



FREQUENTLY ASKED QUESTIONS ABOUT BLADDER CANCER

How common is bladder cancer?

Cancer of the urinary bladder is the fourth most common cancer in men and the ninth in women. Approximately 63,210 people develop bladder cancer each year in the United States, and 13,180 individuals. The spectrum of bladder cancer includes superficial, invasive, and metastatic disease, each with its own clinical behavior, prognosis, and treatment.

What are symptoms of bladder cancer?

The diagnosis of bladder cancer is often delayed due to the similarity of symptoms to those of benign disorders such as urinary tract infection, prostatitis, and the passage of kidney stones. The most common presenting symptom is **hematuria**, which is typically painless. However painless hematuria is not proof of bladder cancer and the majority of these patients (85%) have other causes.

When **pain** is experienced, it is usually as a result of locally advanced or metastatic tumor. Its distribution is related to the size and location of the primary tumor or its metastases: Flank pain may result when a tumor obstructs the ureter at any level (bladder, ureter or renal pelvis). Although usually a sign of a muscle-invasive disease, large superficial tumors located at the ureteral orifice may also cause symptomatic obstruction. The pain is similar to that experienced with the passage of urinary stones, and may or may not be associated with hematuria. Bone pain may indicate the presence of metastases

How is bladder cancer diagnosed?

Radiographic imaging of the upper tract can consist of either a helical computed tomography (CT) scan of the abdomen/pelvis with urography or intravenous pyelography (IVP) plus renal ultrasound (US).

Cystoscopy — Cystoscopy forms the mainstay of diagnosis and staging of bladder cancer. The cystoscope is inserted into the bladder, and urine is obtained to determine the presence or absence of malignant cells. The bladder is inspected visually, and a detailed description of the size, number, location, and growth pattern (papillary or solid) of all lesions is recorded. Biopsy specimens are taken from visible tumors, or the tumors are resected transurethrally in stages to determine the histologic subtype and depth of invasion into the tissue layers of the bladder.

Urine immunocytochemistry and proteomics assays — The limitations of cytology and the invasiveness of cystoscopy for detecting bladder cancer have generated interest in other non-invasive diagnostic tools, such as urine immunocytochemistry (ImmunoCyt test) and proteomics assays for the nuclear matrix protein NMP22 (NMP22 BladderChek test).



NMP22 proteomics assay— Proteomics refers to the analysis of protein expression in tissues, serum, and other biologic samples in order to identify and/or characterize malignant tumors on the basis of unique protein expression patterns. (The NMP BladderChek test is approved in the United States for diagnosis of bladder cancer.

Several other tests are approved in the United States (eg, BTA Stat, BTA TRAK, UroVysion tests) for the detection of recurrent bladder tumors, but none is approved for widespread screening, initial diagnosis, or risk assessment. None of these tests has shown sufficient diagnostic reliability to eliminate the need for cystoscopy for either primary or recurrent bladder tumors

IVP— An intravenous pyelogram (IVP) allows visualization of the bladder and upper tracts, but are gradually being replaced by helical CT scanning. CT may demonstrate extravesical extension, nodal involvement in the pelvis or retroperitoneum, visceral, pulmonary or osseous metastasis, and upper tract function, tumor involvement, or obstruction. Although CT provides better visualization of tumors than US, it may also miss tumors <1 cm in size, particularly those in the bladder trigone or dome, and cannot differentiate depth of bladder wall invasion

Once the diagnosis of cancer is secured, other imaging studies may be appropriate to evaluate for extravesical extension and other sites of disease (eg, metastatic lesions). The decision whether or not to perform additional diagnostic studies is based upon the results of the physical and bimanual examination, cystoscopy and the histologic/cytologic evaluation. Because bladder tumors often occur in the elderly, a general medical evaluation is essential to document significant comorbid conditions which might interfere with appropriate treatment regimens (ie, ability to tolerate general anesthesia, prolonged surgery, chemotherapy).

Chest X ray— Chest x rays are used as an initial screening tool and for periodic monitoring in patients at risk for pulmonary metastasis, although they are insensitive for lesions <1 cm.

Bone scan— Radionuclide bone scans to assess the presence of bone metastasis are recommended only in patients with invasive or locally advanced tumors and either skeletal symptoms or unexplained elevations in serum alkaline phosphatase. Increased uptake is a nonspecific finding that may represent areas of degenerative change, trauma, previous fracture sites, or metastatic disease. Plain radiographs, CT, or MRI of suspicious areas may be necessary to confirm a metastasis

How are bladder tumors classified and what is the survival rate?

Bladder tumors are now classified as either low or high grade.

Nodal and metastatic disease— The staging system categorizes nodal disease based on the number and size of the involved nodes. It also accounts for metastases to specific sites. Once invasion outside the bladder or nodal disease is documented,



outcomes without systemic therapy are poor, with overall 5-year survival rates ranging from 4 to 35 percent. A similar bleak prognosis is also

apparent for patients with distant metastases (i.e. lung, liver, bone), whose median survival rates range from 6 to 9 months. Few patients survive 5 years when metastatic disease is present.

The most important prognostic determinant to be derived from staging is whether the tumor is confined to the bladder or not.

The major concern after surgical removal of the cancer relates to the tendency of the cancer to have already spread, though it may be undetectable by scans or blood tests. Therefore a number of studies have attempted to eradicate “hidden” tumor disease by using chemotherapy as an adjuvant therapy.

Data are conflicting as to the role of adjuvant systemic chemotherapy because no randomized comparisons of an adequate sample size have definitively shown a survival benefit of such therapy. Nevertheless, the results of currently available trials do show that adjuvant chemotherapy can delay recurrences, which, for most patients, is benefit enough to justify the routine administration of chemotherapy in patients at a high risk for relapse. Tumors that have grown through the bladder wall (T3b or T4) **or any tumors with lymph node involvement or growth into blood vessels (vascular invasion)** have a high risk (greater than 50 percent) of systemic relapse and therefore should be treated with adjuvant chemotherapy, such as M-VAC or CMV (cisplatin, methotrexate, and vinblastine). Because of the higher risk of relapse, imaging studies are advised at 3-month intervals during the first 2 years, every 6 months in year 3, and annually for years 4 and 5. A yearly IVP is also recommended for the first 3 years. If a relapse is documented, salvage chemotherapy is advised with a regimen to which the patient has not been previously exposed. ECOG has initiated a randomized trial of four cycles of Taxol/Carboplatin vs. four cycles of MVAC for patients with pT4 and/or node-positive disease.

Patients with tumors of a lesser stage are considered to be at low risk and do not necessarily require adjuvant chemotherapy. They should be monitored with urinary cytology, a urethral wash (if the urethra has not been removed), and liver function tests at 3-month intervals. A CT scan is advised after surgery as a baseline and at 6-month intervals for the first 3 years, along with an annual IVP. Both examinations should be repeated once during year 4 and year 5.