# Non-muscle invasive urothelial carcinoma of the bladder: molecular mechanisms of pathogenesis, diagnosis, and therapeutic strategies

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**Funding:** This research received no external funding.
**Institutional Review Board Statement:** Not applicable.
**Informed Consent Statement:** Not applicable.

## Abstract

Urothelial carcinoma of the bladder (UC) is one of the most common cancers of the urinary tract, characterized by a high recurrence rate, significant morphological and molecular heterogeneity, and complex developmental biology. The purpose of this paper is to comprehensively review current concepts of pathogenesis, diagnosis and treatment of non-muscle-invasive urothelial carcinoma of the bladder. Special attention is given to the two main pathways of tumor development - papillary, associated with FGFR3 mutations, and non papillary, associated with disorders in TP53 and RB1 genes. The significance of the field effect as a mechanism explaining multifocal and recurrent disease is also discussed. The paper considers our own material - documentation of endoscopic images obtained during diagnostic and therapeutic procedures, showing tumor morphology, pathological vascularization, calcification and scarring after transurethral tumor resection (TURBT). The role of endoscopic diagnosis and urine cytology, including marker tests, and the importance of surgical treatment and BCG intravesical immunotherapy in the context of UC surveillance were analyzed. This article points to the need for further clinical research to develop more precise and integrated diagnostic and therapeutic strategies that can realistically improve the prognosis of patients with non-muscle-invasive urothelial carcinoma of the bladder.

**Keywords**: bladder cancer; histopathology; cystoscopy; urothelial carcinoma; papillary tumors; transurethral resection of the bladder tumor; cancer diagnostics; urological oncology; tumor morphology

## Introduction

Bladder cancer is among the most commonly diagnosed urinary malignancies worldwide. In 2020, more than 573,000 new cases were registered, ranking it tenth in terms of the incidence of all malignancies [1–3]. Histopathological diagnosis of bladder cancer is based on two main clinicopathological forms: non-muscle-invasive bladder cancer (NMIBC) and muscle-invasive bladder cancer (MIBC) [4,5]. NMIBC includes papil-lary lesions confined to the mucosa (Ta) or infiltrating the basement membrane but not reaching the muscularis propria (T1), as well as flat foci of carcinoma in situ (CIS, Tis) with a high degree of malignancy [6,7].

The majority (about 90%) of bladder tumors are urothelial carcinomas (UC), while the remaining 10% are less common non-urethral cancers [8–10]. Accurate histopathological

Medicine Physicist & Engineer 1/2026 vol. 1
*received: 06.05.2026; corrected: 18.05.2026; accepted: 27.05.2026*

**Author Contributions:**
A – Conceptualization, B – Validation, C – Formal analysis, D – Resources, E – Writing—original draft preparation, F – Writing—review and editing, G – Visualization, H – Supervision.
All authors have read and agreed to the published version of the manuscript.

classification is crucial for predicting the course of the disease and choosing the optimal therapy. According to the 2004 WHO guidelines (updated in 2016), there are three stages of urothelial bladder cancer:

- PUNLMP (Papillary Urothelial Neoplasm of Low Malignant Potential) - a papillary lesion with minimal atypia and low risk of progression;
- Low-grade urothelial carcinoma (LG) - characterized by moderate cellular atypia and low risk of progression, but increased propensity for recurrence;
- High-grade urothelial carcinoma (HG) - showing significant atypia, deep infiltra-tion of the bladder wall and a high risk of progression and metastasis [6,7].

Approximately 75% of newly diagnosed UC cases are NMIBC, which has a high re-currence rate and risk of progression to invasive form despite local treatment [11–13]. Diagnosis of UC histological variants is complicated by tumor heterogeneity, tissue fixa-tion artifacts and inter-observer variability. Studies indicate that up to 30% of primary diagnoses of urothelial carcinoma change after specialized pathomorphologic re-evaluation, underscoring the importance of accurate and multispecialty diagnostics [14,15].

Imaging techniques, including cystoscopy, are an essential component of UC diag-nosis, allowing direct assessment of cancerous lesions [16,17]. Cystoscopic images of tu-mors of different morphologies provide key information about their structure and extent, which can be important in planning surgical treatment, including transurethral resection of bladder tumors (TURBT) [18]. In turn, observations of pathological vascularization and structural features of the tumor can serve as important prognostic and therapeutic indica-tors [19]. Despite extensive research into the pathogenesis of bladder cancer, there is still considerable controversy over the factors that determine the risk of recurrence and pro-gression of the disease. In particular, there is a lack of clear guidance on the impact of his-topathological features, such as calcifications or morphological differences in tumors, on treatment outcomes and patient prognosis.

In this study, the authors used cystoscopic images obtained from patients with urothelial bladder cancer during diagnostic and therapeutic procedures. The endoscopic shots documented the morphology of the tumor lesions, including tumor characteristics during TURBT. In addition, scarring from this procedure was identified, and pathological vascularization of tumor foci was demonstrated.

A literature search was conducted using PubMed/MEDLINE, Scopus and Web of Science databases.

## Cancer pathways

Two distinct pathogenetic pathways can be distinguished in the development of bladder cancer:

- Papillary pathway
- Non-papillary pathway

These pathways differ in many ways, such as molecular mechanisms, clinical fea-tures and biological behavior. However, they share a common basis in the form of diffuse hyperplastic lesions in the bladder mucosa, which is related to the concept of field effect [20].

### Papillary pathway

The papillary pathway is the predominant pathway for urothelial bladder cancer, accounting for about 80% of all cases of this disease. Tumors arising from this pathway are characterized mainly by superficial growth and typical papillary morphology, often appearing as exophytic, well-demarcated lesions in the bladder lumen. They usually ori-ginate from low-grade intraepithelial neoplasia and show a relatively benign clinical co-urse. Although they have a high tendency to recur even after successful surgical treatment, in most cases they rarely progress to forms that infiltrate the bladder musculature, and they also rarely yield distant metastases [21,22].

At the molecular level, a key mechanism driving the development of these tumors is activation of the FGFR3/RAS signaling pathway. The FGFR3 gene, which encodes the fi-broblast growth factor receptor type 3, plays a fundamental role in regulating cellular pro-liferation and differentiation of epithelial cells. Mutations of this gene are extremely com-mon in low-grade papillary tumors - found in more than half of superficial tumors of this type, as well as in about 20% of tumors of higher clinical and histologic grade [23,24]. Ac-tivated FGFR3 mutations lead to excessive activation of the RAS-MAPK pathway, which promotes uncontrolled proliferation of urothelial cells, and thus - the formation and proli-feration of papillary lesions. This has been confirmed by a number of in vitro and *in vivo* studies, which have shown that bladder cancer cell lines with the presence of FGFR3 mu-tations show a significant dependence on an active FGFR3 pathway to maintain their pro-liferative potential [25,26]. The importance of this mechanism has also been confirmed in animal models. For example, a study by Lan Mo et al. showed that the introduction of a mutated form of the HRAS gene into urothelial cells in mice leads first to the development of hyperplastic lesions and, at higher expression levels, to the formation of tumors with a distinct papillary morphology [27].

### Non-papillary pathway

The non papillary pathway is less characteristic of NMIBC and is more often associ-ated with forms of the disease with a more aggressive course [21,22]. In this pathway, the molecular mechanism is based on loss of function of tumor suppressor genes such as TP53 and RB1. Mutations in the TP53 gene are associated with a markedly worse progno-sis [28]. Loss of RB1 function interacts with TP53 mutations in the development of a more aggressive phenotype, although RB1 mutations alone are less common [29,30]. In addi-tion, amplifications of the MDM2 gene

(which inhibits p53) and deletions of the CDKN2A gene (which regulates the cell cycle) also contribute to the inactivation of the p53 and RB1 pathways [28]. Another important mechanism in this pathway is activation of the PTEN/PI3K/AKT/mTOR pathway. Loss of function of PTEN, which is a negative regulator of the PI3K/AKT pathway, leads to its overactivation. In animal models, the dual loss of PTEN and TP53 results in the development of carcinoma in situ, which rapidly trans-forms into bladder cancer with high metastatic potential [31]. In human cancers, fre-quent activation of the PI3K/AKT/mTOR pathway confirms its involvement in disease progression and its worse prognosis [32–34].

## Field effect

When discussing the two pathways of bladder cancer, papillary and non papillary, it is essential to mention the field effect that underlies the progression of both pathways. The field effect plays a key role in the development of bladder cancer, explaining why the dis-ease is often multifocal and has a high tendency to recur. The concept of the field effect assumes that exposure to carcinogens, such as tobacco smoke or industrial chemicals, leads to extensive genetic and epigenetic changes throughout the bladder mucosa. These changes affect large areas of the transitional epithelium, creating a «field» prone to tumor growth. As a result, even seemingly healthy tissue can carry traces of DNA damage that predispose it to the formation of new cancerous foci [35]. One of the earliest and most common genetic events associated with the field effect is loss of heterozygosity (LOH) on chromosome 9. Regions of LOH occur on both arms of chromosome 9, with particularly significant changes occurring in the 9p region, which contains the p16/ARF gene, and the 9q region, where the TSC1 gene is located [36–38]. The p16 gene is a key regulator of the cell cycle, and its inactivation by LOH, homozygous deletions or methylation promotes uncontrolled cell proliferation [39,40]. On the other hand, the TSC1 gene is a negative reg-ulator of the mTOR pathway, and its loss can lead to activation of this pathway, acceler-ating tumor progression [41,42]. Another important component of the field effect is the in-activation of the interferon-α (IFNα) gene, which is also located in the 9p region. IFNα can induce apoptosis in cancer cells, so its loss reduces the body's ability to eliminate cancer cells, which promotes disease progression [43,44]. In addition, several relatively new can-didate genes have also been identified that may play a role in the field effect. These include P2RY5 and ITM2B, which are often silenced by LOH and methylation in bladder cancer cells. Reintroduction of these genes into cancer cells leads to cell cycle arrest and apopto-sis, suggesting that they act as tumor suppressor genes [45,46].

Whole-organ mapping studies have confirmed that genetic changes characteristic of the field effect are found not only in tumor areas, but also in the apparently normal blad-der mucosa. It has been shown that areas of hyperplasia and atypia often occur adjacent to visible tumor foci, suggesting that the entire bladder mucosa is exposed to carcinogens [47].

## Pathological angiogenesis

Tumor angiogenesis is a key process that enables the growth and survival of cancer cells [48–50]. In healthy tissues, a balance between pro- and anti-angiogenic factors main-tains control over blood vessel formation [51]. In tumors, this balance is disrupted, acti-vating the angiogenic switch and initiating the formation of new blood vessels. The most common mechanism is sprouting angiogenesis, in which existing capillaries dilate, become more permeable and undergo basement membrane degradation. Endothelial cells then migrate and form new vascular structures, which are then stabilized by pericytes. In addition to classical sprouting, tumors can use alternative mechanisms, such as vascular co-optation, in which the tumor integrates pre-existing blood vessels, or intussusceptive microvascular growth (IMG), which involves separation of the vessel lumen by forming internal tissue bridges. IMG does not require endothelial cell proliferation, making an-ti-angiogenic therapies targeting endothelial cell growth potentially ineffective for tumors that rely on this mechanism [52]. The tumor vasculature is characterized by unique struc-tural and functional features, such as a lack of clear distinction between arterial and ve-nous vessels, excessive permeability, abnormal anastomoses and blind ends, and integra-tion of tumor cells into the vessel wall. The tumor vasculature is chaotic, with irregular shapes and diameters, leading to inefficient blood flow. An important aspect of pathol-og-ical angiogenesis is also insufficient coverage by pericytes, which play a stabilizing and regulatory role in normal vessels. Their absence or abnormal distribution contributes to increased vascular permeability and promotes further tumor growth. Paradoxically, de-spite abundant vascularization, tumors often remain hypoxic, which activates hypox-ia-induced factors, stimulating the expression of adaptive genes and enhancing angio-genesis [53].

Elevated serum levels of VEGF-A (vascular endothelial growth factor A) in patients with bladder cancer are an important indicator of the biological aggressiveness of the tu-mor. Values exceeding 400 pg/ml are strongly correlated with the presence of metastasis, while elevated urinary VEGF-A levels have been shown to be associated with NMIBC re-currence [54,55]. Angiogenesis in bladder cancer can also be regulated by genetic disor-ders, such as mutations in the FGFR3 (fibroblast growth factor receptor 3) gene [56]. These mutations are mainly characteristic of low-grade tumors and early stages of the disease, and their presence is associated with increased tumor vascularization, indicating a poten-tial role for FGFR3 in stimulating angiogenesis. Importantly, the expression of this gene decreases with progressive invasion and increasing aggressiveness of the

tumor [57]. Another important factor involved in angiogenesis and UC progression is interleukin 8 (IL-8). High IL-8 expression in bladder cancer cells correlates with advanced disease stage, increased microvessel density, higher risk of metastasis and intense tumor growth. Its ac-tion in the context of tumor biology is partly linked to the regulation of matrix metallopro-teinases activity, but IL-8 functions independently of classical angiogenic factors such as VEGF and bFGF [58,59].

Given the key role of angiogenesis in bladder cancer progression and invasion, ther-apies targeting its inhibition are being developed. Monoclonal antibodies such as bevaci-zumab and ramucirumab, used in combination with chemotherapy, have shown prom-ising results - they are currently in phase III clinical trials. At the same time, phase II trials are underway for VEGF inhibitors such as sunitinib, sorafenib and pazopanib, which also show therapeutic potential in bladder cancer treatment [60].

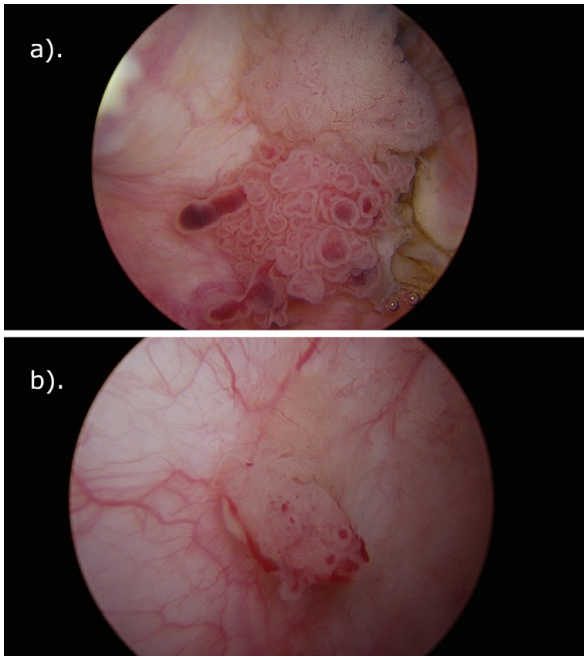


***Fig. 1*** *a) and b) Papillary bladder cancer - during TURBT - pathological tumor vascularization is visible*
*Source : Own study.*

## Diagnostics

Cystoscopy and urine cytology are the gold standard in the diagnostic evaluation of suspected patients, as well as in the surveillance of those with a history of urothelial non-muscle-invasive bladder cancer [61–63].

## Cystoscopy

Cystoscopy is the primary diagnostic method used in the evaluation of urothelial carcinoma [64–66]. In the outpatient setting, flexible cystoscopy is recommended if possi-ble, as it makes the patient more comfortable. Cystoscopy results should be documented using a standardized diagram, noting the location and size of the tumor [7].

Papillary tumors appear as exophytic lesions with a papillary structure, which can be single or multiple. The cystoscopic appearance varies depending on the stage of the tumor. In the case of PUNLMP, the lesions are well demarcated and the sur-face shows fine, thin and branching papillae [69]. In the case of low-grade (LG) cancer, cystoscopy reveals more irregular structures, although they still retain a distinctly papil-lary arrangement. In contrast, high-grade (HG) carcinoma at the non-invasive stage may also present as a papillary lesion, but is characterized by a greater degree of cellular atypia and a more irregular surface appearance, which may suggest a greater risk of progression [70]. During cystoscopy, the key diagnostic elements are tumor size, number and macro-scopic features, which are crucial for planning further therapeutic management [71].

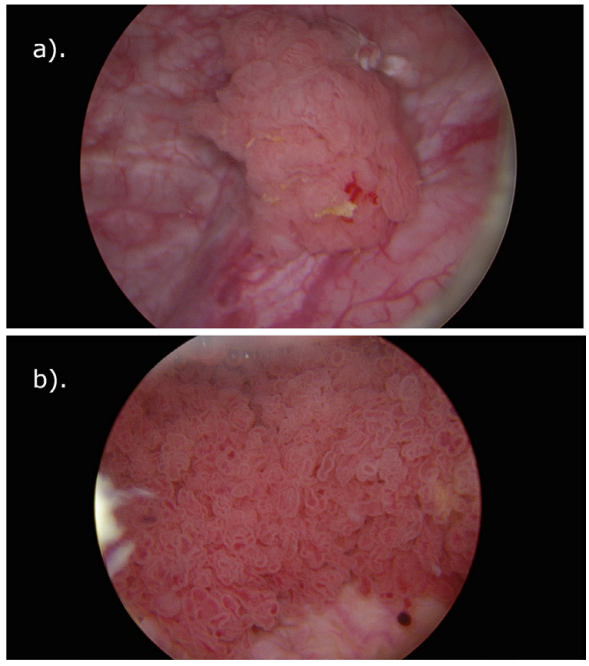


***Fig. 2*** *a) and b) Urothelial carcinoma of the bladder – cystoscopic image*
*Source : Own study.*

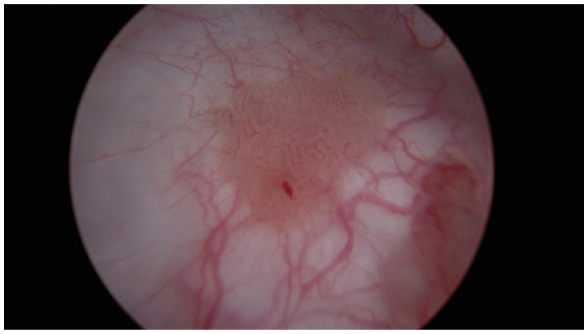

***Fig. 3*** *Urothelial carcinoma of the bladder – cystoscopic image*
*Source : Own study.*

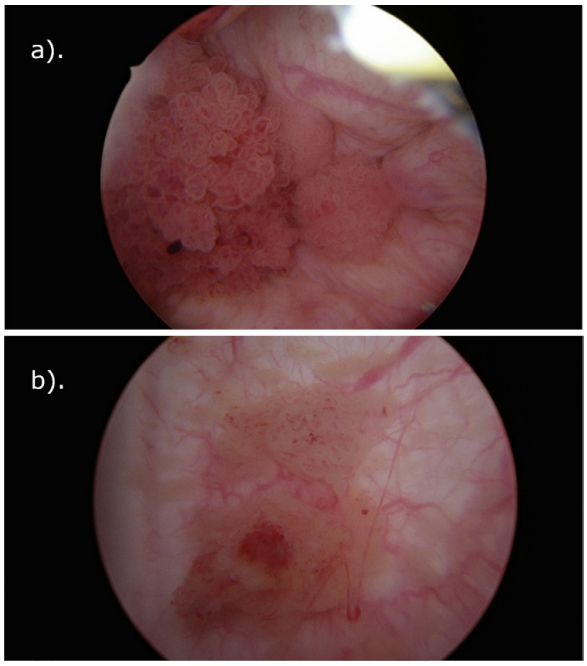


***Fig. 4*** *a) and b) Multiple urothelial carcinoma of the bladder – cystoscopic image*
*Source : Own study.*

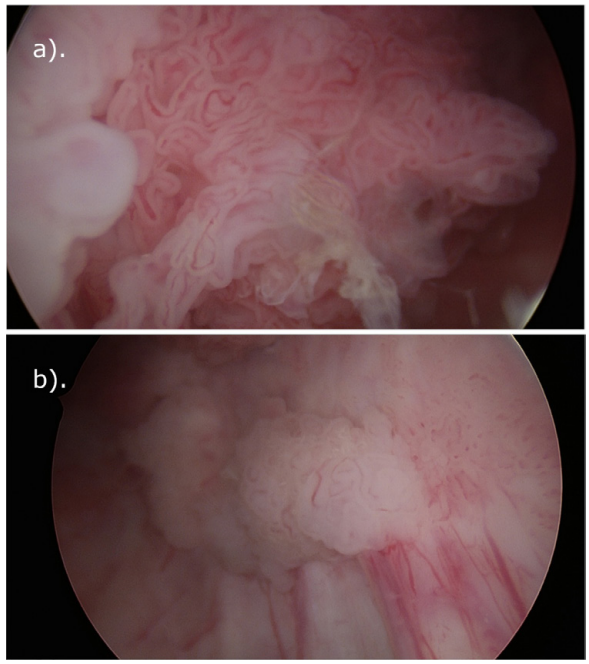


***Fig. 5*** *a) Papillary urothelial carcinoma of the bladder – cystoscopic image; b) Multiple pa-pillary urothelial carcinoma of the bladder – cystoscopic image*
*Source : Own study.*

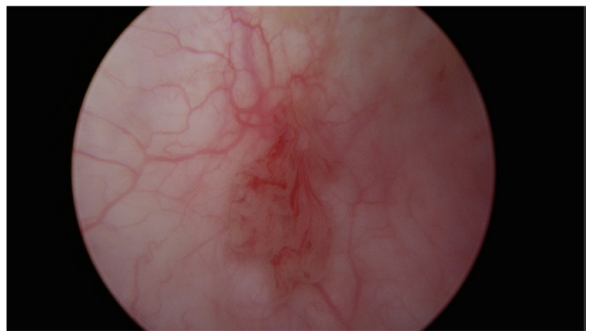

***Fig. 6*** *Pedunculated, small urothelial carcinoma of the bladder – cystoscopic image*
*Source : Own study.*

## Urine cytology

Urine cytology, despite being one of the primary tools in the diagnosis of bladder cancer due to its non-invasiveness and wide availability, has a significantly limited sensi-tivity, especially for urothelial LG tumors. The efficiency of this method in detecting LG le-sions is estimated at only about 16%, which significantly limits its clinical value in the context of early diagnosis of this form of the disease. In the case of HG tumors, the sensi-tivity of cytology increases significantly, reaching a value of about 84%, making it an im-portant tool to help diagnose lesions with greater potential for biological aggression.

In order to increase diagnostic sensitivity in the detection of bladder cancer, a number of molecular and immunochemical tests based on the determination of tumor markers in the urine sample have been introduced. Of these, the BTA Stat and NMP22 BladderChek tests have found the greatest clinical use. Studies have shown that their use makes it po-ssible to detect HG cancer with a sensitivity of 91% and 92%, respectively. However, it should be noted that the increase in sensitivity achieved by these tests comes at the expense of a decrease in specificity, which is relatively high in the case of cytology [72].

A study by Moonen et al. analyzed the sensitivity and specificity of the NMP22 Blad-derChek test compared to conventional urine cytology in patients diagnosed with superfi-cial bladder cancer (pTa, pT1) and carcinoma in situ (CIS). The results show that NMP22 BladderChek has a sensitivity of 57.1% and specificity of 89.8%, while cytology shows 42.9% and 93.2%, respectively. The study's authors emphasized that the marker tests offer higher diagnostic sensitivity than classic cytology, with only a slight decrease in specifi-city, making them a valuable tool to complement the diagnosis of UC [73].

Despite the availability of commercial tests to detect tumor markers in urine, the Eu-ropean Association of Urology (EAU)

does not recommend their use in the routine dia-gnosis of NMIBC. Exceptions are the UroVysion FISH and NMP22 BladderChek tests, which have received formal approval in the context of the diagnosis and monitoring of patients with hematuria of unknown origin [74]. However, it should be noted that the re-liability of the results of these tests may be limited by a number of confounding factors, in-cluding the presence of benign urothelial epithelial lesions, the presence of urinary tract infections, and prior intravesical treatment with BCG preparations [7,74,75].

The effectiveness of marker tests largely depends on the purpose of their use - diffe-rent parameters of sensitivity and specificity will be desirable for screening, others for primary diagnosis, and still others in the context of monitoring patients with different levels of risk for recurrence and disease progression. Additional value may be presented by these tests in patients with negative cystoscopy and normal upper urinary tract images who simultaneously have positive cytology or molecular tests. In such cases, the use of tests such as UroVysion FISH, NMP22 nuclear matrix protein assay, FGFR3 or TERT mu-tation analysis, or microsatellite testing can assist in identifying patients at increased risk of cancer recurrence or progression. Integration of these methods with classical diagnostic techniques may improve diagnostic accuracy and more effective surveillance of patients with urothelial nonmuscle-invasive bladder cancer [7,76].

## Treatment

### Transurethral Resection of Bladder Tumor (TURBT)

TURBT is a key procedure used to treat urothelial bladder cancer. During this procedure, performed under local or general anesthesia, a resec-toscope equipped with a light source and electrodes is inserted transurethrally, allowing precise resection of tumor-like lesions from the bladder mucosa [77–80]. The goal of TURBT is to completely resect the tumor along with margins of healthy tissue and the base of the tumor, ensuring the presence of a layer of the detrusor muscle (muscularis propria) in the histopathological specimen. The absence of muscle in the specimen increases the risk of recurrence and can lead to under-estimation of the local tumor grade [81]. The technique for excision of an exophytic lesion depends on its size and the surgeon's experience. En bloc resection is recommended for tumors up to 3-4 cm in diameter and is not associated with an increased risk of recurrence or complications, such as perforation of the bladder wall [82–85]. The main advantage of this method is the higher quality of the histopathological preparation, including a higher percentage of cases in which the muscle layer is present compared to the conventional TURBT technique [85,86].

TURBT is performed using monopolar or bipolar resectoscopes. The use of a bipolar electrode allows the procedure to be performed in a saline environment, which improves the transparency of the surgical field. In addition, the temperature of the resection loop in the bipolar method is about 55°C, compared to 400°C in the monopolar method, which theoretically reduces the risk of thermal damage to the histopathological specimen. This is confirmed by a study conducted by Ahsan et al. [87], although Kexin et al. dispute this claim, citing a lack of conclusive evidence [88]. Analysis of available data suggests that the only significant benefit of bipolar resection is a shorter hospital stay [89,90]. Other factors, such as complication rates (e.g., postoperative bleeding, urinary retention due to clot for-mation, bladder wall perforation, TUR syndrome, obturator nerve reflex) are comparable between the two methods [88–90]. Because of the risk of missed satellite lesions, including CIS, or inadequate resection margins, which can lead to recurrence and disease progres-sion, complementary imaging techniques such as photodynamic diagnostics and nar-row-band imaging are increasingly being used in clinical practice. Independent prognos-tic factors for recurrence are patient age and the presence of CIS [84].

After TURBT, postoperative intravesical chemotherapy is recommended, including a single insylation of mitomycin C, epirubicin or pirarubicin. The goal of this therapy is to eliminate residual tumor cells and microscopic satellite lesions, reducing the risk of re-currence. However, it should be noted that the benefits of this therapy do not apply to pa-tients experiencing recurrences more than once a year [91–93].

Figures 7a, 7b, 8a and 8b represent the continuity of the process, culminating in excision, fol-lowed by healing and a scar visible in Fig. 8b – such an image is typically observed a few months after bladder cancer resection

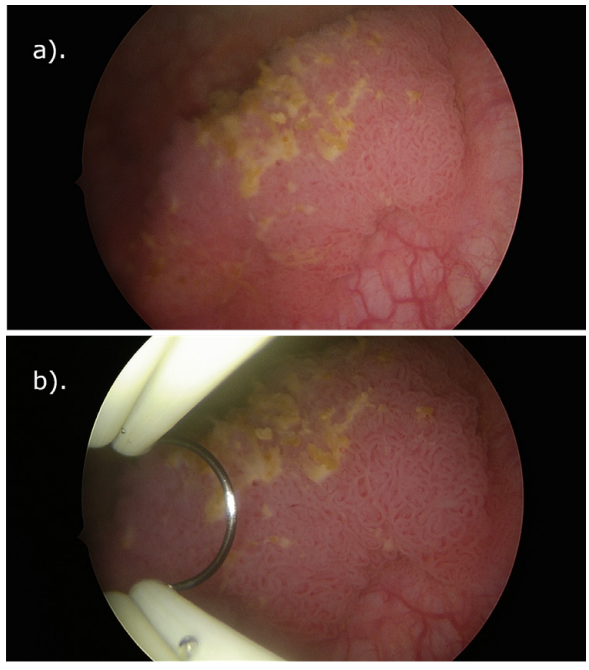


***Fig. 7*** *a) Papillary urothelial carcinoma of the bladder with surface calcifications – cystoscopic image; b) Papillary urothelial carcinoma of the bladder with surface calcifications before TURBT – resectoscope loop visible*
*Source : Own study.*

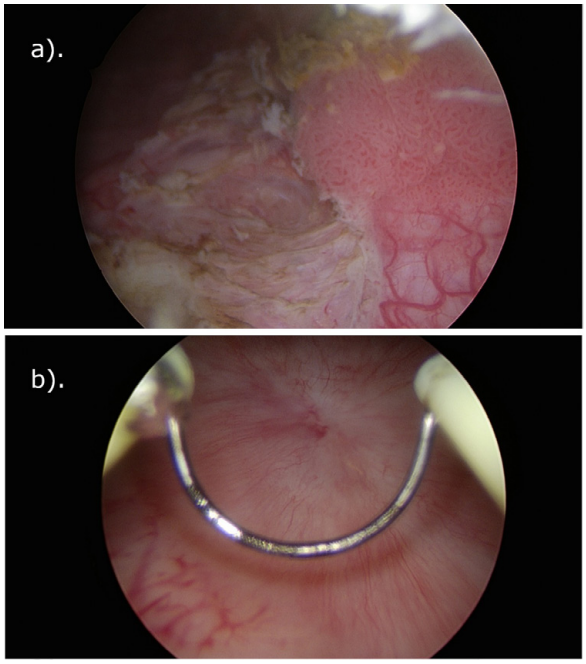


***Fig. 8*** *a) Papillary urothelial carcinoma of the bladder with surface calcifications – during electrosurgical resection – resection site of part of the tumor visible on the left side; b) Scar in the bladder after tumor resection – The image shows a scar in the bladder wall following a previous TURBT – cystoscopic image*
*Source : Own study.*

## Intravesical immunotherapy with BCG vaccine

According to current European Association of Urology (EAU) guidelines, intravesical BCG (Bacillus Calmette-Guérin) immunotherapy is recommended as an integral part of the treatment of patients with urothelial nonmuscle-invasive bladder cancer with mode-rate, high and very high risk of progression. A particular indication for this form of thera-py is the presence of CIS foci, which are an independent risk factor for uncontrolled tumor growth and dissemination [94,95]. The use of attenuated mycobacteria (BCG) intravesical infusions after TURBT is a more effective treatment for NMIBC than TURBT as mono-therapy or TURBT combined with a single dose of intravesical chemotherapy [96–98].

Absolute contraindications to BCG therapy include:

- Presence of active hematuria
- A period of less than 14 days after TURBT has been performed
- Active symptomatic lower urinary tract infection
- History of traumatic bladder catheterization [7].

The regimen of BCG administration according to the Morales protocol involves a total three-year treatment cycle, consisting of two phases:

- Induction: six weekly intravesical infusions, starting 2-4 weeks after TURBT.
- Sustaining: three weekly infusions at the 3rd, 6th, 12th, 18th, 24th, 30th and 36th months after the start of therapy [99].

Patients with NMIBC at high and very high risk of progression are advised to follow the entire three-year regimen, while in the moderate-risk population - in order to reduce toxicity - continuing treatment for the first year is usually sufficient [7]. The results of a multicenter, randomized EORTC trial confirmed that a full three years of BCG therapy le-ads to a significant reduction in recurrence rates in high-risk patients, compared to a one-year treatment regimen, with no effect on progression rates or overall survival [100]. In contrast, an analysis by Malmström et al. showed that skipping the maintenance phase (i.e., limiting therapy to only six induction doses) significantly increases the risk of relapse compared to a full regimen including both induction and maintenance doses [96].

## Conclusions

Non-muscle-invasive urothelial carcinoma of the bladder remains one of the most common urinary tract neoplasms, and its complex biology, high morphologic and molec-ular heterogeneity, and significant rate of recurrence after treatment make it a significant therapeutic challenge. Our article aims to provide a comprehensive assessment of selected aspects of this disease entity, with particular emphasis on the endoscopic picture of the lesions, their pathological vascularization, and the implications of standard and modern diagnostic and therapeutic methods.

In the presented article, we paid special attention to the cystoscopic image of the tu-mors, taking into account the morphological diversity of the tumors - from typical papil-lary lesions to atypical foci with associated calcifications and scarring after TURBT. The author's photo documentation allowed not only the characterization of these lesions, but also highlighted the importance of direct visualization of pathological vascularization, which can indicate increased biological aggressiveness of the tumor. Such observations may, in the future, act as additional prognostic markers, supporting classical histopatho-logical criteria.

From a molecular perspective, the work highlighted the duality of the pathways of urothelial bladder cancer - papillary, associated with FGFR3 mutations and a milder cli-nical course, and non-papillary, characterized by loss of function of suppressor genes (TP53, RB1) and activation of the PI3K/AKT/mTOR pathway, which is associated with a worse prognosis. The inclusion of these pathogenetic pathways in cancer classifications lays the groundwork for the development of more precise targeted therapies. Promising results from studies of FGFR and VEGF inhibitors confirm the growing importance of in-tegrating molecular knowledge into clinical practice.

The so-called «field effect» - a phenomenon that explains the multifocal and recurrent nature of UC in the context of extensive genetic and epigenetic changes in the apparently unaltered bladder mucosa - also plays an isotopic role. Understanding this mechanism opens up new possibilities for recurrence prevention, planning the extent of resection, and implementing

adjuvant therapies that encompass the entire lesional field, not just visible tumor foci.

From a treatment perspective, TURBT still plays a key role, the quality of which, par-ticularly the presence of the detrusor muscle layer in the specimen, has a significant im-pact on subsequent prognosis and the need for re-TURBT. Technological advances in imaging - including the use of blue light, photodiagnostics or narrow-band imaging - are making it possible to assess lesion boundaries with increasing accuracy and detect CIS fo-ci that may be difficult to identify with classic cystoscopy.

BCG intravesical immunotherapy, despite its numerous limitations and side effects, remains the standard of care for intermediate- and high-risk NMIBC, and study results indicate its superiority over intravesical chemotherapy in preventing recurrence and pro-gression.

In conclusion, this article integrates the classical clinicopathological approach with the latest molecular findings, and an important element of the study is the use of imaging documentation obtained during endoscopic diagnosis. The images presented are an im-portant complement to morphological analyses, emphasizing the importance of visual assessment of tumor lesions in treatment planning. The collected data indicate the need for further clinical research aimed at the development of more precise and integrated dia-gnostic and therapeutic strategies that can realistically improve the prognosis of patients with non-muscle invasive urothelial carcinoma of the bladder.

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