What is muscle-invasive bladder cancer?

About a quarter of patients diagnosed with bladder cancer have a muscle-invasive form that has grown into the muscular part of the bladder wall (stages T2–T4). This type of cancer has a higher chance of spreading to other parts of the body (metastatic) and needs a different and more radical form of treatment. Muscle-invasive bladder cancer will be fatal if untreated.

Additional diagnostics

Computed tomography (CT scan) is particularly important for further work-up in muscle-invasive bladder cancer. With a whole-body CT scan, done in less than 10 minutes, the physician can tell if the cancer has already grown out of the bladder and into the surrounding fat tissue or adjacent organs and if there are signs of spreading to other organs (metastatic disease). By adding intravenous contrast agent, which is excreted into the urine by the kidneys, the urinary tract above the bladder can be visualized and tumour growth identified.

Prior to treatment, it is essential to evaluate whether the cancer is metastatic. If the CT scan indicates that the cancer has spread to your soft (visceral) organs, your bones or lymph nodes. This will possibly change the treatment decisions.

Additional magnetic resonance imaging (MRI scans) or bone scans may be performed, although this is not routinely done. Bone and brain metastases are rare at the time that muscle-invasive bladder cancer is diagnosed. Therefore, your doctor would only consider a bone scan or additional brain imaging if you have specific symptoms that suggest bone or brain metastases. Unclear findings might also be probed with a needle biopsy to confirm metastatic disease.

A combination of positron emission tomography (PET scan; uses a radioactive tracer) and CT scan (PET/CT) is increasingly being used in European centres, although it is not generally available in all countries. PET/CT may improve the ability to detect distant metastases. It is not recommended for staging bladder tumours because urinary excretion of the radioactive tracer makes tumour staging very difficult (see leaflet 02, Diagnosis and Classification).
Prognosis and risk stratification

The long-term prognosis for patients with muscle-invasive bladder cancer is determined by the extent of tumour growth (stage). As opposed to non-muscle-invasive bladder cancer aggressiveness (grade) which is determined by the pathologist is less important, since virtually all invasive tumours are high grade. Staging and grading are described in detail in Leaflet 02, Diagnosis.

Treatment options

Removal of the urinary bladder (cystectomy)
The mainstay of treatment for muscle-invasive bladder cancer is surgical removal of the urinary bladder.

Your doctor has several reasons for recommending removal of the whole bladder:

- Presence of a muscle-invasive tumour
- Presence of a tumour that grows aggressively (high grade), that has multiple cancerous areas (multifocal), or that is superficial, but has recurred after chemotherapy or immunotherapy
- Failure of or recurrence after a bladder-sparing approach (chemoradiation) or the occurrence of major side-effects
- Symptoms like bleeding or pain in patients with incurable disease

To evaluate and weight your individual risk of undergoing removal of the bladder, work with your physician to consult a multidisciplinary team (for example, urologist, surgeon, anaesthesiologist, nurse practitioner, general practitioner, cardiologist).

Factors like your biological age (your body’s performance as it ages, measured as performance status or life expectancy) and other diseases that you have (diabetes, heart disease, high blood pressure) are also important. Patients older than 80 years of age have more problems recovering from such an operation. Physicians use special indexed scores to assess the risk of patients undergoing this stressful operation.

Prior abdominal surgery or radiotherapy makes surgery more difficult but is rarely a reason not to have surgery. Being overweight does not influence survival after surgery but does influence the risk of complications from wound healing.

Removal of the urinary bladder includes removal of the bladder, the endings of the ureters and the pelvic lymph nodes. Depending on factors like tumour location and type of urinary diversion part of the adjacent gender-specific organs (the prostate and seminal vesicles in men; the entire urethra, adjacent vagina,

The terms your doctor may use:

<table>
<thead>
<tr>
<th>Term</th>
<th>Description</th>
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<tr>
<td>Urothelial carcinoma</td>
<td>This term refers to cancer that typically occurs in the urinary tract (kidney, bladder, ureters, urethra) and indicates the type of cancer, which affects urothelial cells as opposed to other types of cells in the urinary tract. Most bladder cancers are urothelial carcinoma (also called transitional cell carcinoma).</td>
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<tr>
<td>High grade</td>
<td>Tissue is greatly altered in appearance, indicating aggressive tumour growth.</td>
</tr>
<tr>
<td>Low grade</td>
<td>Tissue is mildly altered in appearance, indicating less aggressive tumour growth.</td>
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and uterus in women) are removed. Men should be aware that prostate cancer is sometimes found in removed prostates but generally does not affect long-term survival or treatment.

**How is bladder removal performed?**

Removal of the urinary bladder is performed through an incision in the abdomen (open) with the patient under general anaesthesia (combination of intravenous drugs and inhaled gasses; you are ‘asleep’). The bladder, the ends of the ureters close to the bladder, the pelvic lymph nodes, and (part of) adjacent gender-specific organs are removed. Now another way to store and empty urine must be created (urinary diversion).

The standard procedure at the moment is open surgery. However, it can be done as a minimally invasive procedure (laparoscopically or robotic assisted) at centres that treat a lot of patients and have experienced and specialised surgeons. Currently a minimal invasive approach is considered experimental for bladder removal.

**How do I prepare for the procedure?**

You are admitted to the urology ward 1 day prior to the operation. A physician or nurse will talk you through the operation and explain what happens before and especially after the surgery.

Part of your intestines will be used to create the urinary diversion. Your doctor will advise you in detail about how to prepare for the procedure.

Before surgery, your doctor will inform you in detail how to prepare for anaesthesia. If you are taking any medications, discuss them with your doctor. You may need to stop taking medications for several days before surgery.

**What happens after the procedure?**

For the first few days you will be closely monitored. Your doctor will inform you in detail about the post-operative routine.

During hospitalisation, you will learn how to manage the urostomy or neobladder. Once you have learned how to use and empty the urostomy or internal urine pouch, a date for your discharge will be set.

**Chemotherapy before removal of the bladder**

Chemotherapy is administered before bladder removal to potentially shrink the tumour and kill cells that have already entered the blood or lymph nodes.

Chemotherapy before the operation may be recommended for patients with muscle-invasive disease. It is also necessary if tumours are large (>3 cm) or if signs indicate that cancer has spread to the lymph nodes (metastatic disease) and the goal is treatment of the disease. The decision to administer chemotherapy is made by a multidisciplinary team (including an oncologist, a urologist, and a radiologist).

Adequate kidney function is necessary. Potential side-effects are usually monitored and managed by an oncologist.

A good response to chemotherapy improves survival but does not change the need for surgery. Although neoadjuvant chemotherapy is currently advised, physicians are unable to identify who will definitely benefit from chemotherapy before removal of the bladder.

**Chemotherapy after removal of the urinary bladder**

If a tumour is large (>3 cm), or could not be fully resected, or if cancer has spread to the lymph nodes (determined by the pathologist), chemotherapy after removal of the bladder is an option. Cancer that has spread to the lymph nodes indicates systemic disease and may need systemic treatment (with chemotherapy) in certain cases.

**Urinary diversion: incontinent or continent**

It is important to understand the two-step approach to bladder removal. First, the urinary bladder and lymph nodes are removed. Second, the urine needs to be diverted. This can be achieved with several techniques.
In general we distinguish between diversions that are incontinent (continuous flow with urine collected outside the body) and continent (urine stored in the body and emptied when necessary). In addition to biological age, kidney function and other illnesses, quality of life and patient compliance (you will need to make certain adjustments) are crucial when deciding on bladder substitution or urinary diversion.

To determine which option best suits your situation, you should understand the limitations and side-effects of each option. In addition to your personal preference, the ability to physically and mentally handle the diversion is important, as is your social and family support.

**Incontinent diversion**

**Rerouting ureters through the skin (ureterocutaneostomy)**

By moving the ureters either together or individually to empty through a new opening in the skin (stoma) at the side of abdomen (Fig. 1), urine can simply exit the body into a stoma bag. This diversion is the most simple. Although it is rarely used, it is safe and feasible for patients who have medically complicated situations (prior operations, multiple health problems, palliative care) or who cannot care for themselves after the operation. Major complications are rare, but recurrent infections and tightening of the orifice (stenosis) are common and might require treatment. Patients often need a stent in the ureter, which has to be changed regularly.

**Placing a piece of small intestine between the ureters and the skin (ileal conduit)**

An ileal conduit can be created by placing a piece of small intestine between the ureters and the skin (Fig. 2). This ‘enteric stoma’ creates more distance between the kidneys and the skin and reduces the risk of infections, which usually enter the body from outside. Another advantage for patients is that this stoma is easier to handle and has less narrowing (stenosis) than smaller stomas. Recurring infections remain a complication, along with long-term complications like tightening/scar formation (stenosis) of the opening, leakage, and formation of stones in the urinary tract (urolithiasis).
This procedure is technically relatively simple and reliable and is therefore the most often used form of diversion.

When choosing this type of urinary diversion you must be aware that adapting to the new situation of living with a stoma will take time and effort. Your healthcare team will help you to adjust your lifestyle and get used to the situation (different body image, sports and hobbies, traveling etc.)

** Continent cutaneous diversion (heterotopic neobladder)**

Creating a reservoir inside the body (cutaneous urinary diversion)

By using small intestine or large intestine and sometimes the appendix, a reservoir is created in the abdominal cavity and then connected to the skin with a valve mechanism ([Fig. 3](#)). With this low-pressure pouch, urine can be stored within the body. The goal of this procedure is to allow control of emptying (continence) or backflow to the kidneys (reflux). The reservoir is emptied by intermittent catheterization with a small plastic catheter every 2–6 hours. The opening can be anywhere on the lower abdomen or in the belly button (umbilicus).

If you choose this diversion, your eye–hand coordination must be sufficient to catheterize and drain the pouch regularly by yourself. Liver and kidney function must be adequate because of reabsorption of urinary components (salts, uric acid, water) by the intestinal lining of the pouch causes extra stress on these organs.

Complications include infections, incontinence, hernia, reflux, tightening of the opening (stenosis), and leakage as well as short bowel syndrome and metabolic and electrolyte imbalances.

Since this procedure is technically challenging, especially creating the valve mechanism is not always successful, this technique is not often used.
Implanting the ureters into the rectum (uretero-colonic diversion)
When the ureters are implanted in the rectum, the urine is stored in the rectal pouch (Fig. 4). The anus and pelvic floor become the continence organ and must function properly. This diversion leads to faecal matter mixing with the urine, so voiding and defecation happen simultaneously. This technique has a high rate of infections, so it is used infrequently and only under certain circumstances. Short-term complications include recurring infections (including inflammation of the abdominal wall and the kidneys), tightening of the opening to the rectum, and leakage. Long-term complications include incontinence from having to void urgently, bowel irritation, and associated colon cancer.

Forming a bladder from small intestine (orthotopic neobladder)
A new bladder can be constructed from small intestine that is isolated from the digestive tract (Fig. 5). A reservoir is shaped from small intestine and placed in the small pelvis as a substitute for the bladder. Depending on the technique used the reservoir is spheroidal shaped, “W” or “V” shaped. The ureters are attached on both sides, and the lower end is connected to the urethra. The urinary sphincter is preserved. This diversion results in a continent reservoir
Fig. 4: Ureterocolonic diversion.

Fig. 5: Orthotopic neobladder.
that should hold a volume comparable to that of a healthy adult bladder.

You will not feel the bladder filling or the need to void with an orthotopic neobladder, so voiding must be initiated every 2–4 hours. The neobladder is emptied by relaxing the pelvic floor muscles and contracting the abdomen (Valsalva manoeuvre). Pressing the abdomen with both hands might help with complete emptying of the neobladder. In women about 20% may need to perform intermittent self-catheterisation to empty completely, in men this is rarely necessary.

This diversion requires you to have a good understanding of its requirements and to comply with them. Acceptable renal and liver function, relatively long life expectancy, good mental fitness, and a functional pelvic floor (no prior incontinence) are necessary for this urinary diversion. If you have had prior extensive abdominal surgery or radiotherapy, you should not have this type of diversion.

Short-term complications include recurring infections (including inflammation of the abdominal wall and the kidneys) and leakage. Long-term complications include tightening of the opening to the neobladder, changes of the upper urinary tract, incontinence, short bowel syndrome and hernia as well as metabolic and electrolyte imbalances.

Close monitoring and guidance is important for the first months after this type of urinary diversion. Your healthcare team will help you to adjust your lifestyle and get used to the new situation. You will need to adapt your habits and daily routines (voiding to a fixed time schedule).

Regular blood test will help evaluate if too much uric acid is being reabsorbed by the used intestine causing pH imbalances which often times require treatment with oral medications (sodium bicarbonate = baking soda).

The newly formed reservoir needs time to settle and start functioning. To increase its capacity you will need to train your bladder. Your healthcare team will provide you with instructions for bladder training. The new bladder needs to be trained to increase its capacity (bladder training). In the beginning incontinence can occur due to post-operative swelling near the pelvic floor and/or the volume deficit of the neobladder in the beginning.

**Bladder-sparing treatments**

A bladder-sparing approach is currently used in a minority of cases worldwide but deserves consideration. Bladder preservation can be achieved at the cost of multiple therapies, including their side-effects. Transurethral resection of the bladder tumour (TURBT) and radiation is used to cure or control the tumour locally. Chemotherapy is used to treat the cancer cells that might already have spread within in the body (systemic disease). The goal is to preserve the bladder and its function as well as quality of life without compromising cancer treatment.

Studies in selected patient groups have shown good results for bladder-sparing approaches, about a third of patients still undergo bladder removal after failure of a bladder-sparing treatment.

**Transurethral resection of bladder tumour**

If you cannot undergo extended surgery, TURBT is possible if the tumour invades only the inner muscle layer of the bladder. With high recurrence and progression rates, this treatment alone cannot be considered a good option for controlling the disease long term.

**Chemoradiation**

Radiation therapy combined with sensitizing chemotherapy is a reasonable alternative for patients who refuse or are not candidates for bladder removal. Evaluation for this approach will consider general fitness (life expectancy), kidney function, prior radiation, prior abdominal operations, and history of other cancers. A consultation with a radiation oncologist is advisable prior to deciding on this treatment.

**Radiotherapy**

Radiation therapy is an option for preserving the bladder in patients who are not candidates for sur-
gery or who do not want surgery. Results from radio-therapy alone are worse than those from complete removal of the bladder, but if combined with chemotherapy (chemoradiation), acceptable results can be achieved. Side-effects include mild to strong irritation of the bladder and digestive tract as well as incontinence, increased risk of infections, and fistulas (abnormal passages that develop between organs).

Chemotherapy

Chemotherapy alone has only limited results and is not recommended as a sole treatment.

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