



What is Non-Muscle Invasive Bladder Cancer?



Non-muscle invasive bladder cancer (NMIBC) is cancer found in the tissue that lines the inner surface of the bladder. The bladder muscle is not involved.

Bladder cancer is the 6th most common cancer in the United States. Nearly 81,000 people will be diagnosed in the United States with bladder cancer in 2020. Bladder cancer is more common in males than females. Four times more men than women tend to get this disease.

Bladder cancer is more common as a person grows older. It is found most often in the age group of 75-84. More Caucasians than any other ethnicities seem to develop bladder cancer. However, there are more African-Americans who do not survive the disease.

What is Cancer?

Cancer is when your body cells grow out of control. When this happens the body cannot work the way it should. Most cancers form a lump called a tumor or a growth. Some cancers grow and spread fast. Others grow more slowly. Not all lumps are cancers. Cancerous lumps are sometimes called malignant tumors.

What is Bladder Cancer?

The bladder is where the body stores urine before it leaves the body. Urine is what we call the liquid waste made by the kidneys. The bladder is a hollow organ in the pelvis with flexible, muscular walls. The bladder can get bigger or smaller as it fills with urine. Urine is carried to the bladder through tubes called ureters. When you go to the bathroom, the muscles in your bladder will contract. They then push urine out through a tube called the urethra.

When cells of the bladder grow abnormally, they can become bladder cancer. A person with bladder cancer will have one or more tumors in his/her bladder.

How Does Bladder Cancer Develop and Spread?

The bladder wall has many layers, made up of different types of cells. Most bladder cancers start in the urothelium or transitional epithelium. This is the inside lining of the bladder. Transitional cell carcinoma is cancer that forms in the cells of the urothelium.

Bladder cancer gets worse when it grows into or through other layers of the bladder wall. Over time, the cancer may grow outside the bladder into tissues close by. Bladder cancer may spread to lymph nodes nearby and others farther away. The cancer may reach the bones, the lungs, or the liver and other parts of the body. With NMIBC, the tumor will not have spread outside the bladder.

Symptoms

How do you know that you may have bladder cancer? Some people may have symptoms that suggest they have bladder cancer. Others may feel nothing at all. Some symptoms should never be ignored. You may need to talk to a urologist about your symptoms. A urologist is a doctor who focuses on problems of the urinary system and male reproductive system.

Talk to your doctor if you have the following symptoms:

- Hematuria (blood in the urine) - the most common symptom, often without pain
- Frequent and urgent urination
- Pain when you pass urine
- Pain in your lower abdomen
- Back pain

Symptoms You Should Not Ignore

Blood in the urine is the most common symptom of bladder cancer. It is generally painless. Often, you cannot see blood in your urine without a microscope. If you can see blood with your naked eye you should tell your healthcare provider immediately. Even if the blood goes away, you should still talk to your doctor about it.

Blood in the urine does not always mean that you have bladder cancer. There are a number of reasons why you may have blood in your urine. You may have an infection or kidney stones. But a very small amount of blood might be normal in some people.

Frequent urination and pain when you pass urine (dysuria) are less common symptoms of bladder cancer. If you have these symptoms, it's important to see your healthcare provider. He/ she will find out if you have a urinary tract infection or something more serious, like bladder cancer.

Causes

People can get bladder cancer when they come into contact with tobacco or other cancer-causing agents. There also are some risks related to genes and certain types of infections. Another known risk factor is a type of radiation beam aimed at the pelvis. Patients with other cancers, such as lymphomas and leukemia, who receive treatment with the drug cyclophosphamide, may be at a higher risk for bladder cancer.

Smoking is a Big Risk Factor

You are more likely to get bladder cancer if you smoke or breathe in tobacco smoke. Smoking tobacco may be the cause of half of all bladder tumors. If you smoke, you are more likely to get bladder cancer than those who have stopped smoking.

Workplace Exposure is another Known Cause

Some things in the workplace may put you at a greater risk for bladder cancer. Contact with chemicals used to make plastics, paints, textiles, leather and rubber may cause bladder cancer.

Diagnosis

Your healthcare provider will first perform a full medical history and physical exam. He/she may refer you to a urologist for more tests and to form a diagnosis. If your diagnosis is bladder cancer, additional tests will find out the stage of your disease. It will also give your doctor an idea of what treatment is best for you. Some of these tests are described here.

Tests for Non-Muscle Invasive Bladder Cancer

The following tests most likely will be done:

- Urine cytology. The color and content of your urine will be checked. This test will also look at body cells under a microscope to test for cancer cells.
- Blood tests: A comprehensive metabolic panel (CMP), which includes kidney and liver function tests will be among the blood tests your doctor will order.
- A Computerized tomography scan (also known as CT or CAT scans) with a bladder scope "cystoscopy" are often good enough to diagnose bladder cancer.
- Cystoscopy: A doctor will use a thin tube that has a light and camera at the end of it (cystoscope) to pass through the urethra into the bladder. It allows your doctor to see inside the bladder cavity. Usually your doctor will use a flexible cystoscope and a local anesthetic for your exam in the office. The doctor will take a tissue sample with a cystoscope in the operating room. Taking the tissue at this time will allow your doctor to look at the cells. The tissue sample will be sent to a laboratory where they will find out the stage of your cancer. This will help with choosing the right treatment.
- Rigid cystoscopy: The scope that the doctor uses when you are put to sleep is not flexible like the one used in the office, but rigid. This means that it is straight and does not bend. This cystoscope is bigger, has a light at the end, and surgical instruments can pass through it. This allows for more extensive work like the transurethral resection of bladder tumor (TURBT) described below.

If any of these tests suggest that you have bladder cancer, the next step to confirm the diagnosis is a transurethral resection of a bladder tumor (TURBT) described below. You will likely be put to sleep for this procedure. During a TURBT the doctor will both try to remove all visible tumors and take tissue. The tissue sample will be sent to a laboratory where they will find out important information about your cancer. They will also see whether the cancer has spread. This will help with choosing the right treatment.

- **Transurethral resection of bladder tumor (TURBT).** This is a very important procedure for accurate tumor typing, staging and grading. Your doctor can look inside the bladder, take tumor samples and resect (cut away) what he/she sees of your tumor.
- **Blue light cystoscopy with TURBT.** For this test, your doctor uses a catheter to place an imaging solution into your bladder through your urethra. The solution is left in the bladder for about an hour. The doctor then uses the cystoscope to inspect the bladder with regular white light and then with blue light. The bladder cancer cells show up better with blue light.

Other Additional Imaging tests: These tests may help your doctor diagnose and stage bladder cancer.

- **Retrograde pyelogram:** This test uses x-rays to look at your bladder, ureters and kidneys. The test is done during a cystoscopy.
- **Magnetic resonance imaging (MRI)** These tests use a powerful magnetic field, radio waves and a computer to produce detailed pictures of the inside of your body.

Grading and Staging

Grade and stage are two important ways to measure and describe how cancer develops. A tumor grade tells how aggressive the cancer cells are. A tumor stage tells how much the cancer has spread.

Tumor Grade

Grading is one of the ways to know if the disease will come back. It also tells us how quickly the cancer may grow and/or spread.

Tumors can be low or high grade. High-grade tumor cells are very abnormal, poorly organized and tend to be more serious. They are the most aggressive type.

Tumor Stage

The tumor stage tells how much of the tissue has the cancer. Doctors can tell the grade and stage of bladder cancer by taking a small sample of the tumor. This is called a biopsy. A pathologist in a lab examines the sample under a microscope and determines the grade and stage of the cancer.

The stages of bladder cancer are:

- Ta: Tumor on the bladder lining that does not enter any layers of the bladder
- Tis: Carcinoma in situ (CIS)-A high-grade cancer but "flat" cancer. It looks like a reddish, velvety patch on the bladder lining
- T1: Tumor goes through the bladder lining, into the second layer, but does not reach the muscle layer
- T2 : Tumor grows into the muscle layer of the bladder
- T3: Tumor goes past the muscle layer into tissue surrounding the bladder, usually fat surrounding the bladder
- T4: Tumor has spread to nearby structures of the bladder such as the prostate in men or the vagina in females

What Does NMIBC Look Like?

Bladder cancer is described by how far into the wall of the bladder the cancer has grown (which is the clinical stage). Non-muscle invasive bladder cancers are found in the inner layer cells of the bladder. These cancers do not invade the muscular wall. These tumors are staged from Ta (lowest stage) to T1 (highest stage for NMIBC).

Over half of patients with low-grade Ta cancers will have a tumor recurrence. About 6% will progress to a higher stage. High-grade T1 cancers recur at a rate of about 45% and 17% of these will probably progress to a higher stage.

Once diagnosed, the rates of survival are quite favorable for patients with NMIBC. Survival in high-grade disease ranges from about 70-85% at 10 years and a much higher rate for low-grade disease. However, it is important that the disease is diagnosed early. This helps doctors predict the course of the disease and choose the best treatment to stop it from growing.

Treatment

A cancer diagnosis can be very frightening. However, your doctor and medical team are there to help you.

Talk with your health care team about all the available forms of treatment. They will tell you about possible risks and the side effects of treatment on your quality of life.

Your options for treatment will depend on how much your cancer has grown. Your urologist will stage and grade your cancer and assess the best way to manage your care considering your risk. Risks are classified as low, intermediate or high and suggests the likelihood of tumor recurrence and/or progression. Treatment also depends on your general health and age.

Options and Choices for Treatment

Treatments for non-muscle invasive bladder cancer include:

- Cystoscopy transurethral resection of the bladder tumor (TURBT)
- Intravesical Therapy
- Surgery

If these options fail to treat your cancer, your doctor may recommend removing the complete bladder.

TURBT

Transurethral resection of bladder tumor (TURBT) is usually done under anesthesia. The surgery is done through the urethra using a cystoscope, so there is no cutting into the abdomen. You will be given general or spinal anesthesia.

A rigid cystoscope is what your doctor will use for this procedure. This scope is straight and does not bend. It has a light at the end and is bigger and allows surgical instruments to pass through it. Your doctor is able to see inside the bladder, take tumor samples and resect (cut away) the tumor.

If a tumor is clearly seen, the doctor will attempt to remove it all. The doctor may also remove very small samples of other areas of the bladder that may look abnormal. These samples will also be checked for grade and stage. You may be left with a Foley catheter in your bladder after this procedure to allow your bladder to heal.

You may need to have a TURBT more than once to remove all potential tumors. During your follow-up examinations your doctor will check to make sure all the cancer is removed.

Intravesical Therapy

Intravesical ("within the bladder") therapy, is when a treatment drug is put directly into your bladder. The drug is put into the bladder with the help of a catheter (a thin tube that is placed through the urethra). You will hold the drug in your bladder for one to two hours and then pass it out. Intravesical chemotherapy is usually given immediately after surgery.

Intravesical Immunotherapy

Immunotherapy is a treatment that boosts the ability of your immune system to fight the cancer. Bacillus Calmette-Guerin (BCG) is the immunotherapy drug that is used for bladder cancer. BCG also has been used as a tuberculosis vaccine.

Your BCG therapy will probably last about six weeks for the first course. It is usually done in your doctor's office, not in the hospital or operating room. You may get BCG treatment more than once and some patients need many courses.

The BCG drug is inserted into the bladder through a catheter. The therapy triggers the immune system to attack bladder cancer cells. It is one of the most effective treatments for bladder cancer, especially carcinoma in situ (CIS). It is not recommended if you have a weak immune system or certain symptoms.

Side effects can include:

- Urinating often
- Pain when urinating
- Flu-like symptoms
- Joint pain
- Fever or chills
- Bacteria infecting whole body (less common)

Intravesical Chemotherapy

Intravesical chemotherapy is usually given immediately after surgery. With intravesical chemotherapy, drugs that are known to kill cancer cells are placed directly into the bladder, not in the bloodstream. As a result, many common side effects of chemotherapy - like hair loss - can be avoided. Because the drugs only reach the bladder lining, this type of treatment is only recommended for NMIBC.

Mitomycin C and gemcitabine are the most common chemotherapy drugs used for intravesical therapy. It is usually given after the initial TURBT. It helps stop cancer cells from going to another place and growing. It also reduces the recurrence rates. It can also be given as a six-week induction course similar to BCG and some people need more than one course.

Common side effects include:

- The need to urinate often
- Painful urination
- Flu-like symptoms
- Skin rash

Repeat Intravesical Therapy

Some patients may respond to repeat therapy if the cancer returns. If you have high-grade Ta or T1 cancer or CIS, or you tried BCG and it did not work, you may need something else to control the cancer. In this case, you should talk to your doctor about surgery to remove the bladder.

Maintenance Intravesical Therapy

After the bladder is free of disease, your doctor may suggest more treatment with the same drugs to keep the tumor from coming back. This may happen at the first three-month appointment after treatment.

Maintenance therapy is a good choice for people who have had BCG, less so for those who have had chemotherapy drugs. It is given for up to three years after treatment, and generally about every six months for three weeks at a time.

Your doctor will talk to you about whether you are a candidate for maintenance therapy. He/she will also talk about whether intravesical chemotherapy or BCG are good options for you.