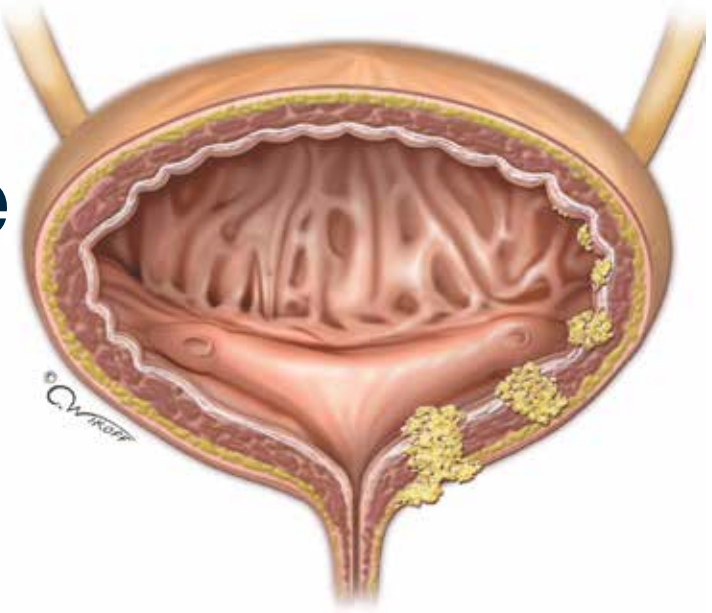

Muscle-invasive bladder cancer

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Early diagnosis of muscle-invasive bladder cancer can be life saving. Treatment will depend on the staging of the cancer.

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Bladder cancer is the ninth most common malignancy worldwide. Although the male to female ratio of those who develop bladder cancer is almost four to one, women are more likely to present with muscle-invasive disease and subsequently have poorer prognosis.

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Given the bladder's key function as a storage unit, it has prolonged exposure to urine and its contents. Smoking (active and passive) and work-related carcinogens remain the key risk factors for developing bladder cancer. Smoking cessation reduces the long-term risk of developing bladder cancer.

Life expectancy in patients with bladder cancer varies with the clinical or pathological stage of the cancer. Patients with muscle-invasive bladder cancer have a five-year life expectancy of 30 to 70%. Although muscle-invasive disease represents a minority of cases, early diagnosis can be life saving.

PRESENTATION

Patients with muscle-invasive bladder cancer typically present with painless haematuria. Painless haematuria has both benign and malignant causes that should be differentiated with further investigation in conjunction with urgent urological assessment. Patient evaluation should include diagnostic imaging, urine-based tests (such as voided urine cytology) and direct cystoscopic examination of the bladder.

Some patients with bladder cancer present with persistent irritative symptoms, such as dysuria, urgency or frequency. These symptoms may reflect the presence of carcinoma in situ or muscle-invasive bladder cancer. Common benign causes for these symptoms, such as infection, should be excluded. Thereafter, patients with persistent irritative symptoms should be referred for further urological assessment.

TUMOUR GROWTH AND CLASSIFICATION

Bladder cancer has the capacity to grow progressively from the urothelium (inner lining of the bladder), through the bladder wall into the perivesical tissues and then spread to distant organs such as lymph nodes, liver, lung and bones.

The tumour (T) component of TNM (Tumour Node Metastasis) staging classification describes this outward growth (depth of invasion) and reflects worsening prognosis (Box).[1] Bladder cancer

THE TUMOUR STAGES OF BLADDER CANCER

Bladder cancers are often described based on their invasion of the bladder wall:

- noninvasive bladder cancers are still in the bladder lining, the urothelium
- invasive bladder cancers are those that have grown into the deeper muscle layer of the bladder wall.

The vast majority of bladder lesions are papillary in nature. Less frequently, tumours are solid, or flat.

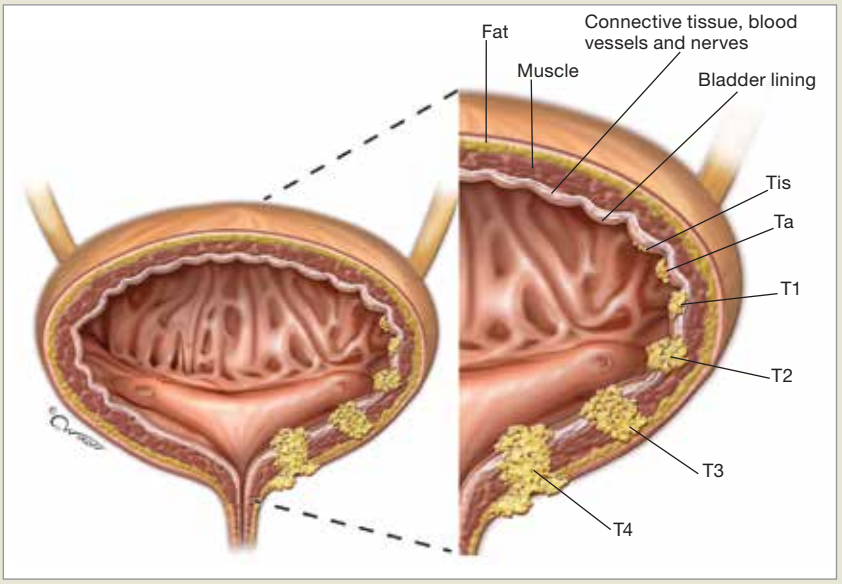

Figure. The T stages of bladder cancer.

The T category of the TNM staging classification for bladder cancer describes the extent of the cancer spread, as listed below.[1] The N category indicates spread to nearby lymph nodes, and the M category, spread to distant sites.

TX: Primary tumour cannot be assessed
T0: No evidence of primary tumour
Ta: Noninvasive papillary carcinoma
Tis: Carcinoma in situ; a high risk flat tumour
T1: Tumour invades the subepithelial connective tissue
T2: Tumour invades the muscle layer, the muscularis propria
T3: Tumour invades through the muscle layer into the perivesical fat layer
T4: Tumour invades surrounding organs or body wall

is broadly regarded to be either nonmuscle-invasive or muscle-invasive. About 30% of patients have muscle-invasive disease at presentation.

Most patients with bladder cancer have low-grade, superficial (or noninvasive) disease. This carries a low risk of progression, but high likelihood of recurrence after treatment. A more serious form of bladder cancer is high-grade disease, with or without carcinoma in situ, which may be superficially invasive (pathological stage T1). This clinical picture presents a high risk of both recurrence and progression, and affected patients benefit significantly from early assessment.

DIAGNOSIS

Bladder cancer is typically diagnosed with a cystoscopy, during which the lesion is resected (transurethrally). Histopathological assessment is used to determine both the grade of the lesion and depth of invasion. Early diagnosis is beneficial, with improved survival rates for patients with high-risk or muscle-invasive disease.

Having made a diagnosis of muscle-invasive disease, staging of the lesion is performed with a CT of the chest, abdomen and pelvis.[2] This should involve delayed-phase imaging to assess the upper tract urothelium, and exclude a lesion in either the kidneys or ureters. MRI may be useful in assessing extravesical disease, to delineate the extent of the tumour beyond the bladder.

TREATMENT

Cystectomy

After adequate resection, patients with high-grade superficially invasive (stage T1) bladder cancer may be offered intravesical treatment with immunotherapy such as Bacillus Calmette-Guerin (BCG) or, in some cases, early cystectomy. Survival after early cystectomy is significantly better in patients with high-risk nonmuscle-invasive disease than in those with disease that has progressed to muscle invasion (about 80% *vs* 50 to 60% five-year survival).[3]

Open radical cystectomy with extended lymph node dissection remains the treatment of choice for patients with localised bladder cancer. Other techniques such as robotic-assisted laparoscopic cystectomy are performed uncommonly in Australia. Reconstruction options include ileal conduit and neobladder. Fitness for surgery, rather than age, is the primary determinant of treatment modality.

Chemotherapy

Neoadjuvant cisplatin-based chemotherapy should be considered in patients at risk of micrometastatic disease, because evidence shows an improved five and 10-year survival rate.[4] The benefit is thought to increase

five-year survival from 50 to 55%, and 10-year survival from 30 to 36%.[4] The downside to chemotherapy is time lag to definitive treatment in nonresponders, and unnecessary treatment in patients who do not have micrometastatic disease. Impaired performance status or reduced renal function may preclude a patient from receiving chemotherapy.

Adjuvant chemotherapy can also be considered post cystectomy. Although there is nonrandomised data to support this use, there is less evidence from randomised controlled trials.

Multimodal therapy

A bladder preserving treatment option is multimodality therapy (chemotherapy and radiotherapy) after maximal resection of the lesion. Multimodality therapy should be considered in well-informed patients and those who are unfit for surgery. Cisplatin-based chemotherapy in combination with radiotherapy, following bladder tumour resection, can have complete response rates of between 60 and 80%. Patients managed this way require stringent follow up, and should be aware that outcomes are poorer if the cancer recurs.

In patients who are not fit for major surgery or multimodality therapy, resection alone may be offered as a palliative option.

CONCLUSION

Early diagnosis of high-risk or muscle-invasive bladder cancer improves survival and can be life saving. Haematuria and persistent irritative symptoms are red flags for bladder cancer requiring further investigation and immediate urological referral.

Treatment options for high-grade disease include cystectomy, chemotherapy and multimodal therapy. Data have clearly shown inferior outcomes in men when treatment is delayed by more than 12 weeks from diagnosis.[5] Therefore, early referral of patients with haematuria remains critical, and smoking cessation as a long-term health strategy is as important for the prevention of bladder cancer as it is for the plethora of other smoking-related diseases. MT

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