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Endourological treatment of non-muscular-invasive bladder tumors

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Abstract

Background: Transurethral resection of the bladder is one of the essential methods in the diagnosis, treatment and management of non-muscular-invasive bladder cancer. The purpose of the procedure is to remove completely all visually detected tumors with a following establishment of a very precise histological diagnosis. The aim of the study is to compare the results of conventional transurethral endoscopic treatment and the En-bloc resection method using different types of energy sources in the treatment of bladder tumors.
Material and methods: A total number of 88 patients underwent endourological interventions. Regarding the distribution, 23 patients had conventional transurethral resection, 22 – En-bloc monopolar resection, 21 – En-bloc bipolar resection and 22 – En-bloc with Thu:YAG laser. Clinical data, intraoperative and postoperative data and also the histopathological examination results were compared.
Results: The compared groups were heterogeneous by age, sex, tumor characteristic (size, number, location). No significant differences were observed during the operations, comparing the intraoperative and postoperative complications of the studied groups. The detrusor musculature was detected in 74% of cases after conventional transurethral resection, in 91% of cases of En-bloc monopolar resection, in 95% of cases of En-bloc bipolar resection and in 96% of cases of En-bloc Thu:YAG laser.
Conclusions: The En-bloc resection technique of non-muscular-invasive bladder tumors is a safe and effective method comparing with the conventional transurethral resection; it allows more favorable postoperative results and obtaining better quality tumor samples which allow establishing correct diagnosis of the disease.
Key words: en-bloc resection, laser, non-muscle-invasive bladder cancer.

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Introduction

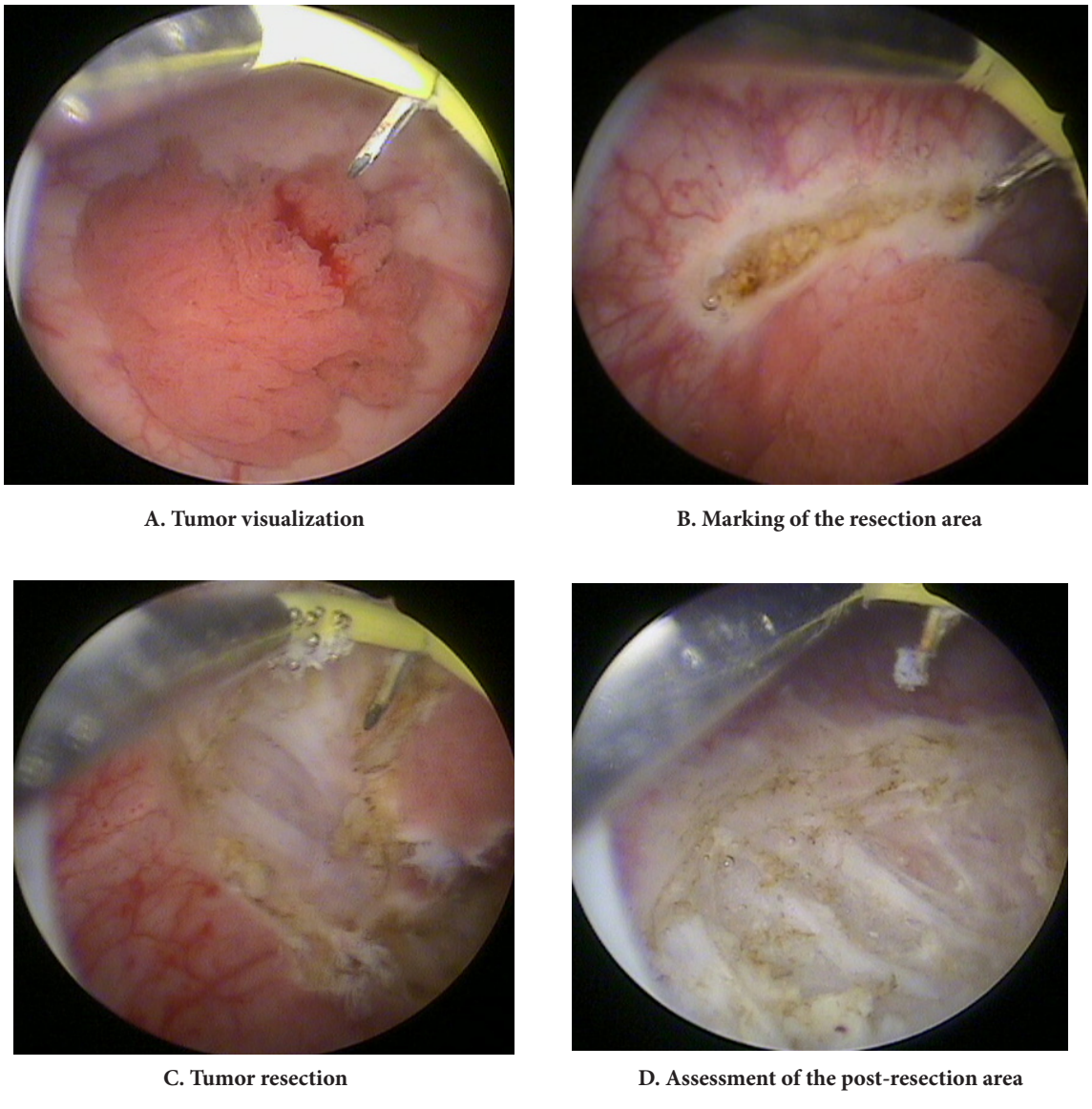
Worldwide bladder cancer is considered to be one of the most common cancers of the urinary tract and is the 11th most common malignancy. It is divided in two types: non-muscle-invasive bladder cancer (NMIBC), accounts about 75% and muscle-invasive bladder cancer (MIBC) about – 25% [1].

Transurethral resection of bladder tumor (TURBT) using white light cystoscopy (WLC) has been the essential procedure in bladder cancer diagnosis, removal, and local staging, since the first endoscopic descriptions of fulguration of papillary bladder tumors in 1910 (Beer E. 1983). The aim of TURBT is the complete resection of the total amount of papillary tumors parallel conducting biopsy of the suspicious flat lesions. For non-muscle-invasive bladder cancer (NMIBC), a high quality TURBT is essential in reducing tumor recurrence and its progression [2].

It must be taken into account the fact that after TURBT recurrences are often developed. Tumor understaging is another danger which should be taken into consideration. In order to overcome these limitations, the surgical strategy was optimized leading to technological improvements, including new energy sources etc. [3]. There is no doubt that the En-bloc resection (fig. 1) represents a promising surgical technique. It involves a 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. A common opinion in the recent literature sources is that this 'no-touch' principle leads to a better specimen quality, as also to an improved surgical radicality, and a reduced recurrence rate [3].

For choosing the treatment strategies an exact pathologic staging of NMIBC is important. For achieving a good prognosis, a complete and correct resection is required [2, 4, 5]. An indicator for a higher risk of residual disease and also for early recurrence is the absence of detrusor muscle in the specimen [6]. The absence of detrusor muscle also represents a poorer surgical experience [6, 7].

The aim of the study is to compare the results of conventional transurethral endoscopic treatment and the En-bloc resection method using different types of energy sources (fig. 2) in the treatment of bladder tumors.



A. Tumor visualization

B. Marking of the resection area

C. Tumor resection

D. Assessment of the post-resection area

Fig. 1. En-bloc resection technique

Material and methods

The study was performed between February 2017 and February 2020, within the Department of Urology and Surgical Nephrology of *Nicolae Testemitanu* State University of Medicine and Pharmacy, in *Timofei Mosneaga* Republican Clinical Hospital. 88 patients were surgically treated with bladder tumor pathology. A transversal descriptive study was performed. The patients were selected from the total amount of bladder tumor patients treated in the department by En-bloc resection using different types of energy sources and transurethral resection of the bladder tumors, according to the following criteria. The inclusion criteria: non-muscular-invasive bladder cancer, patients aging over 18 years old and the Eastern Cooperative Oncology Group (ECOG) score 0-2. The exclusion criteria: other non-urothelial tumors, severe comorbidities, ECOG score ≥ 3 and pregnancy. 88 patients were divided in four groups: 23 patients had conventional transurethral resection (TURBT), 22 – En-bloc monopolar resection, 21 – En-bloc bipolar resection and 22 – En-bloc with Thu:YAG laser resection. The obtained data were comparatively analyzed. Descriptive statistics was applied. The results of this study are demonstrated as absolute and relative values.

Results

The study was done on 88 patients treated endourologically by En-bloc resection and TURB. Intraoperative hemorrhage during the procedure was carried out endoscopic and no blood transfusion was required. These four groups had comparable clinicopathological characteristics: age, gender, tumor size, tumor grade, tumor multiplicity, postoperative complications and histological outcomes (tab. 1, 2).

By gender patients were distributed as follows, from 88 patients included in the study, 73 (83%) were men and 15

Table 1. Patient and tumor demographics

Parameters	Categories	TURBT (n=23)	En-bloc M (n=22)	En-bloc B (n=21)	En-bloc L (n=22)	Total (n=88)
Gender:	Men, n (%)	19 (83%)	18 (82%)	18 (86%)	18 (82%)	73 (83%)
	Women, n (%)	4 (17%)	4 (18%)	3 (14%)	4 (18%)	15 (17%)
Age, years	Mean age (CI 95%)	64,8 (29-82)	65,3 (34-87)	65,6 (27-85)	66,2 (31-83)	65,5 (27-87)
Tobacco/Smoking	Yes, n (%)	12 (52%)	9 (41%)	11 (50%)	11 (50%)	43 (49%)
Tumor size:	< 3 cm, n (%)	18 (78%)	17 (77%)	14 (67%)	16 (73%)	65 (74%)
	≥ 3 cm, n (%)	5 (22%)	5 (23%)	7 (33%)	6 (27%)	23 (26%)
Number of tumors:	Single tumors, n (%)	15 (65%)	14 (64%)	14 (67%)	14 (64%)	57 (65%)
	≥ 2 tumors, n (%)	8 (35%)	8 (36%)	7 (33%)	8 (36%)	31 (35%)

Note: CI – Confidence Interval, TURBT – Transurethral resection of bladder tumor, En-bloc M – En-bloc monopolar transurethral resection of bladder tumor, En-bloc B – En-bloc bipolar transurethral resection of bladder tumor, En-bloc L – En-bloc Thu:YAG laser transurethral resection of bladder tumor.

Table 2. Surgical and histological outcomes

Parameters	Categories	TURBT (n=23)	En-bloc M (n=22)	En-bloc B (n=21)	En-bloc L (n=22)	Total (n=88)
TNM	Ta, (Tis), n (%)	14 (61%)	12 (55%)	12 (57%)	14 (63%)	52 (59%)
	T1, n (%)	9 (39%)	10 (45%)	9 (43%)	8 (37%)	36 (41%)
Detrusor muscle	**n (%)**	**17 (74%)**	**20 (91%)**	**20 (95%)**	**21 (96%)**	**78 (89%)**
Histopathology grade	Low-grade, n (%)	11 (47%)	10 (45%)	10 (48%)	11 (50%)	42 (48%)
	High-grade, n (%)	12 (53%)	12 (55%)	11 (52%)	11 (50%)	46 (52%)
Clavien-Dindo	CD grade I	2 (9%)	3 (14%)	2 (10%)	2 (9%)	9 (10%)
	CD grade II	4 (17%)	4 (18%)	3 (14%)	2 (9%)	13 (15%)
Complications	ONR, n (%)	4 (17%)	3 (14%)	3 (14%)	0 (0%)	10 (11.5%)
	BP, n (%)	3 (13%)	3 (14%)	2 (10%)	1 (5%)	9 (10%)

Note: TURBT – Transurethral resection of bladder tumor, En-bloc M – En-bloc monopolar transurethral resection of bladder tumor, En-bloc B – En-bloc bipolar transurethral resection of bladder tumor, En-bloc L – En-bloc Thu:YAG laser 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.

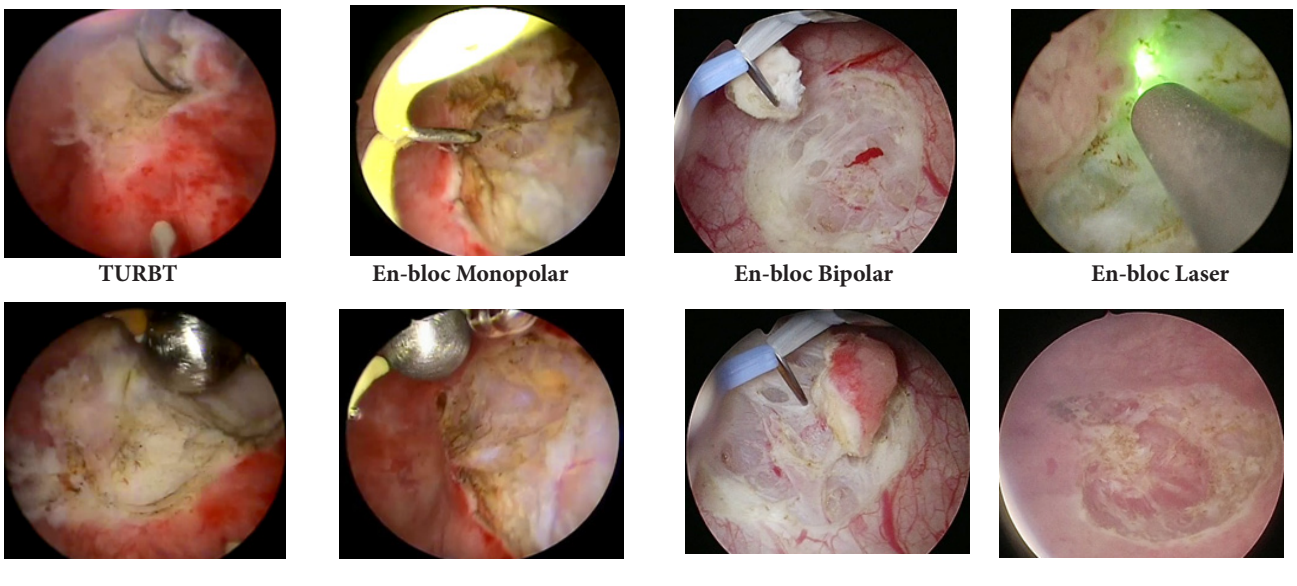


Fig. 2. Resection techniques using different types of energy sources

(17%) – women. The age varies between 27 to 87 years, the mean age encounted 65.5 years, majority of the patients were over 60 – 73 years (69%).

Tumor analysis (tab. 1) showed that in majority of the cases tumors were localized on lateral urinary bladder walls, single bladder tumors were detected in 65% of patients, tumor sizes up to 3 cm were detected in 74% of patients included in the research. An important risk factor for the development of bladder cancer is tobacco abuse which is detected in 49% (from 88 patients) of cases.

According to the Clavien-Dindo classification for surgical complications, only grade I and grade II complications occurred in the study groups (tab. 2). Intraoperative obturator nerve reflex occurred in 17% in the TURB group, 14% in case of En-bloc monopolar resection, 14% – En-bloc bipolar resection and did not occur in En-bloc with Thu:YAG laser. Bladder perforation, hematuria was managed by catheterization for 3-4 days. Histopathological examination showed that fragments of detrusor muscle were detected in 74% of cases after conventional transurethral resection, in 91% of cases of En-bloc monopolar resection, in 95% of cases of En-bloc bipolar resection and in 96% of cases of En-bloc Thu:YAG laser.

Discussion

Since 1997 (Kawada T.) ERBT has been available as a concept for the current-based En-bloc resection. A lot of publications of the last years suggest that transurethral En-bloc resection can potentially change the approach to endoscopic manipulations in the removal, diagnosis, and assessment of NMIBC [8, 9].

Recently an alternative to the standard monopolar TURBT is the bipolar, or plasmakinetic TURBT. There is a couple of advantages comparing them both – the bipolar resection allows the use of isotonic irrigation fluids for decreasing the risk of TUR syndrome. This improves potentially the safety profile comparing with monopolar energy [10]. A lot of studies compared bipolar with monopolar TURBT. It was found that bladder injury decreases and is associated with obturator nerve reflex [11, 12] as also an improved detrusor sampling was observed [13]. The advantages of bipolar resection are limited to safety of the surgical procedure and not to clinical outcomes, the reason is that most of the studies did not find significant effects of bipolar resection on recurrence rates [11, 14].

Pathological interpretation of TURBT samples is a well-known challenge, because the resected tumor fragments are the source for cautery damage, crush artifacts, tangential sections, and lack of spatial orientation which is caused by a random embedding of bladder tissue [15]. En-bloc resection technique improves the pathological assessment due to better preserving tumor architecture and orientation. En-bloc resection can be performed using standard electrocautery, lasers, or water jet combined with monopolar energy [16].

Laser-based En-bloc resection ensures not only a better preservation of tissue orientation, but also reduces surgical morbidity. The reason therefore is the decreasing of bladder perforation through obturator nerve reflex and post-operative bladder irritation [17].

The En-bloc resection has not only the important advantage of conserving the presence of detrusor muscle within specimens, but it also improves the detection of muscularis mucosae or other muscular layers in ERBT specimens. As a consequence these facilitate an accurate T1 substaging. A retrospective comparison between En-bloc resection with the use of green KTP laser and standard monopolar TURB in T1 bladder tumors is reported by Liang et al. [18]. As the primary endpoint the detection of muscularis mucosae in the specimen was regarded. So better outcomes with the En-bloc laser technique (30.7% for En-bloc resection with monopolar electrode versus 11.4% for TURBT) were demonstrated. They also found due to their multivariate logistic regression analysis that the KTP laser resection method is characterized by the presence of muscularis mucosae in specimens. The fact that En-bloc resection leads to a better quality of specimens reveals a more convenient clinical application due to its prognostic possibilities of several pathologic parameters including T1 substaging.

Cheng et al. showed that in spite of the positive surgical margin rate which serves as another indicator of resection quality [19], no significant difference in the positive surgical margin rates between En-bloc resection (98.9%) and TURBT (94.8%) could be demonstrated.

Complications of grades I and II according to Clavien-Dindo complication classification were registered in both groups (tab. 2). The following complications were observed: hematuria of different intensity, obturator nerve reflex, urinary tract infection, bladder perforation and urinary retention which was managed successfully with a standard approach.

The aim of En-bloc resection is not only to improve the resection quality, but also to reach three other goals: to decrease the recurrence rate, to reduce the perioperative complication rates and to decrease the number of repeated resections [15].

Conclusions

The En-bloc resection technique of non-muscular-invasive bladder tumors is a safe and effective method comparing with the conventional transurethral resection. It allows the achievement of more favorable postoperative results and the obtaining of better quality tumor samples. All mentioned above leads finally to the establishment of correct diagnosis of the disease.

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Author's contribution
IV conceptualized the idea, conducted literature review, wrote the manuscript, revised and finalized the text.

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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, 2019).

Conflict of Interest
The author has no conflict of interests to declare.