

**Evaluation of the Role of Early Second
Look Cystoscopy after Complete Resection
of Non-Muscle Invasive Bladder Tumors**

Thesis

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Urology*

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قالوا

لسببائك لا علم لنا
إلا ما علمتنا إنك أنت
العليم العظيم

صدق الله العظيم

سورة البقرة الآية: ٣٢

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List of Abbreviations

Abb.	Full term
<i>AUA</i>	<i>American Urology Association</i>
<i>CIS</i>	<i>Carcinoma in Situ</i>
<i>EUA</i>	<i>European Urology Association</i>
<i>FICBT</i>	<i>First International Consultation on Bladder Cancer</i>
<i>HGUC</i>	<i>High-Grade Urothelial Carcinoma</i>
<i>IQR</i>	<i>Inter-Quartile Range</i>
<i>ISUP</i>	<i>International Society of Urologic Pathology</i>
<i>LGUN</i>	<i>Low-Grade Urothelial Neoplasia</i>
<i>NMIBC</i>	<i>Non Muscle Invasive Bladder Cancer</i>
<i>SPSS</i>	<i>Statistical Package for Social Science</i>
<i>SR</i>	<i>Senior Registrar</i>
<i>TNM</i>	<i>Tumor, Node, Metastasis</i>
<i>TURBT</i>	<i>Transurethral Resection of the Bladder Tumor</i>
<i>UICC</i>	<i>Union of International Cancer Control</i>
<i>WHO</i>	<i>World Health Organization</i>

ABSTRACT

Background: most of the bladder cancers are non-muscle invasion at the time of diagnosis. Non-Muscle invasive tumors confined to the mucosa and invading the lamina propria are classified as stage Ta and T1, respectively, according to the Tumor, Node, Metastasis (TNM) classification system.

Aim of the Study: to determine the efficacy of early second look cystoscopy after complete resection of non-muscle invasive urinary bladder tumors and its impact on subsequent treatment policy.

Patients and Methods: this is a prospective clinical study that was done at Urology Department, Faculty of Medicine, Ain Shams University and Damanhur Oncology Centre. A total of 40 consecutive patients with newly diagnosed non-muscle invasive bladder cancer will be enrolled in this prospective study for second-look cystoscopy with TURBT in two to six weeks after initial TURBT and follow them up in one year.

Results: Single tumor was found in 22 cases (55%), while multiple tumors were recognized in 18 cases (45%) with average sizes ranging from 12mm to 70mm. Low-grade transitional cell carcinoma (TCC) was found in 26 cases (65%), whereas high-grade TCC was found in 14 cases (35%). Stage pTa tumors was found in 12 cases (30%) while 28 cases (70%) have had tumors of pT1 stage. All cases underwent an early second TURBT after (2-6) weeks which has revealed the following data. The majority of cases (28 cases) representing 70% of whole study population were free with no detection of any tumors either residual or recurrence. Residual tumors were detected in six cases (15%) all of which detected in patient with large primary tumor size exceeding 50mm or patients with multiple tumors. Whole detected residual tumors were found at edges of primary tumors ranging 2-5 mm in size which were completely resected and they were of the same stage and grade as the initial tumor.

Conclusion: Our findings in this study support the notion that second-look cystoscopy with or without TURBT is a prerequisite in patients with superficial bladder cancers except for patients with solitary, small low-grade pTa tumors. It is particularly highly recommended for patients with extensive and multiple tumors at the first TURBT

Keywords: Tumor, Node, Metastasis - Transurethral Resection of the Bladder Tumor - Non-Muscle Invasive

INTRODUCTION

Most of the bladder cancers are non-muscle invasion at the time of diagnosis. Non-Muscle invasive tumors confined to the mucosa and invading the lamina propria are classified as stage Ta and T1, respectively, according to the Tumor, Node, Metastasis (TNM) classification system. These tumors can be treated by transurethral resection of the bladder (TURBT), eventually in combination with intravesical instillations and are therefore grouped under the heading of NMIBC for therapeutic purposes. However, molecular biology techniques and clinical experience have demonstrated the highly malignant potential of T1 lesions as compared to Ta lesions. The terms “NMIBC” and “superficial BC” are therefore suboptimal descriptions. However, there is a 50%–70% risk of tumour recurrence, particularly during the first year (*Sylvester et al., 2000*).

This might be related to many factors or theories. Of these the most accepted theory is the recurrence likely due to the persistence or re-growth of residual tumour that has not been adequately resected at initial TURBT. Other related factors that result in the occurrence of new tumours are the progression of a microscopic lesion to a macroscopic one, or the growth of circulating tumour cells at the time of initial TURBT, and/or the aggressive biology of the resected tumour (*Schwaibold, 2000*).

Furthermore, under-staging due to incomplete resection of initial tumour has an impact on the progression rate of 15%–25% of non-muscle invasive bladder cancers. Also, the muscle layer may be missed during the initial resection so, its presence in the second TURBT can change the line of treatment. Consequently, many urologists advocate a second-look check cystoscopy plus/minus TURBT two to six weeks after the initial resection of non-muscle invasive bladder tumours with the aim of improving the treatment outcome (*Jakse et al., 2004*).

Even in patients who are treated appropriately, bladder cancer often recurs. Recurrent cancer can develop anywhere along the urothelium of the kidneys, ureters, prostate, urethra, and bladder. Close follow-up after treatment is required to monitor for recurrence (*Schulze et al., 2007*).

The significant risk of residual tumor after the initial TUR of TaT1 lesions has been demonstrated. Persistent disease after resection of T1 tumors was observed in 33-76% of patient (*Jahson et al., 2005*).

When bladder sparing is a treatment goal, most guidelines recommend re-TUR. According to the recommendations of the AUA guidelines, restaging TURBT provides additional diagnostic and potentially prognostic information for patients with high-grade T1 tumors (*Hall et al., 2007*).

According to the EAU, a repeat TURBT should be performed when the initial resection has been incomplete (eg, cases where multiple and/or large tumours are present) or when the pathologist has reported that the specimen contains no muscle tissue. The EAU also recommends repeat TURBT when a high-grade non-muscle invasive tumor or a T1 tumor was detected at the initial TURB (*Babjuk et al., 2008*).

Currently, there is no consensus on the optimal timing of repeat TURBT. The EAU recommends that repeat TURBT be performed 2–6 weeks after the initial TURBT (*Babjuk et al., 2008*), while the FICBT (*The First International Consultation on Bladder Cancer*) and AUA recommends 1- 4 weeks after the first resection (*Kirkali al, 2005*).

The second TURBT procedure include reassessment of the bladder for detection of any residual tumors after the first resection as well as resection from the primary tumor site (base of the previous resection) for re-staging (*Babjuk et al., 2008*).

AIM OF THE STUDY

The study is aiming to determine the efficacy of early second look cystoscopy after complete resection of non-muscle invasive urinary bladder tumors and its impact on subsequent treatment policy.

REVIEW OF LITERATURE

A. Pathological Review

Accurate pathologic staging requires knowledge of the basic histology of the organ ;

▪ Normal Bladder Urothelium;

The wall of the bladder consists of four layers (figure 1):

○ **Urothelium;**

It is the innermost epithelial lining of the bladder. The urothelium is the site of origin for urothelial carcinomas (*Epestein et al., 1998*).

○ **Lamina propria**

It is separated from the urothelium by a thin basement membrane that is composed of abundant connective tissue containing vascular and neuronal structures (*Epestein et al., 1998*).

○ **Muscularis propria (Detrusor muscle)**

It surrounds the lamina propria and consists of thick, irregularly arranged muscle bundles. In small biopsies, fascicles of muscle in the lamina propria may be confused with the larger smooth muscle bundles of the muscularis propria potentially resulting in an error in tumor staging (*Epestein et al., 1998*).

○ **Adventitia or serosa**

The muscularis propria is separated from the surrounding tissues by a serosal layer (*Epestein et al., 1998*).

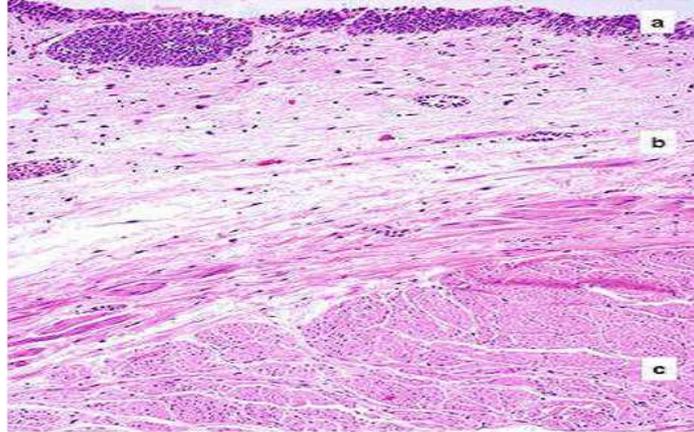


Fig (1): Normal bladder wall.

Transitional Cell (Urothelial) Carcinoma

Urothelial (transitional cell) cancers differ from normal urothelium by having:

- Increased number of epithelial cell layers with papillary foldings of the mucosa.
- Loss of cell polarity.
- Abnormal cell maturation from basal to superficial layers.
- Increased nuclear-cytoplasmic ratio.
- Prominent nucleoli clumping of chromatin.
- Increased number of mitoses (*Epestein et al., 1998*)