

DOI: <https://doi.org/10.17816/uroved632520>

Evaluation of the clinical effectiveness of transurethral bipolar surgery and laser technologies in treatment of patients with non-muscle-invasive bladder cancer

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ABSTRACT

BACKGROUND: Bladder cancer is the most common urinary tract cancer. Transurethral resection of the bladder wall tumor is the gold standard for non-muscle-invasive bladder cancer. In recent years, laser technologies have been actively implemented into clinical practice, including the surgical treatment of bladder cancer, but there are still many questions regarding their use.

AIM: To evaluate the efficacy and safety of bladder wall tumor resection followed by neodymium (Nd:YAG) laser ablation of the tumor.

MATERIALS AND METHODS: Surgical treatment outcomes in 97 patients with non-muscle-invasive bladder cancer were analyzed for the period between 2012 and 2023. Group 1 ($n = 49$) underwent classical transurethral resection of the bladder wall. Group 2 ($n = 47$) underwent the same procedure followed by Nd:YAG laser ablation of the tumor bed. Treatment outcomes were evaluated at 3, 6, and 12 months after surgery.

RESULTS: Analysis of complications using the Clavien–Dindo classification system showed a more favorable postoperative course in group 2. Within 1 year after surgery, the rate of bladder cancer recurrence was significantly lower in group 2 compared to group 1, with 4 and 13 cases, respectively ($p < 0.05$). In addition, no patient in group 2 had a recurrence in the area of the resected tumor bed, whereas 9 patients in group 1 had such recurrence during the specified period.

CONCLUSIONS: The study demonstrates the potential of using laser technologies in the treatment of bladder cancer. Its clinical implementation will facilitate personalized surgical treatment options for patients with urological cancers and reduce the risk of tumor recurrence.

Keywords: bladder cancer; non-muscle-invasive bladder cancer; transurethral resection of the bladder wall tumor; neodymium laser; Nd:YAG laser ablation.

To cite this article

Teodorovich OV, Gameeva EV, Suleymanov SI, Shatokhin MN, Borisenko GG, Babkin AS. Evaluation of the clinical effectiveness of transurethral bipolar surgery and laser technologies in treatment of patients with non-muscle-invasive bladder cancer. *Urology reports (St. Petersburg)*. 2024;14(4):373–380. DOI: <https://doi.org/10.17816/uroved632520>

Received: 23.05.2024

Accepted: 10.11.2024

Published online: 30.12.2024

DOI: <https://doi.org/10.17816/uroved632520>

Оценка клинической эффективности трансуретральной биполярной хирургии и лазерных технологий в лечении пациентов с немышечно-инвазивным раком мочевого пузыря

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АННОТАЦИЯ

Актуальность. Рак мочевого пузыря — наиболее распространенная злокачественная опухоль мочевыводящих путей. Золотым стандартом лечения немышечно-инвазивного рака мочевого пузыря является трансуретральная резекция стенки мочевого пузыря с опухолью. В последние годы отмечается активное внедрение в клиническую практику лазерных технологий, в том числе при хирургическом лечении рака мочевого пузыря, однако многие вопросы их применения остаются неясными.

Цель — оценить эффективность и безопасность резекции стенки мочевого пузыря с опухолью с последующей лазерной абляцией опухоли неодимовым лазером (Nd:YAG).

Материалы и методы. Выполнен анализ результатов хирургического лечения 97 больных немышечно-инвазивным раком мочевого пузыря, проведенного в период с 2012 по 2023 г. Пациентам группы 1 ($n = 49$) выполняли классическую трансуретральную резекцию стенки мочевого пузыря, в группе 2 ($n = 47$) проводили такую же операцию, но с последующей Nd:YAG-лазерной абляцией ложа опухоли. Результаты лечения оценивали через 3, 6 и 12 мес. после операции.

Результаты. Проведенный анализ осложнений по классификации Clavien–Dindo показал более благоприятное послеоперационное течение у пациентов группы 2. В течение 1 года после операции рецидивы рака мочевого пузыря в этой группе отмечались достоверно реже, чем в первой, соответственно в 4 и 13 случаях ($p < 0,05$). При этом ни у одного пациента не выявлено рецидивов в области ложа резецированной опухоли, тогда как в группе 1 такие рецидивы за указанный период обнаружены у 9 человек.

Выводы. Результаты исследования указывают на перспективность применения лазерных технологий в лечении рака мочевого пузыря. Их внедрение в клиническую практику позволит персонифицировать хирургические методы лечения онкоурологических больных и снизить риск рецидивирования опухолей.

Ключевые слова: рак мочевого пузыря; немышечно-инвазивный рак мочевого пузыря; трансуретральная резекция стенки мочевого пузыря с опухолью; неодимовый лазер; Nd:YAG-лазерная абляция.

Как цитировать

Теодорович О.В., Гамеева Е.В., Сулейманов С.И., Шатохин М.Н., Борисенко Г.Г., Бабкин А.С. Оценка клинической эффективности трансуретральной биполярной хирургии и лазерных технологий в лечении пациентов с немышечно-инвазивным раком мочевого пузыря // Урологические ведомости. 2024. Т. 14, № 4. С. 373–380. DOI: <https://doi.org/10.17816/uroved632520>

BACKGROUND

Bladder cancer (BC) is the most common malignant tumor of the urinary tract, ranking tenth in global cancer prevalence. The BC incidence continues to rise worldwide, particularly in developed countries [1]. In the structure of cancer incidence in Russia, BC ranks ninth and sixteenth in men and women, respectively. The incidence rate is 11.58 per 100,000 men and 2.05 per 100,000 women, with mortality rates of 3.8 and 0.52, respectively. The average age of patients diagnosed with BC in Russia is 67.2 years for men and 69.7 years for women [2]. The higher incidence in men is linked to the wider prevalence of smoking and occupations involving exposure to carcinogenic substances. Both men and women who smoke tend to develop BC about 6 years earlier than non-smokers [3, 4].

BC covers a wide range of malignant tumors, from low-risk to high-risk, with significant differences in prognosis and survival depending on the stage, histological subtype, and degree of differentiation, as well as recurrence. Two main categories of BC are distinguished based on the depth of invasion into the bladder wall: non-muscle-invasive bladder cancer (NMIBC) and muscle-invasive bladder cancer (MIBC) [5]. NMIBC includes cases where tumors are confined to the mucosa and submucosa of the bladder wall. Approximately 75% of patients with BC present with non-muscle-invasive cancer (70% at stage Ta, 20% at stage T1, and 10% with carcinoma *in situ*). In other patients, the tumor invades the detrusor muscle (stage T2), the perivesical tissue (stage T3), and surrounding organs (stage T4) [6].

It is advisable that the treatment of NMIBC start with transurethral resection of the bladder wall tumor (TURBT) [7]. At stages Ta and T1, tumors with a predominantly papillary growth pattern are most commonly found. The standard treatment for Ta and T1 papillary bladder tumors is complete transurethral resection, including part of the underlying muscular layer. During TURBT, all visible tumors are removed, which is necessary for accurate staging (pT). A second-look TURBT is recommended in cases of incomplete initial resection (absence of muscle tissue in the sample), for all T1 tumors, and for all high-grade tumors (HG/G3). Second-look TURBT should be performed within 2–6 weeks after the initial operation [8]. Regardless of risk group, all patients should receive immediate single-dose intravesical chemotherapy within 6 hours after TUR.

Alongside the active development of evidence-based medicine, recent years have seen a trend toward modification of surgical techniques, including transurethral resection. In particular, the en bloc TURBT technique, in which the tumor is removed as a single block, has gained widespread use among surgeons. This technique offers several advantages over traditional TURBT, such

as better-quality pathological samples, reduced recurrence rates, and fewer complications [9].

The clinician's desire to minimize complication and recurrence rates, combined with the progressive development of medical technologies, has led to the adoption of laser technologies in the treatment of NMIBC. Compared to electrocoagulation, the use of lasers reduces the frequency of reflexes of the obturator nerve, resulting in fewer complications and providing higher-quality material for pathological examination [10]. Transurethral thulium laser resection of the bladder wall tumor, along with other laser techniques, has become one of the most popular surgical interventions for BC [11]. A study by Teodorovich et al. [12] described the use of a neodymium laser (Nd:YAG laser) for tumor bed ablation following classical transurethral resection, which demonstrated favorable outcomes in terms of recurrence and complications.

However, although studies on the surgical treatment of NMIBC are largely focused on standardization of the surgical procedure stages, the search for the optimal surgical method in multi-specialty hospital setting remains relevant.

The study aimed to clinically evaluate the results of classical TURBT compared with TURBT followed by Nd:YAG laser ablation of the tumor bed in patients with non-muscle-invasive bladder cancer.

MATERIALS AND METHODS

The study was based on the results of surgical treatment of 97 patients with NMIBC, who underwent TURBT at the clinical bases of the Department of Endoscopic Urology of the Russian Medical Academy of Continuing Professional Education, as well as in the urological hospitals of the following institutions: Central Clinical Hospital Russian Railways Medicine, Central Clinical Hospital of Civil Aviation, Medical-Sanitary Unit of the Ministry of Internal Affairs of Russia for Moscow, and City Clinical Hospital No. 13 of the Moscow City Health Department, between 2012 and 2023.

The study design involved three stages. The first stage focused on evaluating the informativeness of modern diagnostic methods for BC, allowing for the determination of the feasibility of surgical treatment. The second stage included a comprehensive assessment of intra- and post-operative complications associated with the transurethral interventions performed using the mentioned methods. The third stage was dedicated to the analysis of long-term treatment outcomes following the application of these techniques, specifically assessment of recurrence-free survival after surgery.

All patients were stratified into two groups based on the surgical intervention method. The first group included patients who underwent classical bipolar TURBT. The second group included patients who underwent the

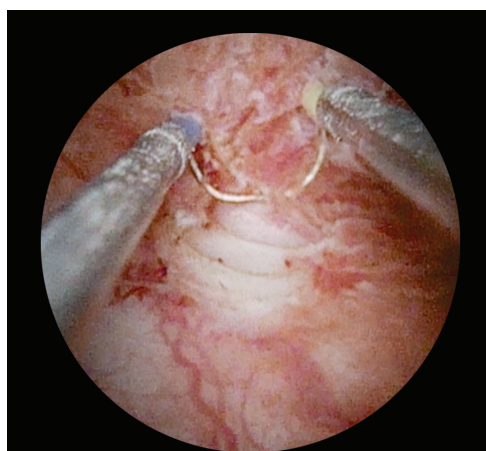


Fig. 1. Transurethral resection of the bladder wall tumor

Рис. 1. Этап трансуретральной резекции стенки мочевого пузыря с опухолью

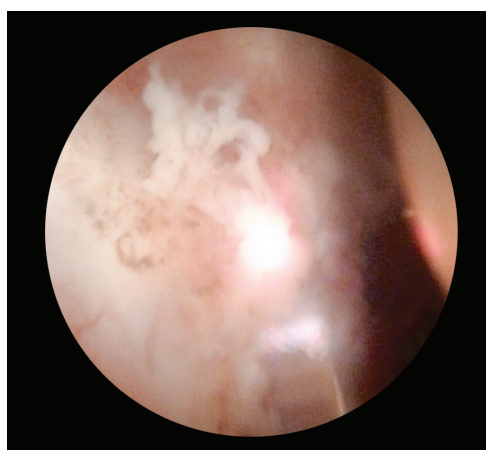


Fig. 2. Nd:YAG laser ablation of the bladder tumor bed

Рис. 2. Этап Nd:YAG-лазерной абляции ложа опухоли мочевого пузыря

same procedure followed by Nd:YAG laser ablation of the tumor bed.

Inclusion criteria: patients aged 30 to 75 years, with histologically confirmed BC, either primary or recurrent NMIBC, ranging from 1 to 3 cm in size at stages pTa–T1. Exclusion criteria: patients with multiple bladder lesions, tumors extending to the bladder neck, ureter, prostatic urethra, or patients with benign bladder lesions as determined by histology. Diagnostic procedures for bladder tumors included urinalysis, ultrasound of the bladder and kidneys, pelvic magnetic resonance imaging (MRI), contrast-enhanced pelvic computed tomography (CT), and diagnostic cystoscopy. In some cases, patients were admitted to the urology department via emergency medical services with an initial diagnosis of ICD10 R31 (unspecified hematuria). Following the confirmation of a volumetric lesion in the bladder, TURBT was performed, followed by histological verification.

Group 1 consisted of 49 patients (mean age 62.4 ± 9.0 years), who underwent classical TURBT, followed by intravesical chemotherapy. Group 2 included 48 patients (mean age 57.7 ± 11.2 years), who underwent TURBT followed by Nd:YAG laser ablation of the tumor bed and postoperative intravesical chemotherapy. All surgeries were performed under spinal anesthesia. The surgical procedure included diagnostic urethrocystoscopy to assess the condition of the urethra, bladder neck, bladder mucosa, the location of the ureteral orifices, and the number and size of lesions. The next step was bladder wall tumor resection down to the muscular layer, using either en bloc resection or standard TURBT with various energy sources (Fig. 1). The final step involved hemostasis using various energy sources (bipolar, laser), and tumor bed ablation with Nd:YAG laser in group 2 patients (Fig. 2).

After surgery, a 3-way Foley urethral catheter (18 Ch) was placed for 1 to 4 days. Within one hour after surgery,

all patients received intravesical chemotherapy with 50 mg of doxorubicin; the exposure lasted 2 hours. Different laser and surgical equipment was used in different medical institutions, including the Auriga XL 50W laser system, FiberLase U3 laser system, AUTOCON III 400 high-frequency generator, Karl Storz bipolar resectoscope, and the Lazurit Nd:YAG laser complex. Endoscopic evaluation of the surgical treatment effectiveness was carried out at the clinical base of the Department of Endoscopic Urology at Central Clinical Hospital Russian Railways Medicine at months 3, 6, and 12 after surgery.

The statistical analysis of the data was performed using the Statistica v. 10.0 software package. Arithmetic mean (*M*) and standard deviation (σ) were used to describe quantitative variables. Statistical significance of the frequency difference was assessed using the chi-squared test (χ^2). The differences were considered statistically significant at $p < 0.05$.

RESULTS

The characteristics of the operated patients in both groups are presented in Table 1.

The average duration of surgery in group 1 patients, who underwent only TURBT, was 20.5 ± 5 min, whereas in group 2 (TURBT followed by laser ablation of the tumor bed) it was 27 ± 6 min ($p < 0.05$). The average length of hospital stay after surgery ranged from 2 to 6 days. The duration of hospitalization in group 2 was slightly shorter (3.2 ± 1.4 days) compared with group 1 (3.6 ± 1.5 days). Group 2 patients had a shorter duration of urethral

catheter placement, which is likely due to better hemostasis during tumor bed treatment.

Early postoperative complications in the operated patients were analyzed. Grade I complications according to the Clavien–Dindo classification (irritative and hemorrhagic symptoms associated with the placement of drainage, a 3-way Foley catheter) were noted in 7 (7.2%) patients; Grade II complications (clinically significant macrohematuria requiring active hemostatic therapy) were observed in 10 (10.3%) patients, with 8 (8.2%) cases occurring after classical TURBT and 2 (2%) after Nd:YAG laser ablation. No Grade III, IV, or V complications were noted in this study.

The patients were monitored for 1 year after surgery, with cystoscopy performed at months 3, 6, and 12 post-surgery. In group 1, 13 recurrences of bladder cancer were observed during the specified period (Table 2), 9 of which were located at the site of the primary tumor bed. In group 2, 4 recurrences were detected, with none occurring at the site of the primary tumor. Within 12 months after surgery, the recurrence rate in group 2 was significantly lower than in group 1 ($\chi^2 = 5.5$, $p < 0.05$).

DISCUSSION

In recent years, there has been a trend toward a steady increase in the incidence of BC among the most socially active population groups. This is largely associated with an unhealthy lifestyle, poor nutrition, harmful habits such as smoking, adverse working conditions, genetic predisposition, and urinary tract infections. All of the above highlights the socio-economic significance of

Table 1. Characteristics of patients in groups 1 and 2 ($n = 97$)

Таблица 1. Характеристика пациентов групп 1 и 2 ($n = 97$)

Group	Age, years ($M \pm \sigma$)	Sex		Hospitalization	
		Male	Female	Planned, n	Emergency, n
Group 1 ($n = 49$)	62.4 ± 9.0	36 (73.5%)	13 (26.5%)	33 (67.3%)	16 (32.7%)
Group 2 ($n = 48$)	57.7 ± 11.23	37 (77.1%)	11 (22.9%)	28 (58.3%)	20 (41.7%)

Note. No statistically significant differences were found between groups ($p > 0.05$).
Примечание. Статистически значимых различий между группами не выявлено ($p > 0,05$).

Table 2. Recurrence of bladder cancer in groups 1 and 2 within 12 months after surgery ($n = 97$)

Таблица 2. Рецидивы рака мочевого пузыря у пациентов групп 1 и 2 в течение 12 мес. после операции ($n = 97$)

Group	Follow-up period			
	3 months	6 months	12 months	Total
Group 1 ($n = 49$)	3	5	4	13
Group 2 ($n = 48$)	–	1	3	4

Note. Differences in bladder cancer recurrence rates between patients in both groups are statistically significant ($p < 0.05$).
Примечание. Различия в частоте рецидивирования рака мочевого пузыря у пациентов обеих групп статистически значимы ($p < 0,05$).

this issue, which requires improvements in the effectiveness of treatment, including the implementation of modern surgical techniques.

The wide use of various energy sources in cancer treatment has significantly enhanced the existing surgical arsenal. However, when analyzing current global experience and achievements of Russia in transurethral bladder surgery using various energy sources over the past decades, it is important to note that the literature describes very few studies dedicated to the use of laser energy in tumor bed treatment, evaluating its effectiveness, and developing individualized approaches to the indications for its application. The insufficiency of information on these issues presents a promising and relevant subject of scientific inquiry, motivating the oncological urology community to conduct large-scale prospective studies in this field.

In an effort to compare classical TURBT with TURBT followed by Nd:YAG laser ablation of the tumor bed, we analyzed retrospective and prospectively supported databases from urological departments at Central Clinical Hospital Russian Railways Medicine, Central Clinical Hospital of Civil Aviation, Medical Sanitary Unit of the Ministry of Internal Affairs of Russia in Moscow, and City Clinical Hospital No. 13 of the Moscow City Health Department. The analysis of the study findings allows us to draw a well-founded conclusion about the high effectiveness of TURBT followed by Nd:YAG laser ablation of the tumor bed in patients with localized bladder neoplasms. We believe that Nd:YAG laser ablation of the tumor bed induces limited irreversible thermal damage to the wound edge and the tissue at the base of the wound, which ensures the radical nature of the surgical intervention. The use of Nd:YAG laser ablation of the tumor bed is associated with a reduction in complications during the early postoperative period and demonstrates fewer recurrences compared to the classical TURBT method. The active implementation of laser technologies in clinical practice could significantly enhance the treatment of patients with NMIBC by minimizing the risk of tumor recurrence and reducing the likelihood of complications.

CONCLUSION

The results of the conducted study indicate the promising potential of using laser technologies in the treatment of BC. The widespread implementation of these technologies in clinical practice will enable personalized

surgical treatment methods for patients with urologic cancer, taking into account the predicted risk for tumor recurrence.

ADDITIONAL INFO

Authors' contribution. All authors made a substantial contribution to the conception of the study, acquisition, analysis, interpretation of data for the work, drafting and revising the article, final approval of the version to be published and agree to be accountable for all aspects of the study. Personal contribution of each author: O.V. Teodorovich — concept and design of the study, analysis of the data obtained, editing the text of the manuscript; E.V. Gameeva, S.I. Suleymanov, M.N. Shatochin — collection of material, analysis of the obtained data, editing the text of the manuscript; G.G. Borisenko, A.S. Babkin — collection of material, literature data analysis, analysis of the data obtained, writing the text of the manuscript.

Funding source. This study was not supported by any external sources of funding.

Competing interests. The authors declare that they have no competing interests.

Ethics approval. Not applicable.

Consent for publication. Written consent was obtained from the patient for publication of relevant medical information within the manuscript.

ДОПОЛНИТЕЛЬНАЯ ИНФОРМАЦИЯ

Вклад авторов. Все авторы внесли существенный вклад в разработку концепции, проведение исследования и подготовку статьи, прочли и одобрили финальную версию перед публикацией. Личный вклад каждого автора: О.В. Теодорович — концепция и дизайн исследования, анализ полученных данных, редактирование текста рукописи; Е.В. Гамеева, С.И. Сулейманов, М.Н. Шатохин — сбор материала, анализ полученных данных, редактирование текста рукописи; Г.Г. Борисенко, А.С. Бабкин — сбор материала, анализ данных литературы, анализ полученных данных, написание текста статьи.

Источник финансирования. Авторы заявляют об отсутствии внешнего финансирования при проведении исследования.

Конфликт интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

Этический комитет. Не применимо.

Информированное согласие на публикацию. Авторы получили письменное согласие законных представителей пациента на публикацию медицинских данных.

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