection (Fig 2) and these patients are analyzed as the study group The

40 patients who underwent a second resection in the group were analyzed in detail. The primary resection and the second resection along with variables like the site, size of the lesion, associated CIS, depth of invasion and the characteristics of the primary lesion were studied.

Of the 40 patients who underwent second resection, 35 were men and 5 were women. The mean age was 56.18 years (37 – 75 years). Three of these patients along with T1G3 had associated CIS (secondary CIS). Characteristics of the lesions have been assessed during the primary resection. They were classified as solitary papillary, multiple papillary, sessile and multiple sessile lesions (Table 2).

Table 2: Characteristics of the primary lesion

Characteristics of the lesion	No. of patients (%)
Solitary papillary	25
Multiple papillary	10
Solitary sessile	05
Multiple sessile	Nil

Most of these tumors were located on the lateral wall (Fig 3). When there were multiple tumors, the site of the largest tumor was considered. 21 of these lesions were ≥ 3 cm in size, and 19 were < 3 cm in size (Table 3)

Table 3: Size of the lesions

Size of the lesion	No. of patients (%)
≥ 3 cm	21 (52.5)
< 3 cm	19 (47.5)

Out of these 45 patients, 34 had intravesical mitomycin instilled. It's a protocol that 40mg of mitomycin diluted in 40ml of saline is instilled after the primary resection if it is not contraindicated. At the completion of the primary resections, all of them had the base of the lesion resected separately, and sent for histopathology. All the histopathological specimens had the deep muscle (detrusor) identified and was not involved with tumor. The second resection is usually planned within a span of 2 to 6 weeks. In the study group, the mean time for the second resection is 4

weeks 5 days . None of the patients had any complaints in the intervening period. During the second resection, the scar was identified at the previous resected sites. The majority of the scars were healthy. 15 patients (37.5 %) had a visible lesion seen during the second resection. Five of them were on or around the area of the previous resection. The other one had multiple papillary lesions all over the bladder. Histopathological examination of the second resection revealed tumor in 11 patients (27.5%) (Figure 5).

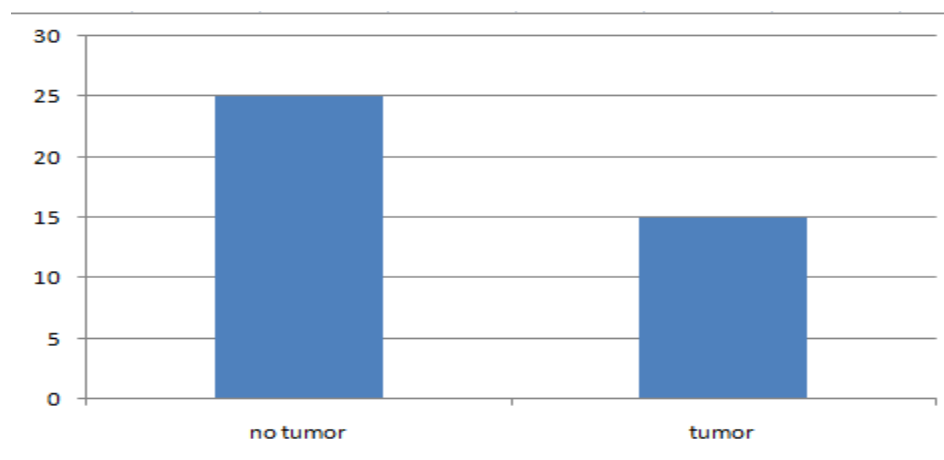


Figure 2: Histopathological examination of the second resection

There is no strong evidence to classify the tumor in the second resection as residual or recurrent tumor. Among the 15 patients with tumor in the second resection, only 3 patient had upstaging to muscle invasive disease (Figure 3).

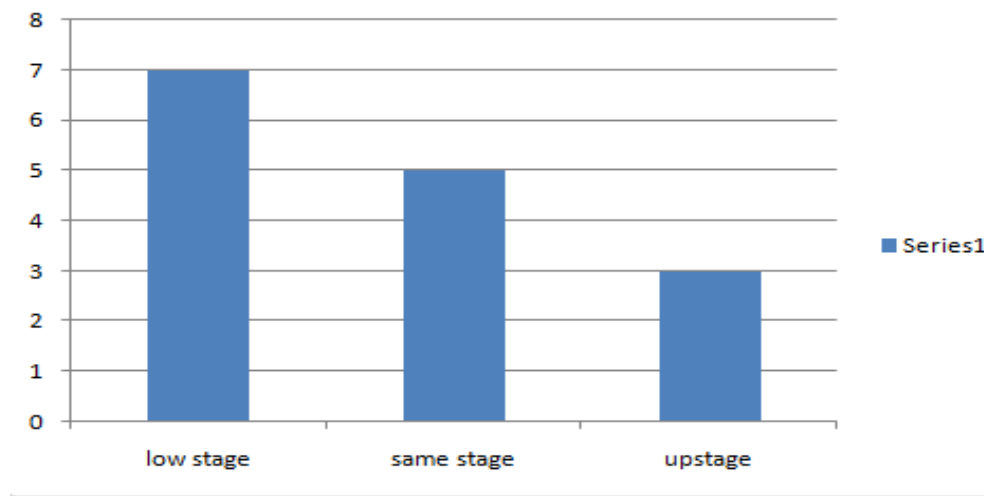


Figure 3: Tumor staging in second resection

Many variables like the primary characteristics of the lesion, the size of the lesion, muscle in the primary resection specimen and associated CIS assessed and correlated with the result of the second resection.

Only 3 patients had a secondary CIS in the primary resected specimen among the study group. On the second resection, two were positive for tumor and one did not have tumor in the second resection. All the primary resections had uninvolved deep muscle in the specimen. When the primary characteristics of the lesions were considered, more than 92% (23/25) of solitary papillary lesions did not have tumor in the second resection. 9 of 10 multiple papillary lesions (90%) and 4 of 5 (80%) sessile lesions had tumor in the second resection (Figure

4). There was a significant association between lesion type and positivity (p=0.04). The chances of tumor positivity in the second resection were maximum in multiple papillary tumors followed by the sessile and least in the solitary papillary lesions.

The relative risk was 4.17 times more in the multiple papillary group when compared to solitary lesions (RR 4.17, CI-95%, 1.01-17.18). The relative risk was 5 times more in the multiple papillary group when compared with the solitary papillary lesions (RR 5.0, CI-95%, 1.1-22.8). The chances of tumor positivity in the second resection in sessile and multiple papillary groups were high and were statistically significant when compared to solitary papillary lesions.

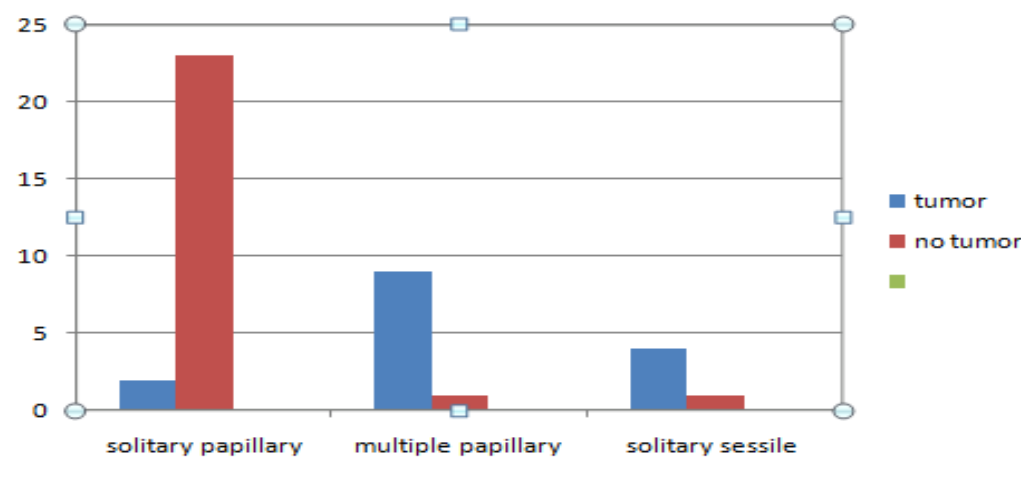


Figure 4: Histopathology in second resection according to lesion characteristics

Tumor size from the primary resection was analyzed with the positivity of the second

resection. There were a total of 21 lesions with more than 3cm in size of which, 12 had tumor

positivity in the second resection (57.14%). Only 3 of the 19 lesions (15.7%) of < 3 cm in size had tumor positivity in the second resection (Figure 8). There was a significant association between the size of the lesion and positivity (p=0.001). The

chances of tumor positivity in the second resection were high with a lesion of more than 3 cm in size. The relative risk was 10 times more in the tumors with size more than 3cm when compared with the lesions of size <3cm. (RR 10, CI-95%, 1.44-69.3).

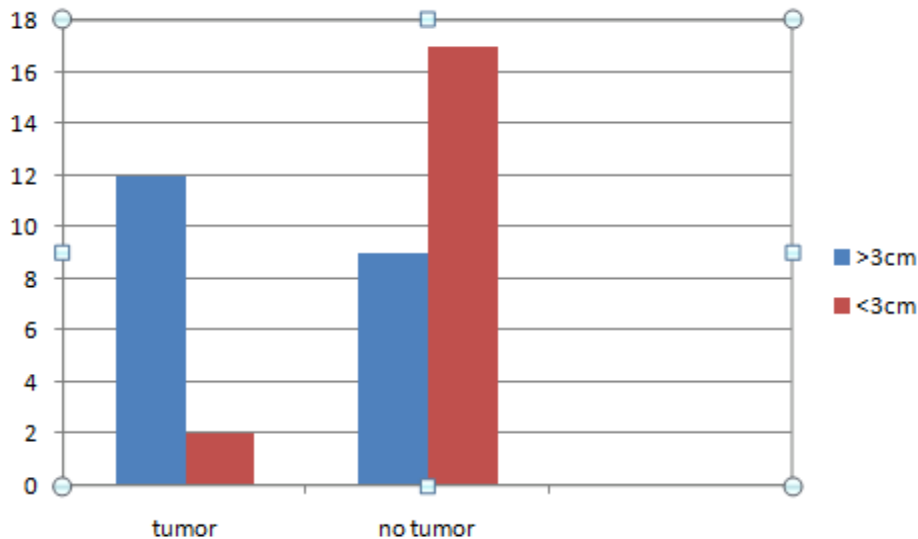


Figure 5: Size of the primary lesion and tumor positivity in second resection

These two variables i.e. the size of the tumor and the characteristics of the primary lesion together were analyzed with the presence or absence of the tumor in the second resection. Of the 15 patients with tumor positivity in the second resection, 11 had ≥3cm primary lesions, and 8 of them were among the multiple papillary lesion (Figure 6). There was 1 lesions from the solitary papillary group and 2 from the sessile group who had >3cm lesion who had tumor positivity in the second resection

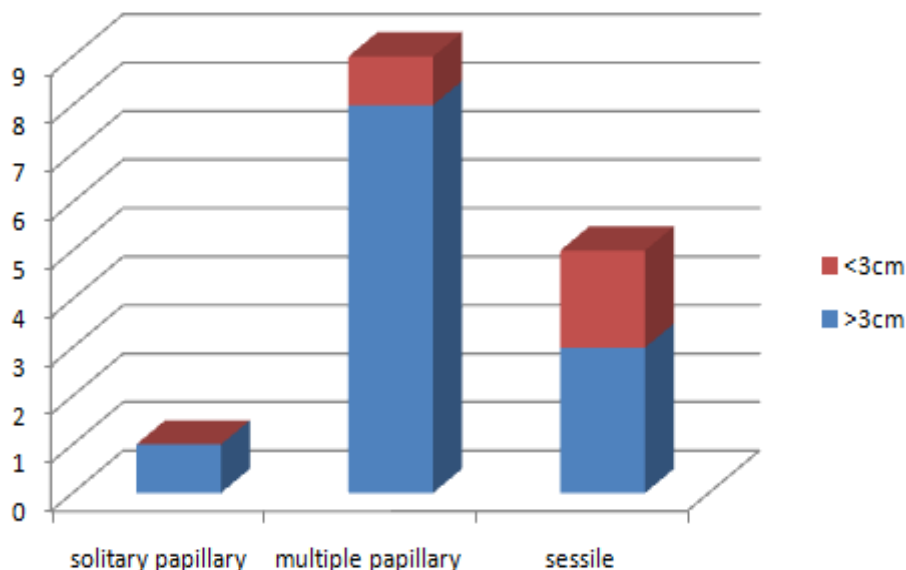


Figure 6: Characteristics and the size of the primary lesion and the tumor positive second resection

Out of the 25 patients who did not have tumor in the second resection, 23 patients were in solitary papillary group, 1 in the multiple papillary and 2 in the sessile group. (Figure 7)

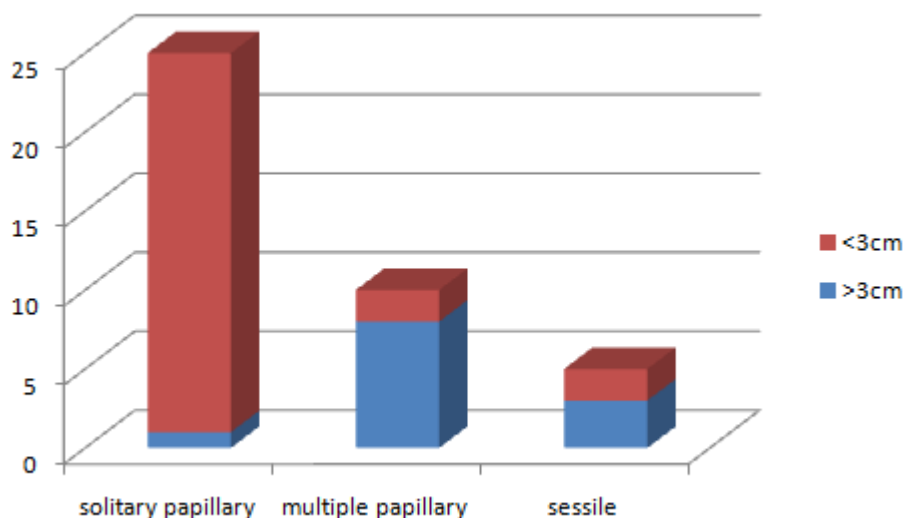


Figure 7: Characteristics & size of the primary lesion and negative second resection

Out of the 15 (37.5%) patients with positive second resection, 7 (46.6%) had low stage disease 5 were solitary papillary and 1 were multiple papillary lesions and one was a sessile lesion. Four of them had lesions <3cm in size. 5 patients (33.3%) had the same stage (T1G3) and 3 patients (20%) had upstaging to T2 disease. Same or higher stage disease in the second TUR is seen in multiple papillary (9 patients) and sessile lesion (4 patient).

Discussion

Bladder cancer is most common in 6th and 7th decade and risk increases with the use of tobacco and cigarette smoking. Bladder cancer is known to occur in the elderly age group, and mostly in the 6th and 7th decade of life. In our study, most of the patients were in the fifth and sixth decade. And most of them had tobacco exposure

TURBT is the 1st step in the management of bladder cancer. It stage and grade the tumor and tell us about whether muscle is present or not and if present whether involved or not. Presence of the uninvolved muscularis propria in the resected specimen is the only identification for a complete resection.

Many Retrospective studies have shown that residual disease can be seen in upto 68% cases due to the fact that no muscle was present in many of the primary TUR specimens. 49% of T1 lesions without muscle in the resected specimen were understated, as compare to muscle 14 % in which muscle were present. Under staging was reported in 64% of T1 tumors when muscle was absent in the specimen versus 30% when it was present. In our entire resections had muscle sample was separately taken at the end of the resection and separately sent for HPE. This can explain why 20

% of our patients were upstaged at the second resection.

Tumor architecture, papillary or sessile, and multifocality of these lesions, and the size of the lesion are important prognostic factors for recurrence and progression of the disease. A solitary papillary lesion is considered to be a good prognostic factor as against multiple papillary and sessile lesions. In our series, among the 25 patients with solitary papillary lesions, two had tumor positive in the second resection and both of them were >3cm lesions.

All the 23 solitary papillary lesions which were <3cm were tumor free in the second resection and 2 of the >3cm lesions were also free of tumor in the second resection. Perhaps this is the subgroup, solitary papillary with <3cm in size lesions, that are least likely to benefit from a second resection. Multiple papillary lesions and the sessile lesions had significant positivity in the second resection. 90 % of the multiple papillary lesions and 80% of the sessile lesions had tumor positivity in the second resection. The relative risk is 4.17 times more in the multiple papillary group when compared to solitary lesions (RR 4.17, CI-95%, 1.01-17.18). The relative risk is 5 times more in the sessile group when compared with the solitary papillary lesions (RR 5.0, CI-95%, 1.1-22.8). The chances of tumor positivity in the second resection in sessile and multiple papillary groups are high and are statistically significant when compared to solitary papillary lesions. The patient who had upstaging of the disease had primary multiple papillary lesions which was >3cm in size.

The size of the primary lesion is one of the useful prognosticating factors in these tumors. Many studies have propagated a lesion <3cm will have very less chances of recurrence and progression

and this is included in the EAU guidelines of non-muscle invasive bladder tumor. In our study, out of 19 patients with a <3cm primary lesion, 17 (93.3%) of them did not have a tumor in second resection. The chances of tumor recurrence in the second resection are high with a tumor of more than 3 cm in size.

The relative risk is 10 times more in the tumors with size more than 3cm when compared with the lesions of size <3cm. (RR 10, CI-95%, 1.44-69.3). The one which had a tumor in the second resection is a multiple papillary lesion which itself carries a poor prognosis even if size is not considered. With consideration of these two good prognostic factors,

i.e size <3cm, and the solitary papillary primary lesion, a select group of patients will not benefit much from the second resection. In our study, all the patients with primary solitary papillary lesion of <3cm size didn't have recurrence. Other factor is the invasion of lamina propria superficial to the muscularis mucosa (T1a) which is considered a good prognostic factor as compared to the lamina propria deeper to muscularis mucosa.

Now the question is that is it really necessary to perform Trans urethral bladder tumor resection in <3 cm and superficial papillary tumor with negative muscle biopsy if intravesical BCG is being planned. Similar studies as shown in table 4.

Table 4:

Study	n	Primary Lesion			Muscle in HPE Primary TURBT	HPE of Second TUR				
		Solitary	Multiple	Sessile		No Tumor	Same tumor	Lower tumor	CIS	Up Stage
Dalbagni et al 2002	15	NS	9	NS	6 (40)	1	13	0	1	0
Schips et al	52	25	14	13	NS	29	9	5	0	9
Herr et al 1999	58	NS	NS	NS	35(63)	13	14	15	0	16
Dalbagni et al 2009	523	NS	NS	NS	242(42)	NS	NS	NS	NS	NS
Our study	27	15	09	03	27(100)	18	03	05	00	01

n = number of patients Percentage in parentheses, NS = not specified

Conclusion

So the conclusion of our study is that 1. do secondary resection in patients with primary characteristic of tumor >3 cm, multiple papillary or sessile, with high grade should receive 2 nd resection 2.

In some subset of patients with < 3 cm of bladder tumor, solitary, with no deep muscle involved 2 nd resection can be safely avoided but this group of patients should be kept in close followup as per the institutional protocol.

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