

## Comparative analysis between En-bloc resection and transurethral resection of non-muscular-invasive bladder tumors

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### Abstract

**Background:** Transurethral resection of the bladder (TURB) tumor was first described by Stern and McCarthy in 1931, and is still considered the gold standard in diagnosis and treatment of non-muscle-invasive bladder cancer. The quality of TURB affects accuracy of histopathologic evaluation, and subsequently impacts the risk of recurrence and patient outcome. New methods that aim to improve the effectiveness of TURB are reviewed, and recent studies are discussed, including resection methods and image enhancement techniques.

**Material and methods:** Between January 2016 and April 2019, within the Urology Clinic of Nicolae Testemitanu State University of Medicine and Pharmacy 108 patients were surgically treated with bladder tumor pathology. Patients were divided in two groups: En-bloc resection group which includes 51 patients and transurethral resection group with 57 patients, the obtained data were comparatively analyzed.

**Results:** Tumor analysis showed that the majority of the patients' tumors were localized on lateral urinary bladder walls, single bladder tumors were detected in 64 (59%) cases, tumor sizes up to 3 cm were detected in 74 (69%) patients included in the study. Detrusor muscles were detected in 49 (96%) cases of En-bloc group and 45 (79%) cases of TURB group. Most recurrences occurred in patients with high-grade histological result, recurrence rate in En-bloc group occurred in 18% and in TURB group in 37%.

**Conclusions:** The En-bloc resection technique of non-muscle-invasive bladder tumor proved to be a safe and effective method compared to the conventional transurethral resection technique (TURB). This method provides more favorable results for obtaining better quality tumor samples (present of detrusor muscle) that allow to establish correct diagnosis and staging of the disease and reduces the number of recurrences.

**Key words:** En-bloc resection, non-muscle-invasive bladder cancer.

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### Introduction

Papillary 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. Flat, high-grade tumors that are confined to the mucosa are classified as carcinoma in situ (CIS) (Tis) [1]. Transurethral resection of the bladder (TURB) is the method which should be chosen for treatment of these tumors. In some cases, it should be combined with intravesical instillations. For this reason, the therapeutic tactics should be chosen regarding the non-muscle-invasive bladder cancer (NMIBC). It is important that all tumors are characterized according to their stage, grade, and other pathological characteristics, taking into account that the term "Non-muscle-invasive BC" is only a generalized definition.

In NMIBC, 60% of patients present with pTa, 30% with pT1, and 10% with (CIS) lesions [2], T1 tumors are mostly high-grade, and high-grade clinical stage T1 (high-grade T1; formerly T1G3) urothelial carcinoma of the bladder

(UCB) is biologically the most aggressive phenotype among NMIBCs [3].

Transurethral resection of the bladder (TURB) tumor was first described by Stern and McCarthy in 1931, and is still considered the gold standard in diagnosis and treatment of non-muscle-invasive bladder cancer [4].

The quality of TURB affects accuracy of histopathologic evaluation, and subsequently impacts the risk of recurrence and patient's outcome. New methods that aim to improve the effectiveness of TURB are reviewed, and recent studies are discussed, including resection methods and image enhancement techniques. The goals of TURB are to obtain an adequate tissue specimen for determining tumor stage and grade (diagnosis) and to resect all visible lesions (therapeutic). Complete resection including a sample of the underlying *muscularis propria* is recommended by the guidelines of the European Association of Urology (EAU) and American Urological Association (AUA) [5, 6].

It is important to take into account that after TURB recurrences often develop. Another danger represents

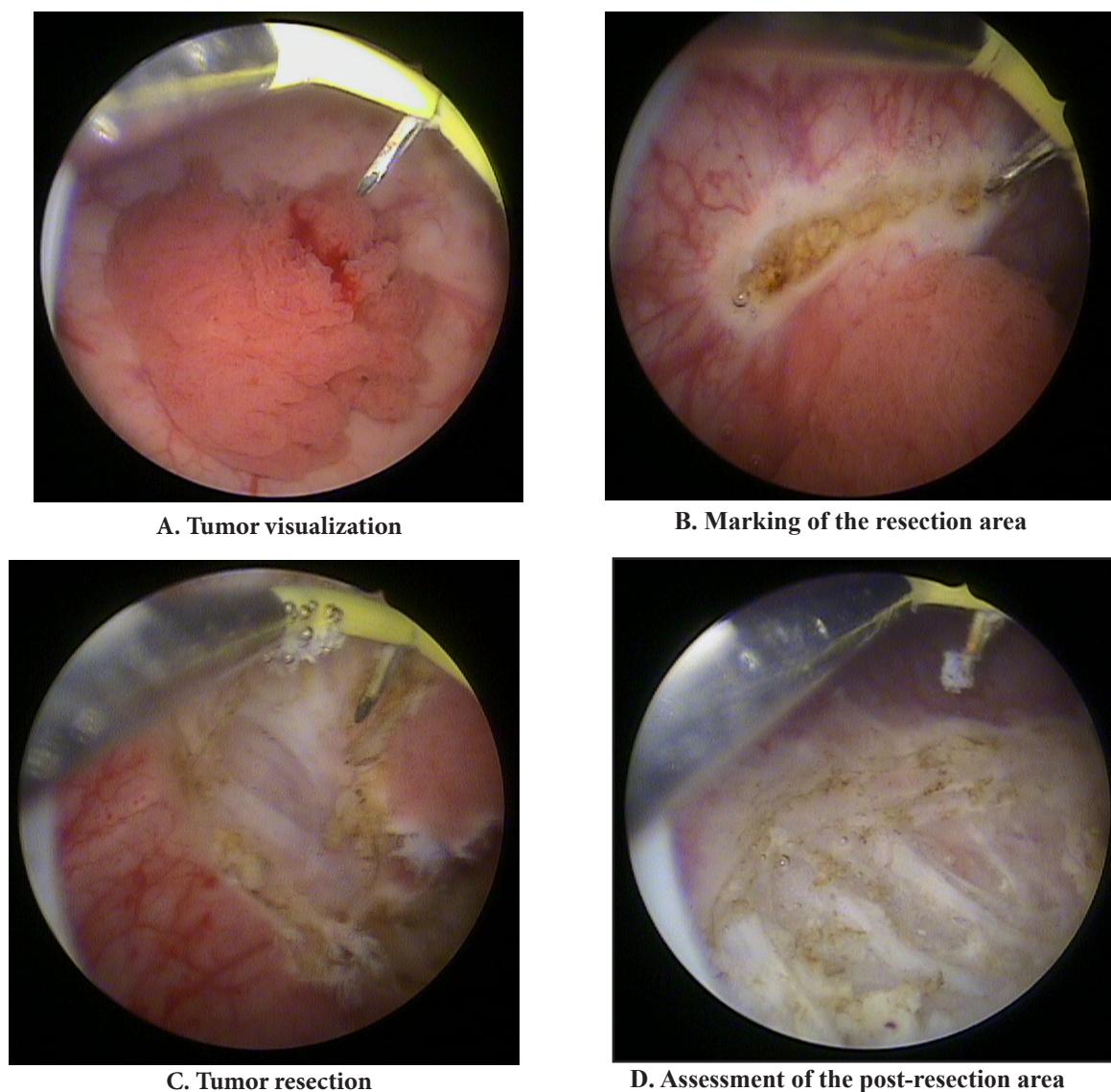


Fig. 1. Operating area

the tumor understaging. To overcome these limitations, an effort has been made to optimize the surgical strategy and introduce technological improvements, including new energy sources and other methods [7]. En-bloc resection is a promising new surgical technique (Figure 1), involving circular incision of the mucosa at a safe distance from the lesion, followed by preparation and removal of the whole tumor, including the underlying detrusor muscle. Many authors believe that this 'no-touch' principle translates into better specimen quality, improved surgical radicality, and a reduced recurrence rate [7].

The aim of the study is to compare the results after En-bloc resection and transurethral resection of non-muscular-invasive urinary bladder tumors.

#### Material and methods

The study was performed between January 2016 and April 2019, within the Department of Urology and Surgical Nephrology of *Nicolae Testemitanu* State University of Me-

dicine and Pharmacy and *Timofei Mosneaga* Republican Clinical Hospital where 108 patients were surgically treated with bladder tumor pathology. A transversal descriptive study was performed. The patients were selected from all amount of bladder tumors patients treated in our department by En-bloc resection and transurethral resection of the bladder tumors, according to the following criteria. The inclusion criteria were: primary non-muscular-invasive bladder cancer, patients over 18-year-old and the Eastern Cooperative Oncology Group (ECOG) score 0-2. The exclusion criteria were identified as follows: other non-urothelial tumors, severe comorbidities, ECOG score  $\geq 3$  and pregnancy. 108 patients were divided in two groups: En-bloc resection group which included 51 patients and transurethral resection group (control group) with 57 patients, the obtained data were comparatively analyzed. Descriptive statistics was applied. In this study the results are demonstrated as absolute and relative values.

## Results

The study was done on 108 patients who were treated endourologically endoscopically by En-bloc resection (51 patients) and TURB (57 patients). No blood transfusion was required and minimal intraoperative hemorrhage during the procedure was observed. These two groups had comparable clinicopathological characteristics: gender, age, tumor grade, tumor multiplicity, tumor size, postoperative complications, histological and oncological outcomes (tab. 1, 2).

Of 108 patients included in the study, according to gender repartition, 89 (82%) were men and 19 (18%) women. The age varied between 26 to 85 years, the mean age was 65.8 years, and the majority of the patients were over 60 – 72 years (66%).

Tumor analysis showed (tab. 1) that the majority of the patients' tumors were localized on lateral urinary bladder walls, single bladder tumors were detected in 64 (59%) cas-

es, and tumor sizes up to 3 cm were detected in 74 (69%) patients included in the study. Of 108 patients 49 (45%) were tobacco users, which is an important risk factor for the development of bladder cancer.

Only grade I and grade II complications occurred in each group (tab. 2), according to the Clavien-Dindo classification for surgical complications. Intraoperative obturator nerve reflex occurred in 10% of En-bloc group and 14% of TURB group. Bladder perforation occurred in 2 patients (4%) in En-bloc group and 3 (5%) in TURB group, which was managed by catheterization for 3-4 days. Histopathological examination showed that fragments of detrusor muscle were detected in both groups: 96% in En-bloc and 79% in TURB, thus we can see benefit of En-bloc tumors samples for an accurate diagnosis.

All interventions were performed as a one-step procedure with patient follow-up during 16-months. Most recur-

**Table 1. Patient and tumor demographics**

Parameters	Categories	En-bloc (n=51)	TURB (n=57)	Total (n=108)
Gender	Men, n (%)	43 (84%)	46 (81%)	89 (82%)
	Women, n (%)	8 (16%)	11 (19%)	19 (18%)
Age, years	Mean age (CI 95%)	65.4 (26-83)	66.3 (28-85)	65.8 (26-85)
Age group	18-30 years, n (%)	3 (6%)	1 (2%)	4 (4%)
	31-60 years, n (%)	16 (31%)	16 (28%)	32 (30%)
	60 years and more, n (%)	32 (63%)	40 (70%)	72 (66%)
Tobacco/Smoking	Yes, n (%)	22 (43%)	27 (48%)	49 (45%)
Tumor size	< 3 cm, n (%)	36 (71%)	38 (67%)	74 (69%)
	≥ 3 cm, n (%)	15 (29%)	19 (33%)	34 (32%)
The number of tumors	Single tumors, n (%)	31 (61%)	33 (58%)	64 (59%)
	≥ 2 tumors, n (%)	20 (39%)	24 (42%)	44 (41%)

Note: CI – Confidence Interval, En-bloc – En-bloc transurethral resection of bladder tumor, TURB – Transurethral resection of bladder tumor.

**Table 2. Surgical and histological outcomes**

Parameters	Categories	En-bloc (n=51)	TURB (n=57)	Total (n=108)
Histopathology grade	Low-grade, n (%)	27 (53%)	32 (56%)	59 (55%)
	High-grade, n (%)	24 (47%)	25 (44%)	49 (45%)
<b>Detrusor muscle</b>	<b>n (%)</b>	<b>49 (96%)</b>	<b>45 (79%)</b>	<b>94 (87%)</b>
TNM	Ta, (Tis), n (%)	32 (63%)	37 (65%)	69 (64%)
	T1, n (%)	19 (37%)	20 (35%)	39 (36%)
<b>Recurrent rate</b>	<b>n (%)</b>	<b>9 (18%)</b>	<b>21 (37%)</b>	<b>30 (28%)</b>
Clavien-Dindo	CD grade I	2 (4%)	3 (5%)	5 (4.5%)
	CD grade II	6 (12%)	7 (12%)	13 (13%)
Complications	ONR, n (%)	5 (10%)	8 (14%)	13 (12%)
	BP, n (%)	2 (4%)	3 (5%)	5 (4.5%)
Operation time	Minutes	34 ± 8	30 ± 11	32

Note: En-bloc – En-bloc transurethral resection of bladder tumor, TURB – Transurethral resection of bladder tumor,

Low-grade – Low-grade papillary urothelial carcinoma, High-grade – High-grade papillary urothelial carcinoma,

Tis (CIS) – Carcinoma in situ, “flat tumor”, Ta – Noninvasive papillary tumor, T1 – Invades subepithelial connective tissue, CD – Clavien-Dindo,

ONR – Obturator nerve reflex, BP – Bladder perforation.



rences occurred in patients with high-grade histological result, recurrence rate in En-bloc group occurred in 18% and in TURB group in 37%.

### Discussion

The initial treatment of all bladder tumors is the gold standard in treatment of non-muscle-invasive bladder cancer which is the accurate transurethral resection of the tumor. Full resection of all visible tumors with the histological examination is the standard care that must be performed [4, 8].

Kawada et al. were the first research group to present a case report on En-bloc resection using a rotational resection technique which remains the method of choice to date [9]. Until now, subsequent research approaches adopted the method described by Kawada et al. or modified it for use with different energy sources (monopolar or bipolar electrical current, Hybrid-Knife, holmium: YAG, thulium: YAG, and KTP laser), although these different energy sources yielded similar results for the evaluated parameters [10].

The specimen is of good quality and well oriented, which makes it easier for the pathologist to assess tumour stage [11]. The En-bloc resection technique seems well tolerated and feasible to use in selected cases. One major goal of En-bloc resection is to improve the quality of endoscopic bladder resection. It is assumed that high-quality resection may decrease the need for second resections and allows for better risk stratification [12]. The presence of detrusor muscle within the specimens serves as a surrogate for resection quality [13-16].

The results of the histopathological examination (tab. 2) according to the WHO/ISUP 2004 and TNM classification in both groups have shown similar results and averaged consist: stage Ta was detected in 69 (64%) cases and stage T1 was in 39 (36%) cases of the patients, Low-grade papillary urothelial carcinoma in 59 (55%) patients and High-grade papillary urothelial carcinoma in 49 (45%) cases of patients included in the research. Detrusor muscles were detected in 49 (96%) cases of En-bloc group and 45 (79%) cases of TURB group.

A complete, high-quality TURB is associated with improved NMIBC outcomes. It was suggested that the quality of tumor resection could be surgeon related [17]. The recurrence rate was so low when TURB was performed by senior surgeons, thus showing a learning curve to perform high quality resections [18].

Recently, Hayashida et al. reported the safety and usefulness of combined endoscopic mucosal resection (EMR) and En-bloc resection in NMIBC patients, where EMR was used to remove the tumor mass that protruded from the mucosa, using a polypectomy snare similar to that used for EMR, while En-bloc resection was used to remove the residual lesion, they demonstrated that EMR combined with En-bloc resection is feasible, safe, and useful for treating patients with NMIBC [13].

According to Clavien-Dindo complication classification

in both groups were registered complications grade I and II (tab. 2). The complications include: obturator nerve reflex, bladder perforation, hematuria of different intensity, urinary tract infection and urinary retention which was managed with standard approach, without additional problems. The tumor recurrence rate shows the benefit of En-bloc resection. In En-bloc group recurrence rate occurred in 18% and in TURB group – in 37%.

Age and grade were the most important prognostic factors for overall survival while the prior disease-recurrence rate and number of tumors were the most important prognostic factors for disease recurrence. Important to mention is that such factors as stage and grade were relevant for disease progression and also for disease-specific survival. T1 high-grade (T1G3) patients do poorly, with one- and 5-year disease-progression rates of 11.4% and 19.8% respectively [19].

### Conclusions

The En-bloc resection technique of non-muscle-invasive bladder tumor proved to be a safe and effective method compared to the conventional transurethral resection technique (TURB). This method provides more favorable results for obtaining better quality tumor samples (present of detrusor muscle) that allow to establish correct diagnosis and staging of the disease and reduces the number of recurrences.

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#### Authors' contribution

IV and AP acquired, interpreted the data, drafted the first manuscript, IV performed most of the analyzed interventions, VG designed the trial and revised the manuscript critically. All the authors revised and approved the final version of the manuscript.

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#### Ethics approval and consent to participate

The research was approved by the Research Ethics Committee of *Nicolae Testemitanu* State University of Medicine and Pharmacy (protocol No 4 of December 16, 2016). Written informed consent was obtained from all participants in the study.

#### Conflict of Interests

The authors have no conflict of interests to declare.

