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Evaluation of the effectiveness of methods of transurethral electroresection of bladder cancer

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Abstract

Aim. To evaluate the treatment outcomes of patients with non-muscle invasive bladder cancer by using transurethral resection alone, transurethral resection combined with electrovaporization and transurethral resection with preliminary tumor fulguration.

Methods. The analysis of the treatment outcomes of 81 patients with non-muscle invasive bladder cancer (Ta–T1N0M0) in the urological clinic of Kazan State Medical University between the period 2000 and 2016 was carried out. The mean age was 63±10.8 years. The patients were divided into 3 groups. The first group included 28 patients who underwent transurethral resection as monotherapy, the second group — 26 patients underwent transurethral resection combined with electrovaporization, and the third group — 27 patients underwent transurethral resection with preliminary tumor fulguration.

Results. In the group of patients who underwent transurethral resection only, recurrences outside the resection zone occurred in 8 (28.57%) patients, recurrences in the resection zone were detected in 6 (21.43%) patients, and tumor progression was diagnosed in 3 (10.71%) patients. In the group of patients who underwent transurethral resection combined with vaporization, recurrences outside the resection zone were diagnosed in 6 (23.08%) patients, recurrences in the resection zone were detected in 4 (15.38%) cases, and tumor progression was detected in 2 (7.69%) patients. In the group of patients who underwent transurethral resection with preliminary tumor fulguration, recurrences outside the resection zone were diagnosed in 4 (14.81%) patients, in the resection zone — in 6 (22.22%) patients, tumor progression in 2 (7.41%) cases.

Conclusion. Transurethral resection alone is not a radical treatment of non-muscle-invasive bladder cancer; transurethral resection combined with vaporization slightly increases the radicality of treatment; transurethral resection with preliminary fulguration reduces the recurrence rate, ensuring the prevention of implant recurrence.

Keywords: bladder cancer, NMIBC, transurethral resection, TUR.

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Background. The main treatment for non-muscle-invasive bladder cancer (NMI BC) is transurethral resection (TUR). TUR is both therapeutic and diagnostic, since it is used to assess both the morphology and degree of muscular invasion of the neoplasm. The main disadvantages of this technique are a high recurrence rate, obturator nerve irritation and, therefore, uncontrolled perforation of the bladder wall. When the tumor is not easily accessible, and has a voluminous exophytic portion, hemostasis could be rather difficult [1–3].

In order to improve the treatment radicality of NMI BC and minimize complications, electrosurgical procedures such as the transurethral electrovaporization (TUEV), fulguration, and bipolar TUR have been introduced into clinical practice.

The use of vaporization in mono-mode is possible if a morphological examination was performed prior to surgery, since it is not possible to obtain material for histological examination during the surgery [4, 5]. For this reason, vaporization is most often preceded by a standard TUR. Some studies state that, this combination can both improve the treatment radicality of BC and minimize complications [6–9].

According to some authors [10–13], fulguration can be used as a monotherapy in patients with minor lesions. The combination of fulguration and TUR is used to prevent implantation recurrence.

Bipolar TUR widens the possibilities and permits operation on patients for whom monopolar TUR is contraindicated. Additionally, the advan-

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Table 1. Patient distribution by gender and age

Groups	Number of patients	Men	Women	Average age, years
TUR	28	20	8	61.75 ± 14.41
TUR + TUEV	26	14	12	63.73 ± 7.78
$p_{1–2}$	—	0.81	0.91	0.61
TUR + F	27	20	7	63.48 ± 10.09
$p_{1–3}$	—	0.22	0.22	0.67

Note: TUR — transurethral resection; TUEV — transurethral electrovaporization; F — fulguration.

Table 2. Localization of non-muscle-invasive (Ta–T1) forms of bladder neoplasms

Surgery	Cervix and trigone of bladder		Lateral walls		Posterior wall		Multiple lesions	
	n	%	n	%	n	%	n	%
TUR	8	28.57	11	39.29	6	21.43	3	10.71
TUR + TUEV	6	23.08	10	34.46	5	19.23	5	19.23
$p_{1–2}$	0.45		0.06		0.20		0.86	
TUR + F	5	18.52	10	37.04	7	25.93	5	18.52
$p_{1–3}$	0.87		0.17		0.39		0.81	

Note: TUR — transurethral resection; TUEV — transurethral electrovaporization; F — fulguration.

Table 3. Morphological characteristics of non-muscle-invasive (Ta–T1) tumors

Surgery	G1		G2		G3		Benign tumor	
	n	%	n	%	n	%	n	%
TUR	7	25	7	25	8	28.57	6	21.43
TUR + TUEV	6	21.43	8	30.77	7	26.92	5	19.23
$p_{1–2}$	0.16		0.46		0.13		0.20	
TUR + F	8	29.63	6	22.22	6	22.22	7	25.93
$p_{1–3}$	0.57		0.24		0.53		0.39	

Note: TUR — transurethral resection; TUEV — transurethral electrovaporization; F — fulguration.

tage of this technique is the absence of obturator nerve irritation [14, 15].

The study aimed at increasing the treatment efficiency of NMI BC patients. Secondly, to evaluate the treatment results of NMI neoplasms of the bladder using TUR, TUR in combination with TUEV (TUR + TUEV), and TUR with preliminary tumor fulguration (TUR + F).

Materials and methods. The treatment results of 81 patients (54 men and 27 women) with NMI BC in the urology clinic of Kazan State Medical University were analyzed. The average age was 63 ± 10.8 years old, with a follow-up period of 5 years.

Patients were separated into three groups. The group 1 included 28 patients who underwent TUR as monotherapy, the group 2 included 26 patients who underwent TUR + TUEV, and the third group included 27 patients who underwent TUR + F of the tumors. The sex and age grouping are displayed in Table 1.

The study was of a retrospective nature. The inclusion criterion was diagnosis of NMI neoplasm (Ta–T1). Detrusor invasion, regional lymph nodes lesions, and distant metastases were the exclusion criteria.

To assess the efficiency of each of the modifications of transurethral electroresection, the study groups included patients who did not undergo additional anti-relapse measures (intraoperative photodynamic or transurethral ultrasound control, intravesical chemotherapy or BCG therapy[1]). Data on the localization of neoplasms and the degree of their morphological differentiation in each of the groups are presented in Tables 2 and 3.

TUR was performed using the classical technique, in the resection mode with 140–200 W, and

[1] BCG therapy involves the use of the Calmette-Guerine vaccine for therapeutic purposes, whose immunostimulating property is applied in modern cancer therapy.

Table 4. Results of transurethral resection in various treatment modifications of non-muscle-invasive bladder cancer (Ta–T1)

Surgery	Recurrence beyond the resection area, %	Recurrence in the resection area, %	Progression, %	Total number of relapses, %	Average relapse-free period, months
TUR	28.57	21.43	10.71	60.71	31.9 ± 26.03
TUR + TUEV	23.08	15.38	7.69	46.15	40.27 ± 24.24
p_{1-2}	0.60	0.53	0.72	0.29	0.81
TUR + F	14.81	22.22	7.41	44.44	40.44 ± 23.79
p_{1-3}	0.05	0.48	0.69	0.19	0.80

Note: TUR — transurethral resection; TUEV — transurethral electrovaporization; F — fulguration.

coagulation with 60–100 W. Vaporization was performed at 200–300 W and 25–400 kHz.

During the case follow-up, all patients underwent standard clinical and laboratory tests (urine cytology, BTA-stat (bladder tumor antigen) test), transabdominal ultrasound examination of the urinary tract, restaging (second-look) cystoscopy after 6 weeks, and then every 3 months during the first year, bi-annually from the second to the fourth year , and then once yearly until a relapse was detected.

Data analysis was performed using Statistica 7.0 and the Microsoft Excel 2003 software package. The survival rate was assessed using the Kaplan–Meier method. Differences in survival rate between the groups were determined using a logarithmic rank test. The significant differences between quantitative group variables were determined through the Student's *t*-test for normally distributed values or by the nonparametric Mann–Whitney test. The analysis of complications and their severity were assessed according to the Clavien–Dindo classification.

Results and discussion. Regarding the mono-TUR patients group, relapses outside the resection area occurred in 8 (28.57%) patients, and relapses in the resection area were detected in 6 (21.43%) follow-up cases (Table 4). This fact indicates insufficient methodic radicality. In 3 (10.71%) patients, the progression of the tumor process to the muscle-invasive form was diagnosed. The total number of relapses in patients with NMI BC after monopolar TUR over a 5-year follow-up period was 17 (60.71%) cases, and the mean relapse-free period in this group was 31.9 months.

The localization based timing occurrence of relapses , as well as their nature (in the area and beyond the area of resection, the tumor progression into a muscle-invasive form) was performed (Fig. 1).

Relapses within the resection area mainly developed in the early post-surgical stages. Their maximum frequency was diagnosed within the first post-surgical year; further relapses did not occur.

Table 5. Complications after monopolar transurethral resection

Complication	Incidence, % (n)	Degree of severity
Exacerbation of chronic pyelonephritis	3.57 (1)	II
Hemorrhage	7.14 (3)	II
	3.57 (1)	III
Perforation of the bladder wall	3.57 (1)	II

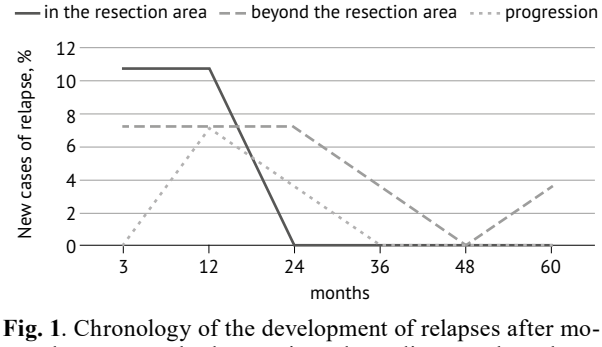

Fig. 1. Chronology of the development of relapses after monopolar transurethral resection, depending on the relapse nature

Progression to the muscle-invasive form was registered in the first two post-surgical years. Relapses outside the resection area occurred with approximately a similar rate during the first three post-surgical years. Such a relapse was not registered in the fourth year., a case was detected by the end of the fifth follow-up year post-monopolar TUR.

Concerning monopolar TUR, complications were detected in 5 (17.86%) out of 28 patients (Table 5). Immediate postoperative hemorrhage found in in 3 (13.63%) resulted from an ineffective intraoperative hemostasis. This was conservatively avoided in two cases, and one patient required a surgical intervention, known as a bladder revision. Bladder wall perforation in 1 (3.57%) case resulted from an obturator nerve irritation and, consequently, an uncontrolled depth of the bladder wall resection. Inflammatory complications in the form of exacerbation of chronic pyelonephritis in 1

Table 6. Complications after TUR and TUR + TUEV

Complication	TUR		TUR + TUEV	
	Incidence, % (n)	Degree of severity	Incidence, % (n)	Degree of severity
Exacerbation of chronic pyelonephritis	3.57 (1)	II	3.85	II
Exacerbation of chronic cystitis, prostatitis	0		7.69	II
Hemorrhage	7.14 (3)	II	0	—
	3.57 (1)	III	0	—
Perforation of the bladder wall	3.57 (1)	II	0	—

Note: TUR — transurethral resection; TUEV — transurethral electrovaporization.

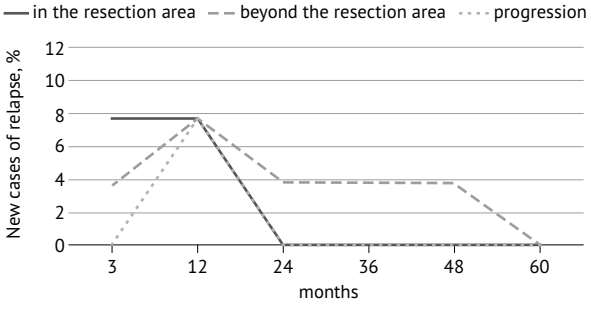

Fig. 2. Chronology of relapse development after transurethral resection associated with transurethral electrovaporization in non-muscle-invasive bladder cancer, relative to the relapse nature

(3.57%) patient resulted from the presence of concomitant chronic urinary tract infection.

Relapses within the resection area mainly developed in the early post-surgical stages. Their maximum frequency was diagnosed within the first post-surgical year; further relapses did not occur. Progression to the muscle-invasive form was registered in the first two post-surgical years. Relapses outside the resection area occurred with approximately a similar rate during the first three post-surgical years. Such a relapse was not registered in the fourth year., a case was detected by the end of the fifth follow-up year post-monopolar TUR.

The results obtained clearly demonstrate that monopolar TUR in mono-mode is a non-radical method for treating NMI forms of bladder neoplasms. The high frequency of relapses both within and beyond the resection area, as well as the early periods of their occurrence, required the search for new methods to improve treatment radicality.

To improve efficiency of TUR, 26 patients underwent monopolar TUR + TUEV. In this group, relapses outside the resection area were diagnosed in 6 (23.08%) patients; relapses within the resection area were detected in 4 (15.38%) cases, occurring during the first follow-up postoperative year (Table 4). The cancerous progression occurring

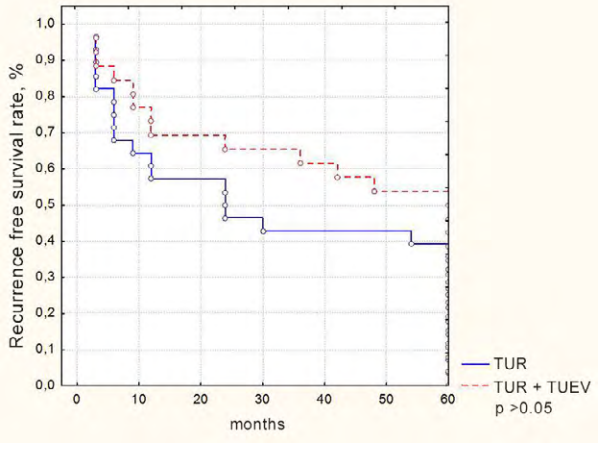

Fig. 3. Five-year survival post transurethral resection (TUR) and transurethral resection with transurethral electrovaporization (TUR + TUEV)

during the first two years follow-up years was diagnosed in 2 (7.69%) cases (Fig. 2). Thus, the total number of relapses was revealed in 17 (46.15%) patients, and the mean relapse-free period was 40.27 months. Relative to the monopolar TUR, there were some positive changes over time in frequency reduction of relapses (Table 4).

The disease-free 5-year survival rate was 53.85% and was higher compared to the monopolar TUR group, where this indicator was 39.29% ($p = 0.18$) (Fig. 3).

An analysis of the TUR + TUEV complications revealed that TUEV prevents hemorrhagic and traumatic complications, since such a combination provides adequate hemostasis and prevents uncontrolled bladder wall perforation. There was a decrease in the number of infectious and inflammatory complications (acute serous pyelonephritis in one patient, exacerbation of cystitis in two patients) caused by resection in the area of the ureteral orifice and insufficient duration of anti-inflammatory therapy (before the postoperative eschar removal) (Table 6). Adjustment of conserva-

Table 7. Complications after transurethral resection (TUR) and TUR with fulguration (TUR + F)

Complication	TUR		TUR + F	
	Incidence, % (n)	Degree of severity	Incidence, % (n)	Degree of severity
Exacerbation of chronic pyelonephritis	3.57 (1)	II	3.7 (1)	II
Hemorrhage	7.14 (3)	II	3.7 (1)	II
	3.57 (1)	III	0	—

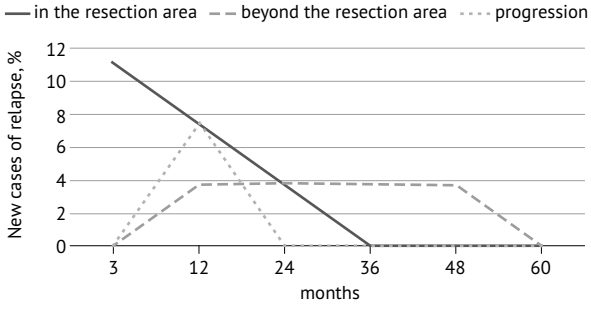

Fig. 4. Chronology of the development of relapses after transurethral resection with fulguration, depending on the relapse nature

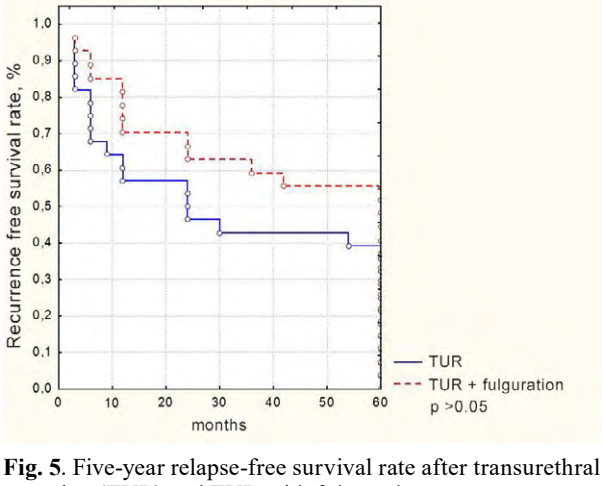

Fig. 5. Five-year relapse-free survival rate after transurethral resection (TUR) and TUR with fulguration

tive antibiotic therapy enabled to a decline in every inflammatory process.

Evaluation of the treatment results of patients with NMI forms of bladder neoplasms by the TUR + TUEV method enables an improvement in surgical radicality, avoiding hemorrhagic and traumatic complications by 14.6%. TUR + TUEV affects the duration of the mean relapse-free period to a lesser extent (8.4 months).

In order to prevent implantation recurrences, 27 patients underwent TUR + F of the tumor. In this group, relapses outside the resection area were diagnosed in 4 (14.81%) patients (Table 4). These results differed significantly from those in the post-TUR monotherapy group ($p = 0.051$). This could probably be due to the appearance of a relapse outside the resection area that occurs in the first postoperative year due to the implantation factor (Fig. 4). The use of fulguration enabled a reduction the number of such relapses by 1.9 folds (up to 14.81%) and increased the operative radicality relative to the same indicator in the mono-TUR group.

The relapse-free 5-year survival rate in this group amounted to 55.56% (Fig. 5), which was 16.27% higher than in the mono-TUR control group ($p = 0.21$).

The number of complications after TUR + F was minimal; these included acute pyelonephritis in 3.7%, and hemorrhage in 3.7% (Table 7). Inflammatory complications arose in association with exacerbation of chronic urinary tract infection in the preoperative period and unsatisfactory drainage function of the urethral catheter in the early postoperative period. The hemorrhage was caused by a large wound surface and insufficient intraoperative hemostasis. A few complications that arose in the immediate postoperative period were stopped by conservative measures.

The results obtained enable to conclude that TUR + F contributes to a decrease in the relapse frequency compared to monopolar TUR, regardless of the size of the tumor and the degree of morphological differentiation.

CONCLUSIONS

1. Monopolar transurethral resection as monotherapy is a non-radical method of treatment of non-muscle-invasive bladder cancer, which requires additional procedures to improve surgical radicality and prevent complications.

2. Transurethral resection with electrovaporization increases the radicality of treatment by 14.56%, provides better hemostasis, and lowers the incidence of traumatic complications.

3. Preliminary electrofulguration of the tumor before transurethral resection raises the surgery radicality by 16.27% due to prevention of implantation recurrence.

4. To prevent complications, it is necessary to strictly adhere to the surgical technique, taking into account the indications and contraindications

for each method, as well as ensure the antibacterial therapy and drainage of the urinary tract in the postoperative period.

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