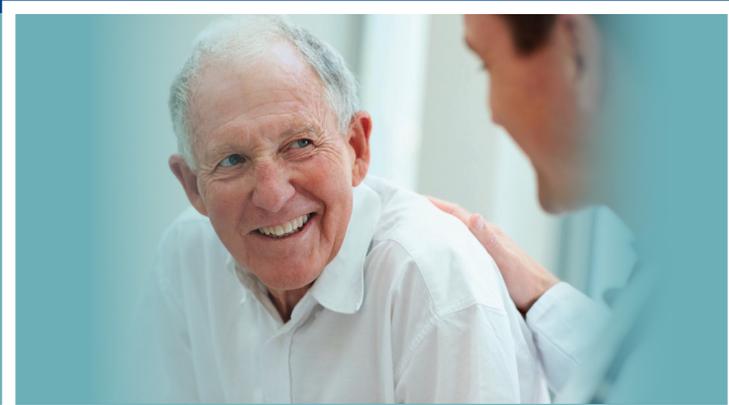




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*The Official Foundation of the  
American Urological Association*



## **PATIENT GUIDE**

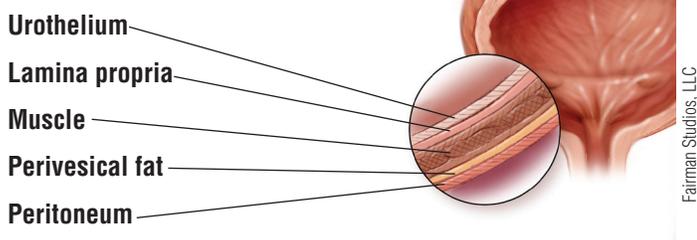
# The Management of Nonmuscle Invasive Bladder Cancer

Based on the recommendations from the Bladder Cancer  
Guideline Update Panel of the American Urological Association

## WHAT IS THE BLADDER?

The bladder is a balloon-shaped organ in your **pelvic** area that stores **urine** and is made up of four layers. The first inside layer is the **mucosa**, which contains **urothelial (or transitional) cells** that can stretch. The next layer is made up of connective tissue and blood vessels called the **lamina propria**. The third layer is the muscular layer, which contains muscles that contract during urination. Finally, urothelial cells line much of the **urinary tract**, including the renal pelvis, the **ureters**, the **bladder** and parts of the **urethra**.

### Layers of the Bladder



## WHAT IS CANCER?

**Cancer** begins in the cells, which are the body's basic unit of life. Normal functioning cells grow and divide in a controlled way. Cells are produced only when they are needed, and always in an effort to maintain a healthy body. Thus, as cells become old or damaged, they die and are replaced with new healthy cells.

Cancer is the abnormal dividing of cells that begin to grow out of control and are able to invade other tissues. "Cancer" is not just one disease, but encompasses hundreds of types of cancer. Most cancers are named for the organ or type of cell in which they start—for example, cancer that begins in the cells of the bladder is called "bladder cancer." Different types of cancers can behave differently.

## WHAT IS BLADDER CANCER?

Bladder cancer is cancer that begins in the bladder. A person with bladder cancer has one or more **malignant** tumors comprised of abnormal and unhealthy cells. Often, the cancer begins in the urothelial cells of the bladder. There are three types of bladder cancer:

- **Urothelial cell carcinoma/Transitional cell carcinoma** accounts for approximately 90 percent of bladder cancer diagnoses and is the most common type of bladder cancer in the United States. This cancer occurs in the cells that line the inside of your bladder. These cells expand when your bladder is full and contract when your bladder is empty.
- **Squamous cell carcinoma** accounts for approximately 5 percent of bladder cancer diagnoses. Development of squamous cell carcinoma is associated with persistent irritation of the bladder. Over time, the cells can become cancerous. This cancer is more prevalent in areas where a bladder infection caused by a certain parasite (schistosomiasis) is common.
- **Adenocarcinoma** is the rarest type of bladder cancer and affects approximately 2 percent of the United States population. This cancer occurs in mucus-secreting glands of bladder cells.

## WHAT ARE THE STATISTICS FOR BLADDER CANCER?

Annually, 69,250 people will be diagnosed with bladder cancer, and an estimated 52,020 will be men and 17,230 will be women. Of the people diagnosed, 14,990 are expected to die from the disease. Bladder cancer is diagnosed most often in older persons with 73-years-old as the average age at diagnosis.

Bladder cancer is the fourth most commonly diagnosed cancer in men, with one in 26 men developing it in his lifetime. Men are also three times more likely than women to develop the disease.

In more than half of bladder cancer diagnoses, patients are diagnosed with cancer that is still confined to the inner layer of the bladder (**carcinoma in situ**, or non-invasive cancer). About 35 percent have bladder cancer that has invaded the deeper tissue layers but is still contained in the bladder. In most of the remaining cases, the cancer has spread to nearby tissues outside the bladder. It is rare that bladder cancer has **metastasized** to other parts of the body.

## WHAT CAUSES BLADDER CANCER?

It is not always clear what causes bladder cancer. Bladder cancer has been linked to smoking, radiation and chemical exposure.

Smoking cigarettes, cigars or pipes may increase your risk of bladder cancer by causing harmful chemicals to accumulate in your urine. When you smoke, your body processes these chemicals in the smoke and excretes some of them into your urine. These harmful chemicals may damage the lining of your bladder, which can increase your risk of cancer.

Exposure to certain chemicals can also increase your risk of developing bladder cancer. Your **kidneys** play a key role in filtering harmful chemicals from your bloodstream and moving them into your bladder. Therefore, breathing in, absorbing or ingesting certain chemicals may increase your risk of bladder cancer. Chemicals linked to bladder cancer risk include arsenic and chemicals used in the manufacturing of dyes, rubber, leather, textiles and paint products. Smokers who are exposed to toxic chemicals may have an even higher risk of bladder cancer.

## WHAT ARE THE SYMPTOMS OF BLADDER CANCER?

While many people will experience symptoms that aid in the detection of bladder cancer, others will report not experiencing any problems that are often associated with the disease. While every person is different, it is important to understand that symptoms associated with bladder cancer could also indicate the presence of other problematic urologic conditions. Thus, it is important to consult with your urologist should you experience any of the following symptoms:

- **Hematuria** (blood in the urine)
- Frequent and urgent urination
- Painful urination
- Abdominal pain
- Back pain

## HOW DO UROLOGISTS SCREEN FOR AND DIAGNOSE BLADDER CANCER?

There are currently no screenings available to determine if a person has bladder cancer. However, through routine examinations such as urinalysis, healthcare providers can detect microscopic levels of blood, which will often warrant further testing to determine conclusively if the blood is a result of bladder cancer. The tests that your doctor may order include:

- **Urine cytology:** A sample of your urine is analyzed under a microscope to check for cancer cells.
- **Imaging tests:** Allow your urologist to examine your urinary tract and its surrounding structures and tissue. One of the commonly preformed tests is the computerized tomography (CT) scan, which is a type of X-ray that allows your urologist to see your urinary tract and the surrounding tissues.
- **Cystoscopy:** A medical procedure in which your urologist inserts a narrow tube through your urethra. This tube has a lens and fiber-optic lighting system that allows your urologist to see the inside of your urethra and bladder. This procedure is generally performed using a local anesthetic to make you more comfortable. It is the only procedure that will allow your doctor to locate a tumor, and then perform a possible transurethral resection of bladder tumor.
- **Transurethral resection of bladder tumor: (TURBT):** This procedure is performed during a cystoscopy. Your urologist will pass the cystoscope through your urethra into your bladder and will collect a sample of cells, which will be biopsied to determine if cancer is present. This procedure is performed under general anesthesia. TURBT can also be used to treat bladder cancer.

## WHAT IS BLADDER CANCER TUMOR STAGE?

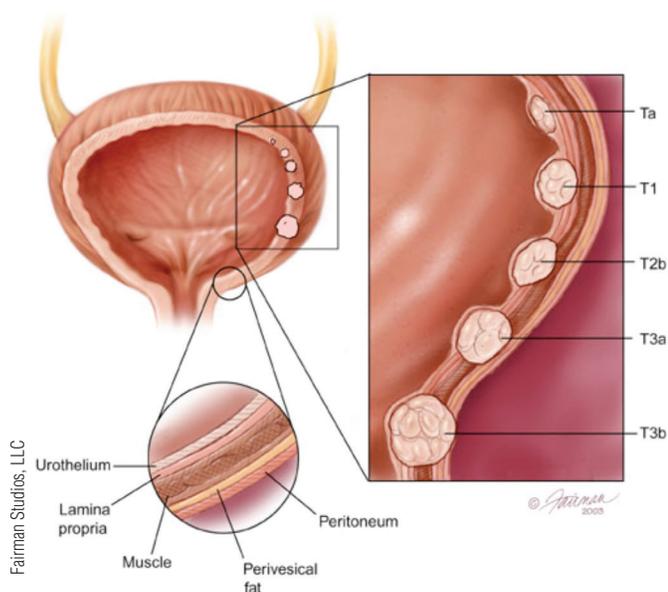
Before any treatment begins, your urologist must first know how far the **tumor** has progressed or moved. The tumor stage and tumor grade provide information about the tumor and how serious it is. Based on that information, your urologist can recommend a course of treatment.

The following are the stages of bladder cancer:

- **Ta:** Noninvasive papillary carcinoma
- **Tis:** Carcinoma in situ—A high-grade cancer that appears as a flat, reddish, velvety patch on the bladder lining
- **T1:** Tumor goes through the bladder lining but does not reach the muscle layer of the bladder
- **T2a and T2b:** Tumor goes into the muscle layer of the bladder
- **T3a and T3b:** Tumor goes past the muscle layer into tissue surrounding the bladder
- **T4a and T4b:** Tumor has spread to neighboring lymph nodes or to distant sites (metastatic disease)

This guide only focuses on Ta, Tis and T1 stages.

### Stages of Bladder Cancer



To determine stage, your doctor may order additional tests such as:

- CT scan
- Magnetic resonance imaging (MRI)
- Bone scan
- Chest X-ray

## WHAT IS BLADDER CANCER TUMOR GRADE?

A **pathologist** is a doctor who specializes in the anatomic (structural) and chemical changes that occur with disease. He or she examines biopsy specimens to determine tumor grade.

A tumor grade depends on the tumors' microscopic appearance. The grade also indicates how aggressive or fast the tumors are likely to grow and spread. The pathologist can see how different the cancerous cells look from normal cells. Grade is one of the most important ways to know if the disease will recur and how quickly it may grow and/or spread. Tumors can be low, intermediate or high grade:

- Low-grade tumor cells are slightly abnormal.
- High-grade tumor cells are very abnormal and disorganized. They are the most aggressive and more likely to grow into the muscle where they are considered more serious.
- Intermediate-grade tumors cells are generally treated like high-grade tumor cells because it is hard to distinguish whether the tumor will be aggressive and in some cases if it will spread.

Stage and grade are two of the most important factors into determining how your cancer will be treated based on its current state.

## WHAT SHOULD BE CONSIDERED IN CHOOSING A TREATMENT?

Patients should talk with their urologist about what to do next. Your urologist can explain the benefits and risks of any type of surgery and other treatments. Other questions to ask include:

- How does your urologist plan to prevent the tumor from recurring or developing to the next stage?
- What kind of discomfort/pain is involved?
- What side-effects may result from the treatments?
- What are the risks of surgery and other treatments?

In addition, some patients seek out the advice of other urologists to get a second opinion about their diagnosis. A second opinion may make sense for patients who have questions about the findings and possible treatment options. There are many valuable resources to help patients find doctors; patients should ask their urologist for the names of specialists who treat bladder cancer. They can also check with their local medical society, nearby hospital or medical school for additional names. Patients wishing to locate a urologist can use the UrologyHealth.org “Find a Urologist” tool to find someone within a 100 miles of their zip code.

## WHAT ARE THE TREATMENT CHOICES FOR NON-MUSCLE INVASIVE BLADDER CANCER?

It is important to understand that no single treatment plan will be the same for every man and woman. You should make sure that you have a thorough conversation with your doctor and medical team about what treatment choice is right for you.

In most cases, before you begin treatment, you will have already undergone a cystoscopic examination, which indicates the presence of the tumor. In addition, you may have had other examinations that allowed your doctor to view the entire urethra and bladder and will assist in future evaluation and follow-up treatment choices. These examinations are critical to providing the following information to your doctor:

1. Position of the tumor
2. Type of tumor
3. Number of tumor(s)
4. Size of tumor(s)

If the tumor(s) is found after close examination of the bladder, your doctor may choose to perform a transurethral resection of bladder tumor (TURBT) as a first step in your treatment.

**TURBT** is generally the initial treatment for non-muscle invasive bladder cancer. The TURBT is a procedure that can be used both for diagnosis and treatment. Using a TURBT procedure to remove the tumor is generally reserved for non-aggressive cancer.

**Benefits:** The TURBT procedure provides a microscopic study of the tumor tissue and tells the tumor type, grade and stage, which help the pathologist with more accurate staging. Repeat TURBT may also improve control of disease.

**Risks:** If TURBT is the only treatment used, the risk is

high that the tumors will return after the TURBT treatment. Approximately 45 percent of patients have a recurrence within one year if TURBT is the only treatment used. This is because some tumors may be missed; they may not be able to be seen or removed; some tumor cells may be shed (come off) during removal and replant in the bladder; and/or a new tumor may be developing. Another risk of the TURBT is bleeding, **perforation** (a hole in the bladder wall) or **dysuria** (painful urination).

Patients with non-muscle invasive cancer located only in the bladder often can receive chemotherapy or immunotherapy drugs after a TURBT via intravesical therapy. This therapy involves chemotherapeutic or immunotherapy drugs placed directly into the bladder by a catheter. This treatment kills only non-muscle-invasive tumor cells and cannot reach tumor cells that have spread to other organs. There are several types of intravesical therapy bladder cancer treatment options:

**Bacille Calmette-Guerin (BCG)** vaccine is an immunotherapy drug therapy. This form of therapy is designed to boost the body’s natural defenses to fight the cancer. It uses substances either made by the body or in a laboratory to bolster, target or restore immune system function. Given through the catheter placed directly into the bladder, BCG attaches to the inside lining of the bladder and attracts the patient’s immune cells to the bladder to fight the tumor. BCG is used mostly for patients with non-muscle-invasive high-grade bladder cancer to reduce the risk of the cancer recurring or progressing. Before BCG treatment, patients may need to have another TURBT to make sure that the cancer has not spread to the muscle. BCG treatment may help patients avoid a **cystectomy**.

**Benefits:** It is a first-line treatment for **carcinoma** that has not spread outside the bladder. It is effective to prevent bladder cancer recurrences following TURBT.

**Risks:** It cannot be used immediately after surgery because of the risk that it will be absorbed into the bloodstream. It may cause flu-like symptoms in some patients as well as infection in a smaller number of patients. Pain and burning may occur during urination and patients may feel the need to urinate frequently.

**Mitomycin C** is a chemotherapeutic agent used to kill cancer cells. It is most often given to patients in their doctor’s office, however, some patients may receive treatment in an outpatient clinic or hospital.

**Benefits:** Mitomycin C is easily absorbed into the bladder and has helped with preventing tumor recurrence. Recently, Mitomycin C has been used more often immediately after TURBT or sometimes within 24 hours after the initial TURBT treatment.

**Risks:** Perioperative Mitomycin C (used immediately after TURBT) should not be used with patients whose bladder may have been punctured during a TURBT since some serious complications can occur. Others include a skin rash, pain and burning during urination, and some patients may feel the need to urinate frequently.

### **Intercalating (inserting) Agents (Doxorubicin, Valrubicin and Epirubicin)**

**Benefits:** These agents are known for good absorption into the bladder, and systemic toxicity is very rare. Doses may vary from three times a week to once a month.

**Risks:** Patients taking intercalating agents may experience bladder irritation, nausea, vomiting, loss of appetite, rash, pain, fatigue, bruising or bleeding.

**Gemcitabine** is used for more advanced bladder cancer.

**Benefits:** In patients who received previous therapy without cure, it is a therapy that may be helpful.

**Risks:** It is still unknown if this treatment is effective for non-invasive bladder cancer.

**Laser-ablation therapy** involves using a laser to “burn” cancer cells.

**Benefits:** The best patients for this therapy have low-grade papillary tumor and a history of low-grade, low-stage tumors.

**Risks:** This technique is not recommended for treatment of new bladder lesions (abnormal areas) because biopsies are required to determine depth of invasion (stage) and tumor grade.

**Conservative management** includes office fulguration (burning of the tumor by electrocautery or laser instrument) and/or cystoscopic monitoring. Certain patients with low risk non-muscle invasive bladder tumors may be managed conservatively.

**Benefits:** Patients can avoid general or regional anesthesia. Only those patients with a well-documented history of low-grade tumors are appropriate for this approach.

**Risks:** The disease may become worse if left untreated. However, the risks of surgery and anesthesia with multiple repeated TURBT procedures in certain patients may be more dangerous than the risk of the disease worsening. This treatment is reserved for only a very select group of patients.

**Cystectomy** is the surgical removal of the bladder. This may be an option for patients with **CIS** or high-grade Ta or T1 cancers that have persisted or recurred after initial intravesical treatment. These cases pose a substantial risk of becoming muscle-invasive cancer. Therefore, these patients should consider having a cystectomy at this point or even as a first choice of treatment. They should ask their doctor for information about the risks of cystectomy. In men, radical cystectomy involves removal of the bladder, prostate and seminal vesicles, and in women, the bladder, urethra, uterus and the front wall of the vagina is removed. Patients should ask their doctors about the methods of urinary reconstruction and the effects of the surgery.

**Benefits:** May be appropriate for high-risk cases when previous treatments have not been successful.

**Risks:** Requires a hospital stay, anesthesia and surgery to remove and replace the bladder with another means of urination. Any of these may result in complications.

## **WHAT FOLLOW-UP CARE WILL I REQUIRE AFTER TREATMENT?**

Bladder cancer patients need lifetime monitoring once they finish treatment. This is because of the high risk that non-muscle invasive bladder cancer tumors frequently reappear or become more aggressive.

Patients usually have follow-up exams every three months during the first two years, every six months for the next two to three years, and once a year thereafter. These exams may include patient history such as voiding symptoms and hematuria, urinalysis and cystoscopy. Follow-up may also include taking images of the kidneys and ureters, especially for high-risk patients. Follow-up treatments may also include intravesical therapies if they are thought to be helpful.



## GLOSSARY

**biopsy:** A procedure in which a tiny piece of a body part (tissue sample), such as the kidney or bladder, is removed (with a needle or during surgery) for examination under a microscope to determine if cancer or other abnormal cells are present.

**bladder:** A thick muscular balloon-shaped pouch in which urine is stored before being discharged through the urethra.

**cancer:** An abnormal growth that can invade nearby structures and spread to other parts of the body and may be a threat to life.

**carcinoma:** Cancer that begins in the skin or in tissues that line or cover body organs.

**carcinoma in situ (CIS):** CIS is a stage of high-grade bladder cancer that appears as a flat, reddish, velvety patch on the bladder lining. CIS is highly malignant and aggressive.

**cystectomy:** The surgical removal of part or all of the urinary bladder.

**cystoscope:** A narrow, tube-like instrument fitted with lenses and a light passed through the urethra to look inside the bladder. The procedure is called cystoscopy (sis-TAW-skuh-pee).

**cystoscopy:** Also known as a cystourethroscopy. An examination with a narrow, flexible tube-like instrument passed through the urethra to examine the bladder and urinary tract for structural abnormalities or obstructions, such as tumors or stones.

**dysuria:** A painful, burning or uncomfortable urination.

**hematuria:** Blood in the urine, which can be a sign of a kidney stone or other urinary problem. Gross hematuria is blood that is visible to the naked eye. Microscopic hematuria cannot be seen but is detected by a urine test.

**immunotherapy:** Also called biologic therapy, it is designed to boost the body's natural defenses to fight the cancer. It uses materials either made by the body or in a laboratory to bolster, target or restore immune system function.

**intravesical therapy:** A treatment method in which drugs are administered directly into the bladder (through a catheter) rather than being given by mouth or injected into a vein. The medications given allow the drugs to affect the cancerous cells in the bladder and bladder lining with little to no effect to other nearby organs and tissues.

**invasive:** Having or showing a tendency to spread from the point of origin to adjacent tissue, as some cancers do. Involving cutting or puncturing the skin or inserting instruments into the body.

**kidney:** One of two bean-shaped organs that filter wastes from the blood and discharge these waste products in urine. The kidneys are located near the middle of the back. The kidneys send urine to the bladder through tubes called ureters.

**lamina propria:** A layer of loose connective tissue between the mucosa and bladder muscle.

**laser:** Device that utilizes the ability of certain substances to absorb electromagnetic energy and re-radiates as a highly focused beam of synchronized single wave-length radiation.

**malignant:** Cancerous

**metabolism:** The chemical processes occurring within a living cell or organism that are necessary for the maintenance of life.

**metastasized:** Cancerous tumor that has spread to another part of the body.

**mucosa:** The inside lining of organs.

**pathologist:** A scientist who is skilled in identifying the cause and progress of diseases by examining tissue and fluid from the body.

**pelvic:** Relating to, involving or located in or near the pelvis

**perforation:** A tiny hole that develops in the bladder after treatment for bladder cancer resection.

**tissue:** Group of cells in an organism that are similar in form and function.

**transurethral resection:** Surgical removal of tissue performed with a special instrument inserted through the urethra.

**tumor:** An abnormal mass of tissue or growth of cells.

**TURBT:** Also referred to as a transurethral resection of the bladder. Surgical procedure performed where a lighted tube is inserted through the urethra into the bladder. It serves as a diagnostic and therapeutic tool in the treatment of bladder cancer.

**ureter:** One of two tubes that carry urine from the kidneys to the bladder.

**urethra:** In males, this narrow tube carries urine from the bladder to the outside of the body and also serves as the channel through which semen is ejaculated. Extends from the bladder to the tip of the penis. In females, this short, narrow tube carries urine from the bladder to the outside of the body.

**urethral:** Relating to the urethra, the tube that carries urine from the bladder to outside the body.

**urothelial:** Cells that comprise a layer of the bladder.

**urinalysis:** A test of a urine sample that can reveal many problems of the urinary system and other body systems. The sample may be observed for physical characteristics, chemistry, the presence of drugs or germs or other signs of disease.

**urinary tract:** The system that takes wastes from the blood and carries them out of the body in the form of urine. Passageway from the kidneys to the ureters, bladder and urethra.

**urinate:** To release urine from the bladder to the outside. Also referred to as “void.”

**urine:** Liquid waste product filtered from the blood by the kidneys, stored in the bladder and expelled from the body through the urethra by the act of urinating (voiding). About 96 percent of which are water and the rest waste products.

**urologist:** A surgeon who specializes in diseases of the male and female urinary systems and the male reproductive system.

## WHERE CAN I FIND ADDITIONAL BLADDER CANCER RESOURCES?

For more information about bladder cancer and other urologic conditions, please visit the AUA Foundation’s Web site, **www.UrologyHealth.org**, or call the Urology Health Line at 1-800-828-7866. You can also refer to the clinical AUA Bladder Cancer Guideline by visiting **www.AUAnet.org/guidelines**.

The purpose of this document is to encourage a discussion between the patient and his/her doctor. This guide was developed by the AUA Foundation and is based on current medical and scientific knowledge. This information is not a tool for self-diagnosis or a substitute for professional medical advice. It is not to be used or relied on for that purpose. Please see your urologist or other healthcare provider regarding any health concerns and always consult a healthcare professional before you start or stop any treatments, including medications.

## About the AUA Foundation

The AUA Foundation is the world’s leading nonprofit urological health foundation – and the official foundation for the American Urological Association – partnering with physicians, researchers, healthcare professionals, patients, caregivers, families and the public to support and improve the prevention, detection and treatment of urological disease. The AUA Foundation relies on contributions to make publications information such as this available to everyone, including those without access to online resources. Please go to **www.UrologyHealth.org** today to make an online donation to help us continue to make this information available and accessible to all. Thank you!

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