PRIMEVIEW

BLADDER CANCER

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Cancer of the urinary bladder is the ninth most common cancer worldwide and the thirteenth most common cause of cancer death. Most bladder cancers originate from the urothelium that covers the inner surface of the bladder, but 10–25% of bladder cancers have variant histology.

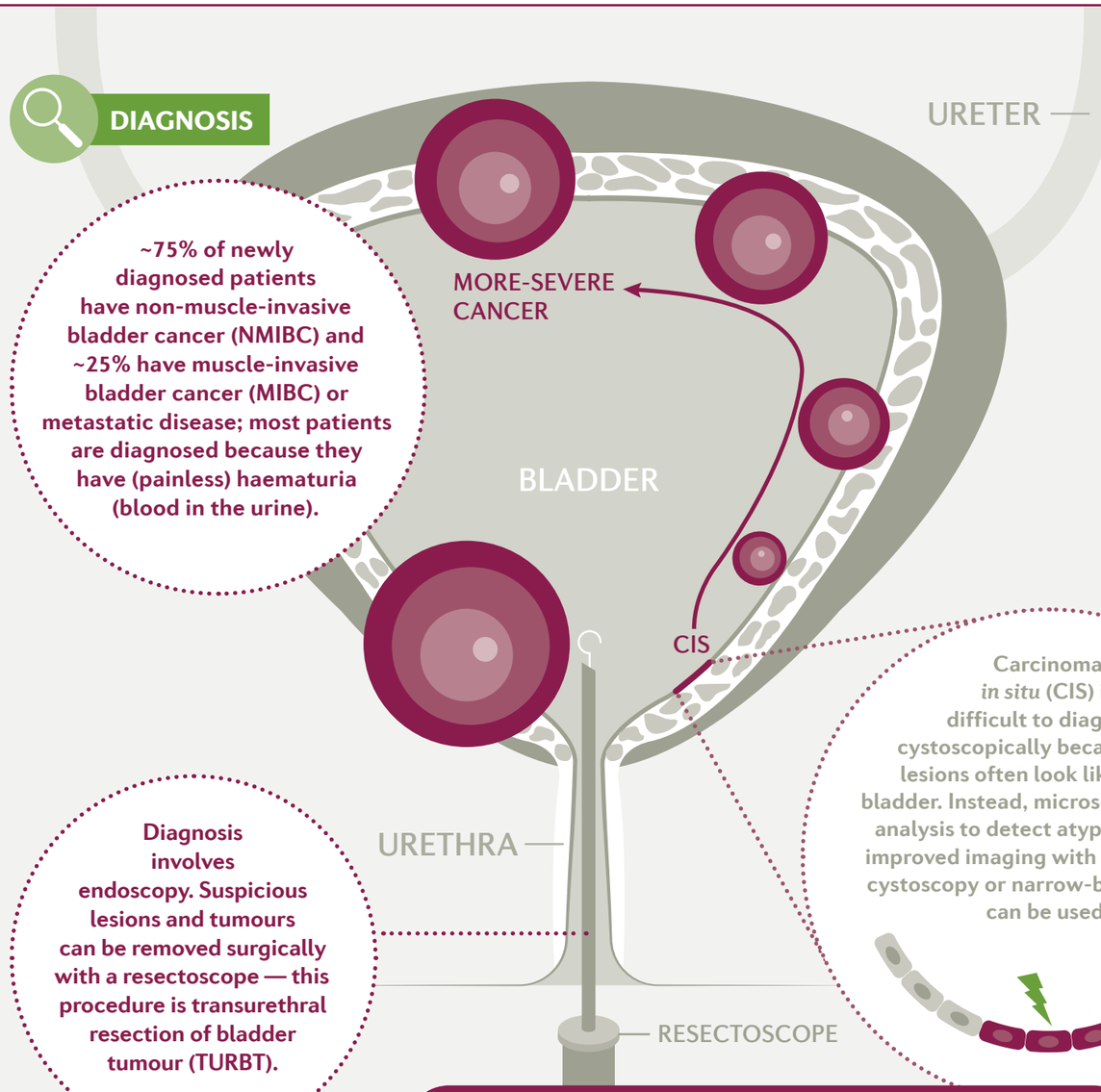
EPIDEMIOLOGY

Bladder cancer is typically diagnosed in people >65 years of age. The incidence of bladder cancer is threefold greater in more-developed areas (9.5 per 100,000 population) than in less-developed countries (3.3 per 100,000 population), but these numbers are expected to almost double in the near future owing to increased life expectancy.

Cigarette smoking is the most common risk factor for bladder cancer, with estimates that tobacco is responsible for half of all cases

DIAGNOSIS

~75% of newly diagnosed patients have non-muscle-invasive bladder cancer (NMIBC) and ~25% have muscle-invasive bladder cancer (MIBC) or metastatic disease; most patients are diagnosed because they have (painless) haematuria (blood in the urine).

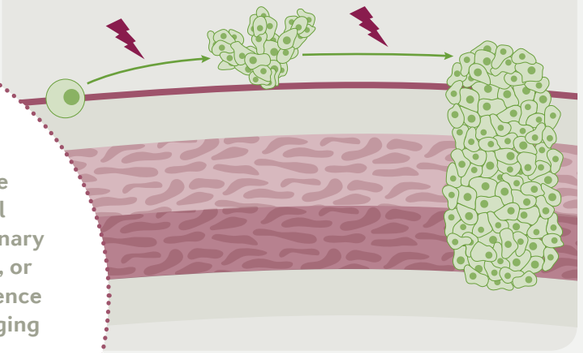


Diagnosis involves endoscopy. Suspicious lesions and tumours can be removed surgically with a resectoscope — this procedure is transurethral resection of bladder tumour (TURBT).

Carcinoma *in situ* (CIS) is difficult to diagnose cystoscopically because these lesions often look like normal bladder. Instead, microscopic urinary analysis to detect atypical cells, or improved imaging with fluorescence cystoscopy or narrow-band imaging can be used.

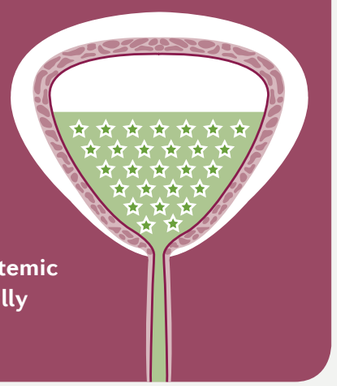
MECHANISMS

NMIBCs are typically preceded by flat or papillary urothelial hyperplastic lesions, commonly harbouring deletion of chromosome 9 and point mutation of *FGFR3* (frequently leading to activation of the RAS–MAPK pathway and cell overgrowth). By contrast, MIBCs are preceded by CIS lesions that often show mutations in *TP53*, upregulated expression of *CK20*, *HER2* and the PI3K pathway, and reduced expression of *PTEN* — features that facilitate cell proliferation and survival. Genome-wide analysis also indicates the importance of both DNA methylation and histone methylation in gene silencing in MIBC.



MANAGEMENT

After TURBT resection, patients with NMIBC typically have adjuvant intravesical therapy with Bacillus Calmette–Guérin (BCG), the tuberculosis vaccine. Patients with MIBC or who do not respond to BCG undergo radical cystectomy (removal of the bladder), with urinary diversion to reroute the urine flow. Patients with metastatic disease are treated with systemic chemotherapy, usually cisplatin based.



In the research setting, several molecular subtyping systems of bladder cancer have been reported based on transcriptional profiles. However, assessing which signatures are clinically useful will be essential to develop a unified clinically meaningful nomenclature system.

QUALITY OF LIFE

Patients with bladder cancer face deficits in sexual, urinary and bowel function as a result of their disease and its treatment, which are compounded by high rates of recurrence and progression.

To better understand these issues, the integration of patient-reported outcomes into routine cancer care has resulted in improved patient satisfaction, symptom management and quality of life. Such data could also inform our understanding of the comparative effectiveness of different bladder cancer treatment options.

OUTLOOK

Efforts to reduce bladder cancer-related mortality are rooted in early detection and more-effective therapies. For example, urinary biomarkers (such as microRNA detection) might help to identify bladder cancer in at-risk individuals. Robot-assisted surgery is being prospectively scrutinized to determine whether it can improve perioperative and oncological outcomes compared with open or laparoscopic surgery. Additionally, systemic therapies for metastatic disease that are being investigated include immune checkpoint inhibitors, which have witnessed success in other cancer types.

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