5th CONGRESS OF MACEDONIAN ASSOCIATION OF UROLOGY

&

6th CONGRESS OF BALKAN ASSOCIATION OF UROLOGY

Balkan Association of Urology

17-19.10.2025

Hotel Drim - Struga, R.N. Macedonia

Up-to-date strategies in the treatment of non-muscle invasive bladder cancer

Maja Sofronievska Glavinov, Ass.Prof.

University Surgery Hospital St.Naum Ohridski, Skopje
Faculty of Medical Sciences, Goce Delcev University, Stip

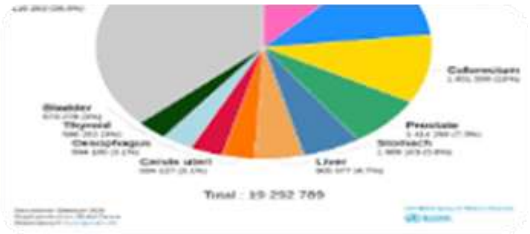
Understanding Bladder Cancer Epidemiology

Bladder Cancer Incidence Rates

95 in men and 24 in women per 100,000 person-years

Survival Rates Across Stages

Different survival rates between Ta/T1 and T2/T4



The ***age-standardized mortality rate illustrates a significant gender disparity*** , 7.5 for men, and 2.2 for women

Long-Term Monitoring and Follow-Up

focusing on recurrence prevention and quality of life improvements.

Ibrahim Jubber, Sean Ong, Laura Bukavin et al. (2023) Epidemiology of Bladder Cancer in 2023: A Systematic Review of Risk Factors. European Urology 84(2) 176-190 https://doi.org/10.1016/j.eururo.2023.03.029

Aetiological Factors in Bladder Cancer Development

Impact of Tobacco on Bladder Cancer

Attributed to carcinogenic compounds such as **aromatic amines.**

Prolonged exposure increases incidences.

Occupational Hazards Linked to Cancer

Occupational exposure to agents like **polycyclic aromatic hydrocarbons and chlorinated hydrocarbons** has been linked to a higher risk of bladder cancer.

Environmental Sources of Carcinogens

Environmental exposures, including **arsenic in drinking water and trihalomethanes**, contribute to bladder cancer incidence.

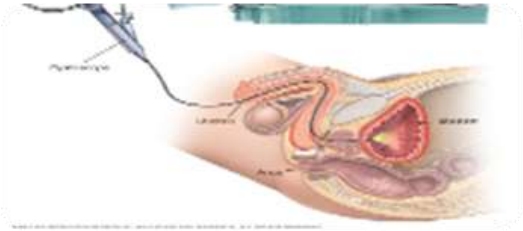
Genetic and Dietary Influences

Genetic predispositions play a **minimal role.**

Dietary factors such as the **Mediterranean diet are protective** against bladder cancer, providing key insights for public health strategies.

Ng KL. The Etiology of Bladder Cancer. In: Barber N, Ali A, editors. Urologic Cancers [Internet]. Brisbane (AU): Exon Publications; 2022 Sep 12. Chapter 3. Available from: https://www.ncbi.nlm.nih.gov/books/NBK585966/ doi: 10.36255/exon-publications-urologic-cancers-etiology-bladder-cancer

Diagnostic protocols for nonmuscle invasive bladder cancer

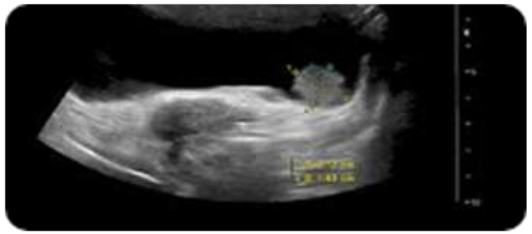


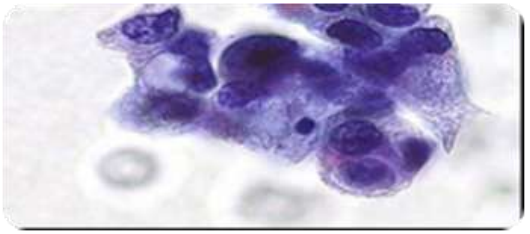
Utilize cystoscopy effectively

Cystoscopy, preferably flexible, is a **critical diagnostic tool** in identifying bladder tumors.

Bladder ultrasound

Initial evaluation of **patients with hematuria** to identify potential abnormalities.



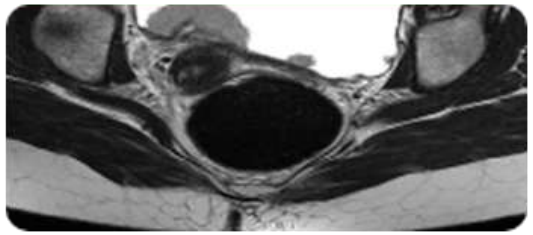


Emphasize urine cytology

Highlight the role of voided urine cytology as an adjunct diagnostic procedure to detect **high-grade tumors** in bladder cancer patients.

MRI for local staging

Recommend **MRI for local staging before TURB** when assessing bladder cancer, ensuring thorough preoperative evaluation.



EAU Guidelines 2025 https://uroweb.org/guidelines/non-muscle-invasive-bladder-cancer

Advanced diagnostic techniques in bladder cancer

Importance of imaging in bladder cancer diagnosis

Computed IVU tomography -for detecting **filling defects,** enhances diagnostic precision.

NMP22 and UroVysion tests in bladder cancer

Though urinary molecular marker tests can assist in diagnosis, **none have achieved routine use** in clinical practice, underlining the critical role of cystoscopy.

Emerging diagnostic methodologies

Innovative diagnostic approaches like **photodynamic diagnosis** and **narrowband imaging** are enhancing the visualization of bladder tumors.

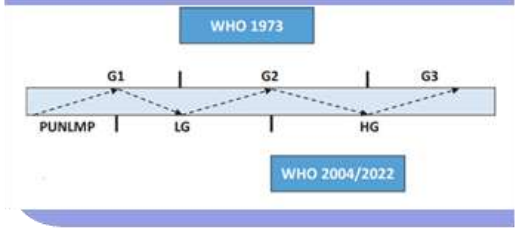
EAU Guidelines 2025 https://uroweb.org/guidelines/non-muscle-invasive-bladder-cancer

Guidelines on classification and grading of bladder cancer

Staging using the TNM classification system

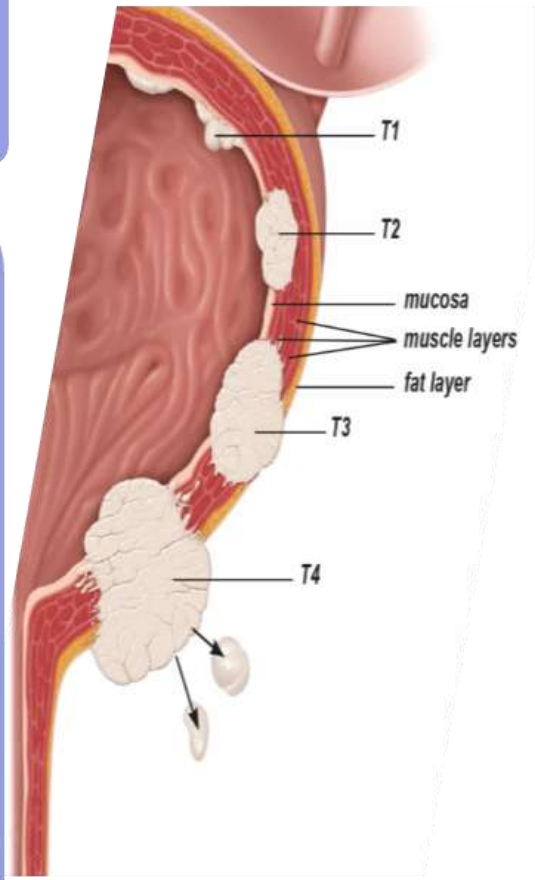
The 2017 TNM system is recommended for classifying bladder cancer, providing a standardized approach to evaluate tumor invasion depth

Both the 1973 and the 2004-2022 WHO grading classifications should be employed to assess tumor grades



The presence of **lymphovascular invasion** is **associated with poorer prognoses** and should be noted in pathological evaluations

Certain subtypes of urothelial carcinoma exhibit worse outcomes, necessitating tailored treatment approaches based on subtype classification



Cheng, L., Lopez-Beltran, A. and Montironi, R. (2025). Classification and Grading of Bladder Cancer. In Bladder Pathology (eds L. Cheng, A. Lopez-Beltran and R. Montironi). https://doi.org/10.1002/9781119707677.ch9

Treatment frameworks for NMIBC management

TURB is a **crucial procedure in diagnosing and treating nonmuscle invasive bladder cancer**, requiring careful surgical techniques for optimal outcomes.

Second TURB to ensure complete resection in cases of initial incomplete treatment or high-risk tumor presentations.

Intravesical therapy protocols should be considered as part of a comprehensive treatment strategy **to reduce recurrence rates**.

Regular follow-up and monitoring are essential after initial bladder cancer treatment **to detect any recurrences early.**

EAU Guidelines 2025 https://uroweb.org/guidelines/non-muscle-invasive-bladder-cancer

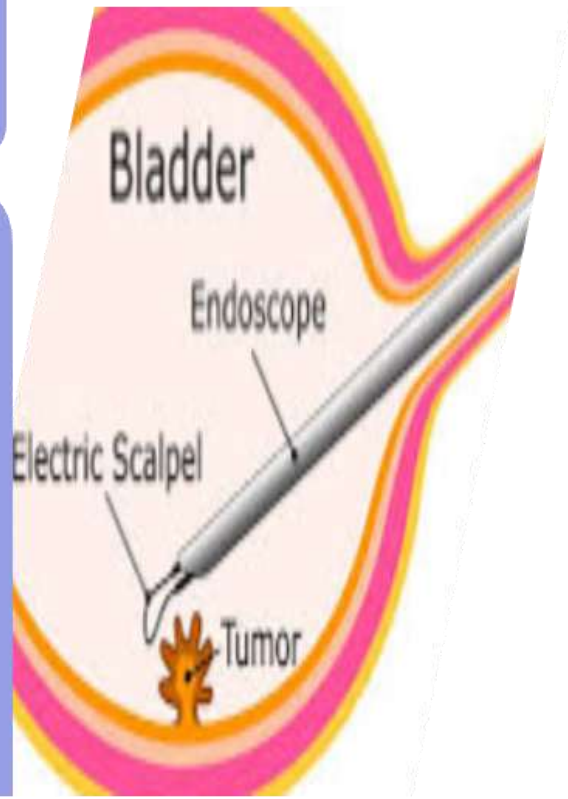
Methods to Enhance Resection Completeness in Bladder Surgery

Achieving a **complete resection during surgery** is crucial for minimizing tumor recurrence.

En-bloc resection improves the quality of the resected specimen and **reduces the risk of residual disease** compared to traditional piecemeal resection.

Photodynamic diagnosis and **narrowband imaging** enhances visualization of tumors during surgery, **ensuring complete resection** and accurate staging of bladder cancer.

The absenceof **detrusor muscle in resected specimens** is linked to **increased risk of recurrence.**



EAU Guidelines 2025 https://uroweb.org/guidelines/non-muscle-invasive-bladder-cancer

Role of Second Resection in Bladder Cancer Treatment

Timing of Second TURB

Performed **14-42 days (2-6weeks)** after the initial surgery to confirm pathological staging and clear residual disease.

Benefits of Second Resection

Significantly **increases recurrence-free survival rates** and provides critical prognostic information to guide further management strategies.

Guidelines for Effective Resection

Second resection can **improve the identification of any remaining cancer and ensure complete staging**, which is crucial for patient outcomes.

Impact on Subsequent Treatments

A second TURB not only aids in clearing residual cancer but also **influences the effectiveness of subsequent therapies**, such as intravesical chemotherapy and immunotherapy.

EAU Guidelines 2025 https://uroweb.org/guidelines/non-muscle-invasive-bladder-cancer

Understanding the implications of carcinoma in situ in urology

Defining carcinoma in situ

Carcinoma in situ (CIS) represents a ***non-invasive form of cancer*** found in the urothelium, often difficult to distinguish during examination.

Importance of accurate diagnosis

Accurate diagnosis of carcinoma in situ is critical, as it can be misclassified as inflammation, leading to inadequate treatment.

Multifocal nature of CIS

CIS is frequently multifocal, potentially affecting various areas including the bladder and upper urinary tract.

Clinical classifications of CIS

Primary: isolated CIS with no previous or concurrent papillary tumours and no previous CIS;

Secondary: CIS detected during follow-up of patients with a previous tumour that was not CIS;

Concurrent: CIS in the presence of any other urothelial tumour in the bladder.

EAU Guidelines 2025 https://uroweb.org/guidelines/non-muscle-invasive-bladder-cancer

Management strategies for carcinoma in situ

CIS diagnosis using a combination of **cystoscopy, urine cytology, and histological** evaluation of bladder biopsies.

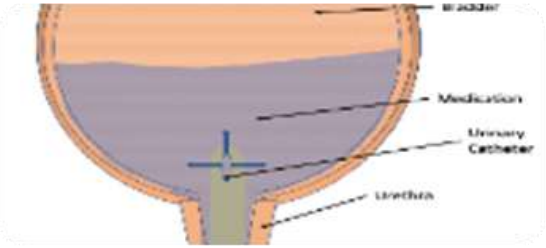
Institute **mandatory follow-up** treatment for carcinoma in situ, as TURB alone is insufficient to eradicate the condition.

Performing **mapping biopsies in normal-appearing mucosa to rule out** carcinoma in situ effectively.

Implement **additional treatment protocols** following TURB to address persistent carcinoma in situ and prevent recurrence.

EAU Guidelines 2025 https://uroweb.org/guidelines/non-muscle-invasive-bladder-cancer

Advancements in Chemotherapy and Immunotherapy for Bladder Cancer



Intravesical Chemotherapy Techniques

Immediate post-surgerysingle instillation of chemotherapeutics (mitomycin C) - effectively eliminates residual tumor cells, reducing the chance of recurrence.

Hyperthermic intravesical chemotherapy-technologies which increase the temperature of the instilled single Mytomicin C

Role of BCG Therapy in Bladder Cancer

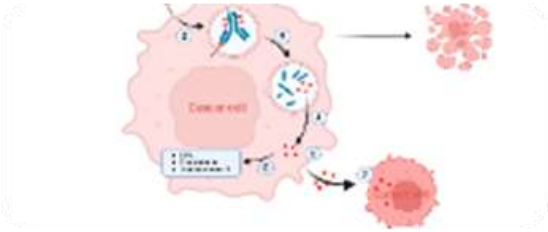
BCG therapy **activates the immune system to target bladder cancer cells.** Understanding its mechanisms is crucial in developing alternative strategies for patients who experience BCG failure.

Combination Immunotherapy Approaches

Combining different immunotherapy agents, such as pembrolizumab and nivolumab, may enhance therapeutic efficacy by preventing tumor cells from evading immune detection.

Emerging Treatments Antibody-Drug Conjugates

Exploring **antibody-drug conjugates** offers a targeted approach to deliver cytotoxic agents directly to cancer cells, minimizing damage to surrounding healthy tissues.



EAU Guidelines 2025 https://uroweb.org/guidelines/non-muscle-invasive-bladder-cancer

Intravesical bacillus Calmette-Guérin (BCG) immunotherapy

7.4.3.7 Summary of evidence - BCG treatment

Summary of evidence	LE
In patients with intermediate- and high-risk tumours, intravesical BCG after TURB reduces the risk of tumour recurrence; it is more effective than TURB alone or TURB and intravesical chemotherapy.	1a
For optimal efficacy, BCG must be given in a maintenance schedule. A complete BCG schedule comprises an induction phase of six-weekly instillations, followed by a maintenance phase of three-weekly instillations at 3, 6, 12, 18, 24, 30 and 36 months, respectively.	1a
Three-year maintenance is more effective than one year to prevent recurrence in patients with high-risk tumours, but not in patients with intermediate-risk tumours.	1a

EAU Guidelines 2025 https://uroweb.org/guidelines/non-muscle-invasive-bladder-cancer

Alternatives to BCG failure

- Combining intravenous and intravesical immunotherapy
- Combining viral- and bacterial-based intravesical therapies
- Combination intravesical chemotherapy regimens based on their complementary mechanisms to enhance cancer cell eradication.

Figure 2. Intravesical chemotherapy drugs and their combinations approved or are currently being studied in bladder cancer.

Cystoscopy scheduling for low-risk Ta tumours

Initial cystoscopy at 3 months

Patients with low-risk Ta tumours should undergo an ***initial cystoscopy at 3 months after treatment*** to monitor for recurrence.

Follow-up cystoscopy at 9 months

If the initial cystoscopy result is negative, a **follow-up cystoscopy should be conducted 9 months later** to ensure ongoing monitoring.

Annual cystoscopy thereafter

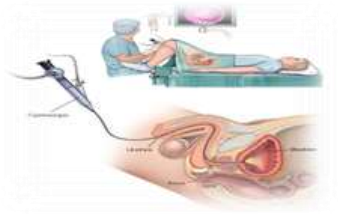
After the 9-month follow-up, cystoscopy should be performed **annually for a duration of five years** to check for any recurrence.

Importance of regular monitoring

Regular cystoscopy management is vital to detect any abnormalities early, **ensuring appropriate treatment and better patient outcomes.**

EAU Guidelines 2025 https://uroweb.org/guidelines/non-muscle-invasive-bladder-cancer

Follow-up of intermediate-risk Ta low-grade tumours

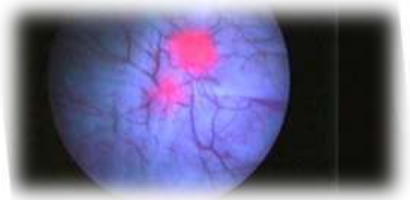


Cystoscopy every 3 months

Patients with intermediate-risk Ta low-grade tumours should receive ***cystoscopy every 3*** months to track progression and manage risks.

Six-monthly cystoscopy after initial follow-up

If the results from the 3-month cystoscopy are negative, subsequent cystoscopies can then be conducted every six months for two years.



Transition to annual cystoscopy

Following the two-year period, patients should transition to annual cystoscopy for the next ten years for ongoing surveillance.

Risk assessment for intermediate tumours

Regular monitoring is essential for intermediate-risk tumours to identify any changes that may necessitate further intervention.

EAU Guidelines 2025 https://uroweb.org/guidelines/non-muscle-invasive-bladder-cancer

Cystoscopy protocols for high-risk tumours

Cystoscopy and cytology at 3 months

Patients with high-risk tumours must undergo ***cystoscopy and urinary cytology at 3 months*** to assess for recurrence or progression.

Frequent monitoring for high-risk patients

If initial results are negative, ***cystoscopy and cytology should be repeated every three months for the first two years.***

Long-term follow-up strategy

After the initial two years, monitoring ***should shift to every six months until the five-year mark,*** followed by annual assessments.

Imaging and biopsy recommendations

High-risk patients may require **additional imaging and biopsies** based on cystoscopy findings to ensure thorough investigation and care.

EAU Guidelines 2025 https://uroweb.org/guidelines/non-muscle-invasive-bladder-cancer

Thank You