Early Stage Bladder Cancer

Can it be cured?

by Dr Gerald Tan

The bladder is a hollow muscular organ whose twin functions are to store and to empty urine produced by the kidneys. Bladder cancer refers to the uncontrolled growth of cells in the lining of the bladder wall, and occurs most commonly in chronic tobacco smokers. Occupational exposure to chemicals, such as benzidine and 2-naphthylamine, are also well-known risk factors.

Diagnosing Bladder Cancer

Bladder cancer classically presents with painless blood in the urine (known as haematuria). Other symptoms may include frequent or painful urination associated with pain in the lower abdomen. Cystoscopy of the bladder, wherein a flexible endoscope is passed through the urethra into the bladder under local anaesthesia, is the most accurate way to determine if cancer is present and to obtain tissue for biopsy. On cystoscopy, most early bladder cancers have a papillary frond-like appearance, similar to how corals in the seabed appear to divers **[Figure 1].** Narrow band imaging has been an important recent advance in endoscope technology,

Figure 1. ***Early stage bladder cancers often have a frond-like appearance (similar to seabed corals) on cystoscopy evaluation of the bladder.***

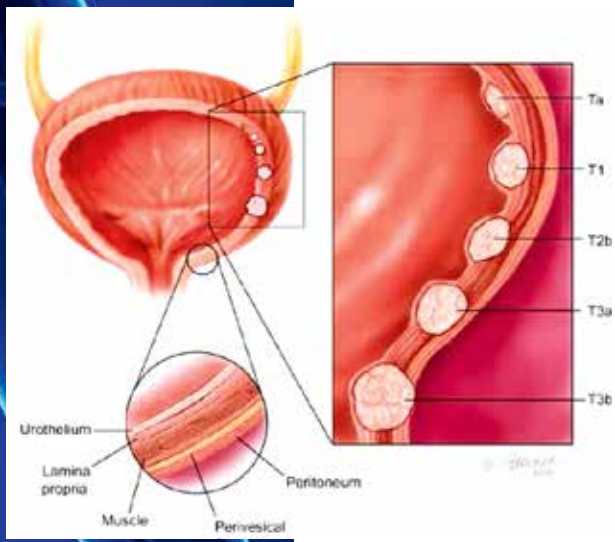


Figure 2. ***Staging of bladder cancer, based on depth of invasion into the muscular wall of the bladder.***

Despite innovations in surgical technique, muscle-invasive bladder cancer is still a difficult diagnosis for patients to accept. Many cannot accept the loss of their natural urination after surgical removal of the bladder, and the possible need for a permanent stoma for urine to leave the body.

enabling better visualisation and earlier detection of cancerous areas of the bladder that would have been missed on conventional white light cystoscopy.

Once the diagnosis of bladder cancer is confirmed, accurate staging of disease would include (1) computer tomography of the urinary tract (CT urogram) to determine the local extent of the cancer and if other parts of the urinary tract are affected; (2) endoscopic removal of the bladder tumour under general anaesthesia to ascertain the grade of cancer and whether it is confined only to the bladder lining (superficial bladder cancer) or if it has invaded into the muscular wall **[Figure 2];** and (3) chest X-ray and bone scan to determine if there is spread of cancer to distant organs (known as metastasis).

Current Recommended Treatment for Superficial Bladder Cancers

The good news is that most bladder cancers nowadays are detected early and are confined to the epithelial lining of the bladder (stage pTa or pT1, also known as superficial bladder cancer). Transurethral resection of these bladder tumours (TURBT) alone is oftentimes curative **[Figure 3],** and this is achieved without any incisions by simply passing a large calibre cystoscope through the urethra into the bladder where the tumour(s) may be scraped out piecemeal using a high energy cutting loop. The procedure is performed under general anaesthesia, and in most cases, the patients may be discharged the same day or the next day, once no further significant bleeding is seen in the urine. Known complications of TURBT surgery include bladder perforation or significant bleeding requiring corrective surgery. Thankfully, bipolar electrocautery has been a significant advance in endoscope and energy technology, and has reduced these complications considerably.

Preventing a Recurrence of Superficial Bladder Cancer

After these superficial bladder tumour(s) are completely removed, the next treatment goal will be to minimise the chances of recurrence and progression of disease. Patients will need to return for regular

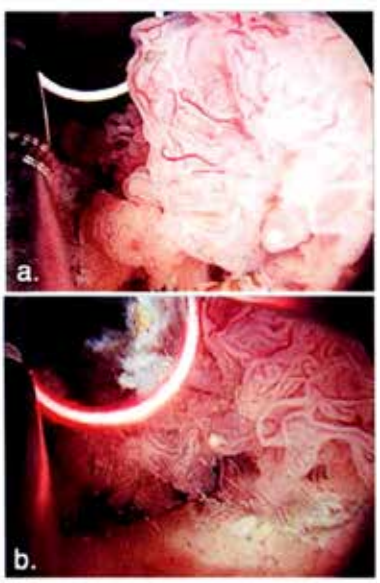


Figure 3.
a) Endoscopic view of the bladder tumour.
b) Endoscopic piecemeal removal of the tumour down to the bladder wall using a high energy cutting loop through the cystoscope.

For patients at moderate to high risk of bladder cancer recurrence, they should comply with a further course of intravesical chemotherapy to reduce the likelihood of recurrence. This is usually painless and is administered in the urologist's clinic via a urinary catheter inserted into the bladder.

surveillance cystoscopy to detect any recurrence of new bladder tumours. Risk factors for early recurrence include (1) large size of bladder tumours; (2) multiple sites of cancer involvement in the bladder wall; (3) high-grade type of cancer cells seen under microscopic evaluation; (4) presence of carcinoma-in-situ (flat tumours) or recurrent tumours.

Immediately after endoscopic surgical removal of these bladder tumours, the attending urologist will usually administer a single dose of chemotherapy (e.g. Mitomycin C) into the bladder through the urinary catheter once the urine is no longer blood stained. This will reduce the likelihood of stray cancer cells re-implanting into the bladder wall. The intravesical chemotherapy agent is then emptied from the bladder two hours after instillation and the urinary catheter removed.

For patients at moderate to high risk of bladder cancer recurrence, they should comply with a further course of intravesical chemotherapy to reduce the likelihood of recurrence. This is usually painless and is administered in the urologist's clinic via a urinary catheter inserted into the bladder. BCG (bacillus Calmette-Guerin) is the preferred chemotherapy agent for this treatment, although it has slightly more reported side effects compared to Mitomycin C. However, not all patients are suitable for intravesical BCG treatment, and there is a risk of toxic side effects in patients with compromised immunity. Previously given once a week for six weeks, large-scale studies now report that regular intravesical BCG should be continued for one to three years after initial surgery to successfully reduce the risk of disease recurrence or progression.

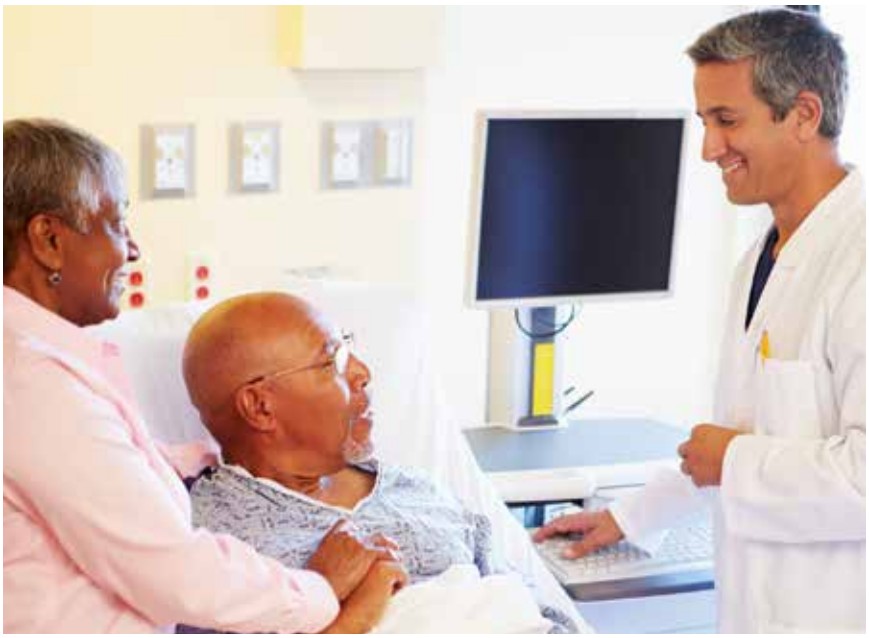
Figure 4. ***Patient who underwent robotic-assisted radical cystoprostatectomy for muscle-invasive bladder cancer. An ileal conduit is required to divert urine out of the body after the bladder is removed.***

Problems Due to Invasion of Cancer into the Bladder Muscle Wall

Muscle-invasive bladder cancer (MIBC) is unfortunately not very good news for the patient. Such cancers that have invaded into or beyond the muscular wall of the bladder (stage pT2-T4) are more aggressive, and without definitive surgical treatment, the cancer will quickly spread to the lymphatic system outside the bladder and then to distant organs.

Once the cancer cells have invaded into the muscular wall, the only effective cure lies chiefly in radically removing the whole bladder and its surrounding pelvic lymph nodes, and diverting the urine outwith of the body through either an artificial conduit using a loop of intestine **[Figure 4]**, or fashioning a new bladder from a segment of small intestine (known as an ileal neobladder). This challenging surgery is routinely performed through a lower midline incision under general anaesthesia, and is often associated with significant blood loss and need for blood transfusion.

In recent years, urologists have been pushing the envelope and developing new techniques for performing the same surgery through small incisions using the da Vinci® surgical robot. This affords the surgeon improved vision and dexterity during the surgery, leading to significantly less blood loss and perioperative complications, quicker recovery of bowel function, and shortened hospital stay. Recently published studies have demonstrated that using the da Vinci



robot to perform this surgery is safe in older patients above seventy years of age – this is widely attributed to the benefits of less blood loss encountered during robotic surgery. With standardisation of the surgical techniques involved and increasing published evidence reporting benefits, many centres are now adopting robotic surgery to deliver improved clinical outcomes for this challenging surgery.

Despite innovations in surgical technique, muscle-invasive bladder cancer is still a difficult diagnosis for patients to accept. Many cannot accept the loss of their natural urination after surgical removal of the bladder, and the possible need for a permanent stoma for urine to leave the body. As such, many MIBC patients unfortunately go into denial when faced with this prospect, and do not follow-up with their urologists, resulting in loss of valuable time and the opportunity for curative surgery.

Non-surgical Treatment Modalities for Muscle-invasive Bladder Cancer

In older patients or those with many co-morbid medical illnesses for whom radical surgery carries high peri-operative risk, external beam radiation to the bladder with adjuvant chemotherapy is an alternative. This should be part of a multi-modality approach, and is usually given after transurethral surgery has been performed to debulk as much tumour burden from the bladder as possible. However, these patients have a much higher risk of disease progression and shorter survival compared to patients undergoing radical surgery.

Dr Gerald Tan Yau Min is a Consultant Urologist at Mt Elizabeth Hospital with over 18 years of clinical experience. He is internationally renowned for his expertise in minimally-invasive and robotic surgery for prostate, kidney and bladder diseases, and performed the first successful robotic surgery for aggressive bladder cancer in Singapore in 2011. In 2012, he was named the Outstanding Young Urologist of Asia by the Urological Association of Asia. Dr Tan also consults at Mt Elizabeth Hospital (Orchard & Novena campuses).

Advice for Patients with Newly Diagnosed Bladder Cancer

In this age of medical innovations, bladder cancer is often curable. For best long-term results, patients must cooperate with their urologists to undergo stage-appropriate treatment based on published international guidelines. The diagnosis of muscle-invasive bladder cancer is often difficult for patients to accept, as the only long-term cure is radical surgery to remove the cancerous bladder and divert the urine. If possible, surgical removal of the bladder and urinary reconstruction should be performed by an experienced team of surgeons. MG

References:

1. Babjuk M, et al. EAU guidelines on non-muscle invasive bladder cancer (TaT1 and CIS). European Association of Urology. http://www.uroweb.org/gls/pdf/05_TaT1_Bladder_Cancer_LR.pdf.
2. Witjes JA, Comperat E, Cowan NC, et al. EAU guidelines on muscle-invasive and metastatic bladder cancer. European Association of Urology. http://www.uroweb.org/gls/pdf/07_Bladder%20Cancer_LR.pdf.
3. Stenzl A, Cowan NC, De Santis M, et al. Treatment of muscle-invasive bladder cancer: update of EAU Guidelines. European Urology 2011;59:1009-1018.
4. Yu H-Y, Hevelone ND, Lipsitz SR, et al. Comparative analysis of outcomes and costs following open radical cystectomy versus robot-assisted laparoscopic radical cystectomy: results from the US nationwide inpatient sample. European Urology 2012;61:1239-1244.
5. Coward RM, Smith A, Raynor M, et al. Feasibility and outcomes of robotic-assisted laparoscopic radical cystectomy for bladder cancer in older patients. Urology 2011;77:1111-1115.