

Cancer of the Urinary Bladder

What is the urinary bladder?

The urinary bladder or the ‘bladder’ is a hollow organ present in the pelvis. Most of it lies behind the pubic bone of the pelvis but when full it can extend up into the lower part of the abdomen. Its primary function is to store urine that drains into it from the kidney through tube-like structures called the ureters. The ureters from both the kidneys open into the urinary bladder. The bladder forms a low-pressure reservoir, which gradually stretches out as urine fills into it. From time to time, the muscular wall of the bladder contracts to expel urine through the urinary passage (urethra) into the outside world.

What are the layers of the bladder?

The bladder consists of 3 layers of tissue. The innermost layer of the bladder which comes into contact with the urine stored inside the bladder is called the “mucosa” and consists of several layers of specialized cells called “transitional cells” which are almost exclusively found in the urinary system of the body. These same cells also form the inner lining of the ureters, kidneys and a part of the urethra. These cells form a waterproof lining within these organs to prevent the urine from going into the deeper layers.

The middle layer is a thin lining known as the “lamina propria” and forms the boundary between the inner “mucosa” and the outer muscular layer. This layer has a network of blood vessels and nerves and is an important landmark in terms of the staging of bladder cancer (described in detail later in the article).

The outer layer of the bladder comprises of the “detrusor” muscle and is called the “muscularis”. This is the thickest layer of the bladder wall. Its main function is to relax slowly as the bladder fills up to provide low-pressure urine storage and then to contract to compress the bladder and expel the urine out during the act of passing urine. Outside these 3 layers is a variable amount of fat which lines and protects the bladder like a soft cushion and separates it from the surrounding organs such as the rectum and the muscles and bones of the pelvis.

What is bladder cancer?

Bladder cancer is an uncontrolled abnormal growth and multiplication of cells in the urinary bladder, which have broken free from the normal control mechanisms of the body. Bladder cancer (like cancers of other organs) has the ability to spread (“metastasize”) to other body parts including lungs, bones and liver.

Bladder cancer invariably starts from the innermost layer of the bladder i.e. the mucosa and may invade into the deeper layers as it grows. Alternately, it may remain confined to the mucosa for a prolonged period of time. Visually, it may appear in various forms. Most common is a shrub-like appearance (“papillary”) but it may also appear as a nodule, an irregular solid growth or a flat barely perceptible thickening of the inner bladder wall (details in subsequent sections).

What are the types of bladder cancer?

Bladder cancer is classified on the basis of the appearance of its cells under the microscope (“histological type”). The type of bladder cancer has implications in selecting the appropriate treatment for the disease. For example, certain types may not respond to radiation and chemotherapy as well as others. The extent of surgery required for maximizing the chances of cure may also be impacted by the histological type of the cancer.

The more common types of bladder cancer and their relative incidence is given below:

- Urothelial carcinoma (previously known as “transitional cell carcinoma”) is the most common type and comprises 90-95% of all bladder cancers. It is strongly associated with cigarette smoking.
- Adenocarcinoma of the bladder comprises about 2% of all bladder cancers and is associated with prolonged inflammation and irritation.
- Squamous cell carcinoma comprises 1-2% of bladder cancers and is also associated with prolonged infection, inflammation and irritation such as that associated with long standing stones in the bladder. In certain parts of the Middle East and Africa (e.g. Egypt), this is the predominant form of bladder cancer and is associated with chronic infection caused by Schistosoma worm (blood fluke or bilharzia).
- Other rare forms of bladder cancer include small cell cancer, pheochromocytoma and sarcoma.

What are bladder cancer causes and risk factors?

The most common type of bladder cancer i.e. urothelial carcinoma is very strongly associated with cigarette smoking. As many as 50% of all bladder cancers in men and 30% in women may be caused by cigarette smoke. The longer and heavier the exposure, greater are the chances of developing bladder cancer. The toxic chemicals in cigarette smoke, many of which are known cancer causing substances (“carcinogens”), travel in the bloodstream after being absorbed from the lungs and get filtered into the urine by the kidneys. They then come in contact with the cells in the inner lining of the urinary system including the bladder, and cause changes within these cells, which make them more prone to developing into cancer cells. Quitting smoking decreases the risk of developing bladder cancer but takes many years to reach the level of people who have never smoked. However, as time passes after the quit date, the risk becomes lesser and lesser. In view of the above, it is extremely important for patients with bladder cancer to stop smoking completely since the chances of the cancer coming back after treatment are more in those people who continue to smoke.

People who smoke also have a higher risk of many other types of cancer, including leukemia and cancers of the lung, lip, mouth, larynx, esophagus, stomach and pancreas. Smokers also have a higher risk of diseases like heart attacks, peripheral vascular disease, diabetes, stroke, bone loss (osteoporosis), emphysema, and bronchitis.

Age and family history are other risk factors as is male sex. Most bladder cancer is diagnosed in people over 60 years though in exceptional cases it may be seen in the 3rd or 4th decade of life. Men are more prone to developing bladder cancer probably due to a higher incidence of smoking and exposure to toxic chemicals. A close relative with a history of bladder cancer may increase the predisposition for the development of this disease.

Exposure to toxic chemicals such as arsenic, phenols, aniline dyes, arylamines etc. increase the risk of bladder cancer and may be responsible for up to 25% of cases in some regions. Dye workers, rubber workers, aluminum workers, leather workers, truck drivers, and pesticide applicators are at the highest risk.

Radiation therapy (such as that for prostate or cervical cancer) and chemotherapy with cyclophosphamide (Cytosan) has been shown to increase the risk for development of bladder cancer. Moreover, it may also delay the diagnosis of bladder cancer in patients presenting with symptoms of bleeding in urine since this bleeding may be incorrectly attributed by the patient and/or the physician to the bladder irritation caused by the chemotherapy or radiation (“radiation cystitis”).

Long-term chronic infections of the bladder, irritation due to stones or foreign bodies and infections with the blood fluke prevalent in certain regions of the world (as mentioned earlier) are some other factors, which predispose to bladder cancer.

What are bladder cancer symptoms and signs?

The most common symptom of bladder cancer is bleeding in the urine (“hematuria”). Most often the bleeding is “gross” i.e. visible to the naked eye, occurs in episodes (“episodic”) and is not associated with pain (“painless hematuria”). However, sometimes the bleeding may only be visible under a microscope (“microscopic hematuria”) or may be associated with pain due to the blockage of urine by formation of blood clots. There may be no symptoms or bleeding for prolonged periods of time between episodes lulling the patient into a false sense of security (“I don’t know what the problem was, but it is fine now!”).

Some types of bladder cancer may cause irritative symptoms of the bladder with little or no bleeding. The patients may have the desire to urinate small amounts in short intervals (“frequency”), inability to hold the urine for any length of time after the initial desire to void (“urgency”) or burning sensation while passing urine (“dysuria”). These symptoms occur more commonly in patients with high grade, flat urothelial cancers called “carcinoma in situ” or “CIS” (described subsequently in the section on staging of bladder cancer).

Rarely, patients may present with signs and symptoms of more advanced disease such as a distended bladder (due to obstruction by a tumor at the bladder neck), pain in the flanks (due to obstruction of urine flow from kidney to the bladder by the growing tumor mass in the bladder), bone pains or cough/blood in the phlegm (due to spread to cancer cells to bones or lungs).

How is bladder cancer diagnosed?

Bladder cancer is most frequently diagnosed on investigating the cause of bleeding in the urine that a patient comes in with. The investigations that come in handy in such circumstances are:

- **Urine analysis:** A simple urine test that can confirm that there is bleeding in the urine and can also provide an idea about whether an infection is present or not. It is usually one of the first tests that is asked for by a physician. It does not confirm that a person has bladder cancer but can help the physician in short listing the potential causes of bleeding.
- **Urine cytology:** This test is performed on a urine sample, which is centrifuged and the sediment is examined under the microscope by a pathologist. The idea is to detect malformed cancerous cells that may be shed into the urine by a cancer. A positive test is quite specific for cancer i.e. it provides a high degree of certainty that cancer is present in the urinary system. However, many early bladder cancers may be missed by this test so a negative or inconclusive test doesn't effectively rule out the presence of bladder cancer.
- **Ultrasound:** An ultrasound examination of the bladder can detect bladder tumors. It can also detect the presence of swelling in the kidneys in case the bladder tumor is located at a spot where it can potentially block the flow of urine from the kidneys to the bladder. It can also detect other causes of bleeding such as stones in the urinary system, prostate enlargement etc. which may be the cause of the symptoms or may co-exist with a bladder tumor.
- **CT scan/MRI:** A CT scan or MRI provides greater visual detail than can be afforded by an ultrasound exam and may detect smaller tumors in the kidneys or bladder than can be detected by an ultrasound. It can also detect other causes of bleeding more effectively than ultrasound specially when intravenous contrast is used.
- **Cystoscopy and biopsy:** This is probably the single most important investigation for bladder cancer. Since there is always a chance to miss bladder tumors on imaging investigations (ultrasound/CT/MRI) and urine cytology, it is recommended that all patients with bleeding in the urine, without an obvious cause, should have a cystoscopy performed by a urologist as a part of the initial evaluation. This entails the use of a thin tube-like optical instrument connected to a camera and a light source ("cystoscope"). It is passed through the urinary passage into the bladder and the inner surface of the bladder is visualized on a video monitor. Small or flat tumors which may not be visible on other investigations can be seen by this method and a piece of this tissue can be taken as a biopsy for examination under the microscope. The presence and type of bladder cancer can be diagnosed most effectively by this method.
- **Newer biomarkers like NMP 22 and Fluorescent in-situ hybridization (FISH)** are currently in use to detect bladder cancer cells by a simple urine test. However, they have not yet achieved the level of accuracy to replace cystoscopy and cytology in the diagnosis and follow up of bladder cancer.

How is bladder cancer staging determined?

Bladder cancer is staged using the Tumor Node Metastases (TNM) system developed by the International Union against Cancer (UICC) in 1997.

The Tumor or the T stage is accorded by a pathological examination of the tumor specimen removed surgically. This refers to the depth of penetration of the tumor from the innermost lining to the deeper layers of the bladder. The T stages are as follows:

- Tx - Primary tumor cannot be evaluated
- T0 - No primary tumor
- Ta - Noninvasive papillary carcinoma (tumor limited to the innermost lining or the “epithelium”)
- Tis - Carcinoma in situ or CIS ("flat tumor")
- T1 - Tumor invades connective tissue (lamina propria) under the epithelium (surface layer)
- T2 - Tumor invades muscle of the bladder
 - T2a - Superficial muscle affected (inner half)
 - T2b - Deep muscle affected (outer half)
- T3 - Tumor invades perivesical (around the bladder) fatty tissue
 - T3a – microscopically (visible only on examination under the microscope)
 - T3b - macroscopically (e.g., visible tumor mass on the outer bladder tissue)
- T4 - Tumor invades any of the following: prostate, uterus, vagina, pelvic wall, abdominal wall

The Node or the N stage is determined by the presence and extent of involvement of the lymph nodes in the pelvic region of the body near the urinary bladder. The N stages are as follows:

- Nx - Regional lymph nodes cannot be evaluated
- N0 - No regional lymph node metastasis
- N1 - Metastasis in a single lymph node < 2 cm in size
- N2 - Metastasis in a single lymph node > 2 cm, but < 5 cm in size, or Multiple lymph nodes < 5 cm in size
- N3 - Metastasis in a lymph node > 5 cm in size

The Metastases or the M stage signifies the presence or absence of the spread of bladder cancer to other organs of the body.

- Mx - Distant metastasis cannot be evaluated
- M0 - No distant metastasis
- M1 - Distant metastasis

The proper staging of bladder cancer is an essential step, which has significant bearings on the management of this condition. The implications of bladder stage are:

- It helps select proper treatment for the patient. Superficial disease (Ta/T1/Tis) can generally be managed with less aggressive treatment as compared to Invasive disease (T2/T3/T4)
- Invasive tumors have a higher likelihood of spread to lymph nodes and distant organs as compared to superficial tumors
- The chances of cure and long term survival progressively decrease as the bladder cancer stage increases
- Staging allows proper classification of patients into groups for research studies and study of newer treatments

What is bladder cancer grading?

Grading of bladder cancer is done by the pathologist by examination of the tumor specimen under a microscope. It is a measure of the extent by which the tumor cells differ in their appearance from normal bladder cells. Greater the distortion of appearance, higher the grade. High grade cancers are more aggressive than low grade ones and have a greater propensity to invade into the bladder wall and spread to other parts of the body.

- Grade 1 cancers have cells that look very much like normal cells - they are called 'low grade' or 'well differentiated' and tend to grow slowly and are not likely to spread
- Grade 2 cancers have cells that look more abnormal - they are called 'medium grade' or 'moderately differentiated' and may grow or spread more quickly than low grade
- Grade 3 cancers have cells that look very abnormal - they are called 'high grade' or 'poorly differentiated' and are more quickly growing and more likely to spread

In 2004, the World Health Organisation developed a new grading system for bladder cancer. This system divides bladder cancers into the following groups.

- Urothelial papilloma - non cancerous (benign) tumour
- Papillary urothelial neoplasm of low malignant potential (PUNLMP) - slow growing and unlikely to spread
- Low grade papillary urothelial carcinoma - slow growing and less likely to spread
- High grade papillary urothelial carcinoma - more quickly growing and more likely to spread

Stage and grade of bladder cancer play a very important role not just in deciding the treatment that an individual patient should receive, but also in quantifying the chances of success with that treatment. Of note, Carcinoma in situ (CIS or Tis, as mentioned in the section on staging) is always high grade.

What is surgery for bladder cancer?

The initial surgical procedure that a patient undergoes after the diagnosis of bladder cancer is established is usually a “Transurethral resection of bladder tumor” or “TURBT”. It is done with the help of special instruments attached to a cystoscope

(mentioned earlier in the section on investigations) and involves cutting out the tumor and removing it from the bladder with the help of an electrical cautery device. This surgery is done through the normal urinary passage and does not involve an external cut on the body. It is the initial treatment of bladder cancer as well as a staging procedure since the specimen retrieved from the surgery is sent to a pathologist who gives his/her inference on the depth of invasion of the tumor in the bladder wall (T stage) as well as the grade (high/low). Further treatment depends to a large extent on the findings of this initial surgery as well as the other staging investigations and is covered in the sections to follow.

What is the treatment of superficial bladder cancer?

Superficial bladder cancer is a cancer which has not invaded the muscle wall of the bladder and is confined to the inner lining of the bladder. The T stage is Ta, T1 or Tis (also known as Carcinoma in situ or “CIS”). After the initial TURBT or biopsy in case of CIS, the subsequent treatment in these cases may involve observation with regular follow up with cystoscopy examinations of the bladder, instillation of medications in the bladder, or in certain cases, surgical removal of the bladder (“radical cystectomy”).

Small low grade, superficial bladder cancers may not require aggressive management after the initial TURBT and may be simply followed up by doing repeated cystoscopy examinations at regular intervals (usually every 3 to 6 months for the first year and then at increasing intervals). Recurrent tumors may be surgically removed or fulgurated (“burnt out”) with special instruments passed through the cystoscope. It is very important to note that 30-40% of these tumors tend to recur and these recurrences may not be associated with any symptoms. Hence, it is imperative to stick to a regular follow up protocol to ensure that the disease does not go out of control. It has also been shown that a single dose of a chemotherapy medication (e.g. Mitomycin C) put inside the bladder immediately after a TURBT can decrease the chances of recurrence within the first 2 years after surgery.

High grade, larger, multiple or recurrent superficial bladder cancers may require additional treatment after the initial TURBT. One of the most effective and widely used medications is called the Bacille Calmette Guerin, commonly referred to as BCG. It is a modified form of a bacterium that causes tuberculosis in cattle (*Mycobacterium bovis*). It is also commonly used for vaccination against human tuberculosis. It is instilled into the bladder in the form of a solution using a catheter placed in the urinary passage. It acts by stimulating the immune system of the body to act against the cancerous bladder cells and prevent their growth and development. It has been shown to decrease the chances of recurrence of bladder cancer as well as its invasion into the muscle layer of the bladder. However, it is only partially effective in achieving these objectives and its use does not obviate the need for a regular follow up. It is usually administered in 6 initial doses at weekly intervals followed by a “maintenance” schedule which is usually recommended for at least 1 year but may last as long as 3 years.

Patients, who do not respond to BCG treatment, recur in spite of treatment or those who have medical issues which preclude the use of BCG, may require other forms of treatment. These include bladder instillation of immunotherapy agents such as

Interferon or chemotherapy medicines like Valrubicin, Mitomycin C, Epirubicin or Adriamycin. In general, these medications are not as effective as BCG and help only a small minority of patients who have not responded to BCG.

In patients who have an aggressive form of high grade superficial bladder cancer and those who have not responded or recurred in spite of treatments mentioned above, a more aggressive form of treatment may be warranted. This is usually in the form of a major surgical procedure called “radical cystectomy”. It entails removal of the bladder and the prostate and diverting the urinary stream using parts of the intestine. This surgery will be described in the subsequent section on treatment of invasive bladder cancer.

What is surveillance for bladder cancer?

Patients diagnosed and treated with superficial bladder cancer need to be followed up regularly to detect recurrences and treat them effectively. A typical follow up protocol includes:

- Cystoscopy and Urine cytology every 3 months for 2 years, every 6 months for the next 2 – 3 years and annually thereafter.
- Imaging study (CT scan/Intravenous Urogram) of the kidneys and ureters once every year (especially for high grade tumors/those associated with CIS)

Cystoscopy and cytology detects recurrence in the bladder itself while CT/IVU is used to detect a tumor in the kidneys and ureters. Patients with bladder cancer are more likely to get “upper tract” tumors, which arise from the inner lining of these organs and share a common origin with bladder tumors. The risk of upper tract recurrence depends on the stage and grade of the initial disease and the response of the tumor to BCG. Individuals with recurrent high grade bladder tumors can have up to a 20% risk of developing a tumor in the upper tracts and need to be followed closely in this regard.

Commercially available tumor markers which are used to test urine samples for evidence of bladder tumor recurrence are also being used in follow up protocols. However, their exact role is undefined as of now and they are not considered an adequate substitute for cystoscopy and cytology. Some of these markers are NMP 22, BTA Stat, BTA Trak and UroVysion.

What is the treatment of muscle-invasive bladder cancer?

Muscle invasive bladder cancer generally requires a more aggressive treatment plan than superficial bladder cancer. The standard and most effective treatment is the surgical removal of the bladder and diversion of the urinary stream using intestinal segments. This procedure, known as radical cystectomy, is a major operation and a thorough discussion and counselling of the risks, complications and benefits is warranted prior to it.

In short, the procedure entails removal of the bladder, prostate, seminal vesicles and the fatty tissue around the bladder through an incision made in the abdomen. The surgery also includes removal of lymph nodes in the pelvis on both sides of the

bladder to detect their involvement with the cancer. This helps in deciding further management after surgery including the need for chemotherapy. It has been shown that patients who undergo a thorough lymph node dissection have a better chance of cure as compared to patients who either do not receive one or undergo a less extensive dissection.

Radical cystectomy can be performed via open surgery, laparoscopy or with robotic assistance. It has been shown that the outcomes in term of cancer control and cure rates do not differ between these different approaches. However, the use of laparoscopic and robotic approaches significantly decreases blood loss during the surgery, decreases the need for blood transfusions and may help in early recovery by decreasing post operative pain at the surgical site. An additional advantage of the robot is that it permits an enhanced magnification of the surgical field with 3 dimensional vision which helps to enhance surgical precision. It is very important to note that all these approaches can achieve comparable results in terms of cancer control in the hands of surgeons skilled and experienced in a particular modality. So, the comfort factor and experience of an individual surgeon in a particular approach should play a major role in the patient's decision regarding selection of the approach for surgery.

Once the bladder has been removed, the urine needs to be diverted. There are 3 popular ways of doing that. All of them require the use of segments of the intestine which are still connected to their blood supply but have been disconnected from the gastro-intestinal tract.

- **Ileal conduit** is the most extensively used form of urinary diversion. It is also the simplest and the least time consuming form of diversion and has the least chances of complications in the short and long term. This entails the use of an intestinal segment, one end of which is connected inside the body to the ureters that drain urine into it from the kidneys, while the other end is brought out to the level of the skin and is covered by an external appliance (a "urostomy bag"). The urine from the kidneys continuously drains into the bag through the ureters and the "ileal conduit". The bag can be emptied at regular intervals or when it is nearly full by opening a tap-like attachment at the lower end of the bag. The major advantage of this procedure is that is relatively straightforward to perform with least chances of complications. The disadvantages include the need to wear a bag all the time and the resultant negative impact that may occur on body image.
- **Orthotopic neobladder** entails the creation of a new bladder ("neobladder") with the help of an intestinal segment and connecting it to the natural urinary passage so that a person may be able to pass urine "more normally". The major advantage of this procedure is that it avoids the need to wear a bag and the patient can pass urine in a more natural fashion. However, this is a more difficult procedure with a longer recovery period and may lead to some short term and long term complications including persistent urinary leakage and inability to pass urine requiring the use of self intermittent catheterization (passage of a tube into the urinary passage to empty the bladder). Some senior patients and those with certain medical conditions that affect the

function of the kidneys or impair their ability to self catheterize may be best served by the ileal conduit rather than the neobladder.

- **Continent catheterizable pouch (e.g. “Indiana pouch”)** is a form of neobladder which is not connected to the normal urinary passage but instead has an opening or a “stoma” at the level of the skin on the abdomen through which a catheter can be passed to empty it periodically. This has a valve-like mechanism which prevents the leakage of urine through this opening thereby precluding the need to wear a bag. It is used in patients desirous of and fit for a continent urinary system while being unsuitable for an orthotopic neobladder due to certain circumstances such as cancer at the point where the bladder joins the urethra.

Radical cystectomy (open, laparoscopic or robot assisted) combined with one of the 3 urinary diversions is the “gold standard” for the treatment of muscle invasive and selected cases of high grade superficial bladder cancer. Certain patients, however, may be unfit or unwilling to undergo this surgery. These patients can often undergo a combination of extensive TURBT + Chemotherapy + Radiation in an attempt to cure or control the disease without the need to remove the urinary bladder surgically. Most experts believe that this regime may not be as effective as a radical cystectomy but can be used as an option in unfit/unwilling patients. Radiation to the bladder can however lead to its own set of problems and complications including radiation damage to the bladder and rectum giving rise to bleeding and irritative symptoms (“radiation cystitis” and “radiation proctitis”).

What is chemotherapy for bladder cancer?

Patients who are diagnosed with metastatic bladder cancer (M stage – M1), i.e. cancer, which has spread to other parts of the body, are usually treated with chemotherapy. Besides, chemotherapy may also be used in cases of “locally advanced” bladder cancer (T stage – T3 and above and/or N stage – N1 and above) in an attempt to decrease the chances of the cancer coming back after radical cystectomy. This is known as “adjuvant chemotherapy”. Another strategy entails administering “neoadjuvant chemotherapy” by giving these medications before radical cystectomy in an attempt to improve the results of surgery and decrease the size of the tumor.

It has been shown that chemotherapy has the potential to control metastatic bladder cancer and increase the chances of cure when used in a “neoadjuvant” or “adjuvant” setting along with surgery. However, chemotherapy has its own set of side effects and may not be tolerated by all individuals.

The time honored chemotherapy regimen for bladder cancer is called the MVAC. It is a combination of 4 medications given in cyclical form.

- M – Methotrexate
- V – Vinblastine
- A – Adriamycin (Doxorubicin)
- C – Cisplatin

Some patients with heart disease may not be in a condition to receive Adriamycin and may receive CMV instead (CMV = MVAC - Adriamycin)

An alternative regimen is a combination of two medications, Gemcitabine and Cisplatin. This is increasingly being used nowadays since some studies have shown that it is equally effective as the MVAC regime with fewer side effects.

Cisplatin, which is the main medication in all these regimens, can not be given to patients who have an abnormal kidney function. In this case, it may be substituted by Carboplatin, which however, is not as effective as Cisplatin based chemotherapy.

What is the prognosis for bladder cancer?

The most important factors that impact the prognosis (or the chances of control and cure) of bladder cancer are the Stage and Grade of the tumor. Lower the Stage and Grade, better the outlook. Other factors such as number, size, pattern of recurrence (if any), response to initial treatment like BCG, coexistent carcinoma in situ and certain genetic mutations also play a role.

For low- risk superficial bladder cancer (Ta, low grade), the chances of recurrence are about 15% in 1 year and 32% in 5 years after the initial diagnosis. This necessitates regular follow up, even in these low risk tumors. However, unlike the more aggressive variants of bladder cancer, the chances of progression (i.e. chances of the tumor invading into the deeper layers of the bladder) are less than 1%. Typically, these tumors, even when they recur, do so in the same stage and grade as the original tumor and do not compromise the life expectancy of the patient.

High-risk superficial tumors are those that are high grade, T1 tumors and/or are associated with extensive areas of carcinoma in situ. Multiple tumors, large tumors and those that recur despite BCG treatment are also at an increased risk for recurrence and progression. These tumors have a recurrence rate in the range of 61% and 78% at 1 and 5 years respectively. They are also much likely to invade into the deeper layers with progression rates of 17% and 45% at 1 and 5 years. These tumors need to be managed and followed up more aggressively since they have a potential to invade and spread to other parts of the body thereby shortening the life expectancy of the patient.

After radical cystectomy, survival depends mostly on the stage of the disease. 5-year disease specific survival (i.e. the percentage chance that an individual will NOT die because of bladder cancer in the first 5 years after surgery) for various stages after a radical cystectomy is as follows.

- T2, N0: 70 – 80%
- T3, N0: 40 – 50%
- T4, N0: 25 – 30%
- N+ (patients with lymph node involvement): 15 – 20%

5-year survival is rare in patients with metastatic disease despite chemotherapy. It is important to note that these are statistics compiled for large groups of patients. Every individual patient is different from the others and may have outcomes starkly different from those mentioned in the average analysis above.

Can bladder cancer be prevented?

The best way to prevent bladder cancer is to avoid exposure to agents that cause the disease. People who don't smoke are 3 – 4 times less likely to get bladder cancer as compared to smokers. Continuing to smoke after the diagnosis of bladder cancer portends a poorer outcome and increases the chance of the disease coming back after treatment. Avoidance of occupational exposure to cancer causing chemicals such as aniline dyes may also be important. Despite research in this area no medication or dietary supplement has been conclusively demonstrated to decrease the risk of bladder cancer in normal individuals.

Where can people find more information on bladder cancer?

A number of online resources are available for bladder cancer patients to gain more insight into this disease and its management. Bladder Cancer Advocacy Network (www.bcan.org) is one such resource, which provides a downloadable patient information handbook and links to patient support groups.

<http://www.cancer.gov/cancertopics/types/bladder> provides a link to bladder cancer information at the website of the National Cancer Institute.

<http://www.eortc.be/tools/bladdercalculator> features a calculator, which predicts the chances of recurrence and progression of superficial bladder cancer after initial treatment on the basis of certain tumor characteristics.

What research is being done on bladder cancer?

Bladder cancer is a topic of intense scientific research currently. Basic science research is focused on finding and studying the genetic alterations (or changes in the human DNA) that predispose to bladder cancer in the hopes to discover new medications and treatments for curing the disease. Other areas of research include:

- Newer molecular diagnostic tests to detect and follow up bladder cancer thereby avoiding the need for invasive tests like frequent cystoscopy examination.
- Targeted therapy, which acts on genetic pathways responsible for bladder cancer as the next generation of chemotherapy for the disease.
- Newer surgical techniques, such as robotics have been incorporated to improve precision and accelerate patient recovery after bladder cancer surgery.
- Stem cell research for creation of urinary diversion during radical cystectomy without the need for intestinal segments.

This field is likely to see significant advances in the years to come and hopefully would provide effective treatment strategies and hope for the millions of bladder cancer patients worldwide.

Bladder cancer at a glance

- Bladder cancer is one of the common cancers affecting men and women

- The most common symptom is bleeding in the urine (hematuria)
- Cigarette smoking is the most significant risk factor with smokers 3 – 4 times more likely to get the disease than nonsmokers.
- Bladder cancer can be sub-divided into superficial and muscle invasive with the former having much better treatment outcomes than the latter
- The initial treatment for bladder cancer is transurethral resection (TURBT), which removes the tumor from the bladder and provides information regarding stage and grade of the tumor.
- Low-grade superficial tumors (Ta) are treated with TURBT followed by an optional instillation of a single dose of a chemotherapy medication in the bladder to reduce recurrence rates. These tumors have a high recurrence rates but a very low chance of progression to higher stages.
- High-grade T1 tumors have high chances of recurrence and progression and may need additional treatment in the form of BCG or chemotherapy instillation in the bladder. Patients unresponsive to these may be best treated by radical cystectomy.
- Radical cystectomy provides the best chances of cure in patients with muscle invasive disease.
- Cisplatin based chemotherapy is used in patients with metastatic disease at presentation or those in which bladder cancer cells are present outside the bladder wall or in lymph nodes during radical cystectomy.

Reference

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