

Kidney cancer - Transitional cell carcinoma (TCC)



What is transitional cell carcinoma (TCC)?

Transitional cell carcinoma (TCC) (or upper urinary tract urothelial cancer) is a cancer that grows in the cells that line parts of the kidney called the renal pelvis (also called the collecting duct) or the ureter. The ureter is the tube that connects the kidney to the bladder, while the renal pelvis is the funnel-like dilated beginning of the ureter where it joins the kidney (see *Essential guide: The Kidneys* for more information).

The ureters are lined with a membrane called urothelium. Urothelium is a type of tissue called epithelium. Epithelium lines the cavities and surfaces of organs and structures throughout the body and forms many glands.

Cancer of the ureter and renal pelvis starts in a type of cell called a transitional cell in the urothelium (lining of the ureter). TCC can start in either the renal pelvis or the ureter or, sometimes, both. Bladder cancer is also a type of urothelial cancer. More information about bladder cancer can be found from

www.fightbladdercancer.co.uk. This guide focusses on TCC of the ureter and renal pelvis (sometimes called renal TCC).

Occurrence

TCC of the renal pelvis or ureter is considered a rare cancer. Only 7-8% of all kidney cancers affect the renal pelvis and 5% affect the ureter.

There are about 650-750 cases of TCC of the renal pelvis and about 480 cases of TCC of the ureter in the UK each year. TCC of the ureter or renal pelvis becomes more common as people get older and is very rare in people under 65. TCC is twice as common in men than women.

Risk factors

A risk factor is anything that might increase a person's chance of developing cancer. Although risk factors can influence the development of cancer, they are not necessarily causal. A cause is a

factor that has proven to give rise to cancer, for example cigarette smoking can cause lung cancer. Some people with several risk factors never get cancer, while others with no known risk factors do. However, knowing your risk factors and talking about them with your GP may help you make more informed lifestyle and health care choices.

The cause of TCC of the ureter and renal pelvis is unknown; however, there are several risk factors that are associated with an increased risk of developing this cancer, including:

- **Smoking tobacco** may increase the risk of developing TCC of the ureter and renal pelvis. Chemicals that cause cancer (carcinogens) that are present in tobacco smoke are absorbed by the blood and filtered by the kidneys to end up in the urine. These chemicals damage the lining of the ureters over a number of years. The risk increases the longer a person smokes and the more cigarettes they smoke
- **Gender.** TCC of the ureter and renal pelvis is more common in men than in women
- **Age.** The risk of developing TCC of the ureter and renal pelvis increases with age and it is rare in people under 65
- **Exposure to certain workplace chemicals** used in the manufacture of dyes, rubber, plastics, leather goods, pesticides and aluminium may increase the risk of TCC
- **Phenacetin.** Kidney damage caused by the long-term use of certain painkillers, such as phenacetin, can increase the risk of developing TCC in the renal pelvis. Phenacetin is no longer available in the UK, but can be found in some illegal recreational drugs, such as cocaine
- **Cyclophosphamide.** Previous treatment with a chemotherapy drug called cyclophosphamide for another cancer can increase the risk of TCC
- **Balkan nephropathy,** a specific form of kidney damage only found in people living in the Balkan countries, may increase the risk of developing TCC of the renal pelvis
- **Lynch syndrome,** a rare condition also called hereditary non-polyposis colorectal cancer (HNPCC) is associated with an increased risk of colorectal and endometrial tumours, and also TCC.

Symptoms

Often kidney cancer in its early stages has no signs or symptoms and maybe found by accident on an ultrasound or CT scan carried out for other reasons or to investigate nonspecific symptoms, such as high blood pressure, weight loss, high temperature, problems with muscles or nerves in

the body, and abnormal blood tests.

Symptoms of TCC of the ureter and renal pelvis are often like those caused by urinary tract infections or stones in the bladder or kidneys. However, it is important to have any of the symptoms mentioned below checked by your GP, because the earlier TCC is diagnosed, the more likely it is to be cured. Some people do not show any of these symptoms, while others may experience a number of them. Symptoms of TCC of the ureter and renal pelvis include:

- The most common symptom is blood in the urine (haematuria), which may appear suddenly and may come and go. The urine may look pink, red or brown and you may see streaks of blood or blood clots. It is important to have blood in the urine checked by your GP immediately. Sometimes the blood cannot be seen (microscopic haematuria) and is picked up when you have your urine tested
- Occasionally, the ureter may become blocked by blood clots causing the urine to be held in the kidney and ureter (hydronephrosis). This may lead to more severe symptoms and



an infection (high temperature/fever, a burning sensation when passing urine and a need to pass urine more frequently or urgently)

- Pain or cramps in the flank/mid-back
- Unexplained weight loss
- Extreme tiredness (fatigue) and lack of energy
- Very rarely, you may suffer from anaemia (low red blood cell count) if you have been passing blood in your urine for a long time. The symptoms of anaemia are tiredness, breathlessness, and a pale complexion.

For information about the kidneys and diagnosis of kidney cancer, please see *Essential guide: The kidneys and Essential guide: Diagnosis and tests for kidney cancer*.

Staging of TCC

Before your oncologists can discuss treatment options with you, they need to know how far your cancer has progressed. Staging is used to describe how big a cancer is and how far it has already spread. The TNM system is a common system used for staging tumours:

- **T** (tumour) plus a number indicates the size of the primary tumour and how far it has grown locally
- **N** (nodes) plus a number indicates that the cancer has spread to nearby lymph nodes
- **M** (metastases) plus a number refers to places elsewhere in the body where the cancer has spread, for example M0 means the cancer has not spread (metastasised) and M1 means the cancer has spread to other parts of the body, such as the lungs, liver, or bones to form small tumours called metastases. MX is used when metastases cannot be assessed.

Oncologists assign the stage of the cancer by combining the T, N, and M classifications:

- **Stage 0a:** There is a small area of cancer only in the lining of the ureter and/or renal pelvis. The tumours may look like tiny mushrooms and this stage is sometimes called non-invasive papillary carcinoma
- **Stage 0is** or CIS (carcinoma in situ): is a flat tumour where the cancer cells are only found in the very inner layer of the lining of the ureter and/or renal pelvis
- **Stage I:** the cancer has started to grow into the layers of tissue beyond the lining of the ureter and/or renal pelvis
- **Stage II:** The cancer has grown into the muscle layer of the ureter and/or renal pelvis
- **Stage III:** The cancer has grown through the muscle layer of the ureter and/or renal pelvis and into the fat layer surrounding the ureter or into the kidney tissue or fat surrounding the kidney
- **Stage IV:** The cancer has spread to a nearby organ, the layer of fat surrounding the kidney, the lymph nodes or to

other parts of the body, such as the lungs, liver, or bones. This is also called advanced or metastatic cancer

- **Recurrent cancer:** The cancer comes back after initial treatment.

TCC of the renal pelvis and ureter is also referred to as:

- **Localised** – the cancer is only found in the kidney or ureter
- **Regional** – the cancer has spread to the tissues around the kidney and to nearby lymph nodes and blood vessels in the pelvis
- **Metastatic** – the cancer has spread to other parts of the body.

Finding the stage of a cancer helps oncologists advise on what is the best treatment and gives them a reasonable indication of the outlook (prognosis). It also describes the cancer in a standard language which is useful when oncologists discuss patients, and when patients are involved in clinical trials. When discussing your treatment options, your oncologist will also take into account how well you are overall.

Treatments for TCC

Making treatment decisions

Your surgeon and oncologist will discuss with you the treatments they think would be best for you (please see the treatment options detailed below). Sometimes they may offer you a choice of surgical treatments. Your healthcare team should always make sure you are part of the decision-making process and that your views and preferences have been considered. You should make sure you have been given enough information and you understand the options, before you give permission for the treatment to start. Don't be embarrassed about asking people to explain things again and remember to ask about any particular aspects that are worrying you.

You should be told:

- The type of treatment that is recommended for you

- How and when this will be carried out
- The advantages and disadvantages of this type of treatment
- Any possible other treatments that might be available
- Any significant risks or side effects of the treatment.

When making treatment decisions, you might also be encouraged to consider a clinical trial as an option. A clinical trial is a research study to test a new treatment or procedure to evaluate whether it is safe, effective, and possibly better than the standard of care (standard treatment).

Treatment options depend on several factors, including the type and stage of your cancer, possible side effects to the treatment, your preferences and your overall health (see below).

Before your operation, you will have a talk with your surgeon about what treatment options are available for you. You might like to ask:

- Will I need a segmental or complete (radical) nephroureterectomy (removal of the kidney and a part of the ureter)?
- Can I have keyhole surgery (laparoscopic or robotic surgery)?
- What are the chances that I'll need a complete

nephroureterectomy even if a partial nephroureterectomy is planned?

- Is this surgery curative?
- What other related procedures or treatments might I need?

What surgical treatments are available for TCC?

Surgery is the main treatment for TCC of the ureter and renal pelvis. The extent of the surgery will depend on the stage of the cancer and the location of the tumour. Surgical removal of TCC tumours is usually carried out by a urologist (a doctor who specialises in diagnosing and treating urinary, bladder and kidney problems). The operation is usually carried out under general anaesthetic. The following surgical treatments are available for TCC of the ureter and renal pelvis:

Radical nephroureterectomy

This is an operation to remove the affected kidney, ureter and top part of the bladder. Sometimes, the surrounding lymph nodes, fat and tissues are also removed during this operation. Radical nephroureterectomy gives patients the best chance of getting rid of the cancer completely.

Segmental resection of the ureter or renal pelvis

This is an operation to remove only the affected part of the ureter or the affected part of the renal pelvis without removing the whole kidney. This procedure is usually done for small, low-grade tumours that are contained within the ureter or the renal pelvis. Segmental resection may be done to save kidney function when the other kidney is damaged or has already been removed.

Ureteroneocystostomy

Ureteroneocystostomy is an operation to remove the lower part of the ureter and a small portion of the bladder. The remaining ureter is then implanted into the bladder. This operation is done for tumours that are contained in the lower part of the ureter.

Laser treatment

Laser treatment may be used for early-stage tumours that only affect the lining of the ureter. It can also be used for people who are not able to have an operation, or for people who only have one kidney, or their kidneys aren't working properly.

A thin, flexible telescope, called a ureteroscope, is inserted through the tube through which urine flows to leave the body (the urethra) into your bladder and from there into the ureter or kidney. During laser treatment, a narrow beam of laser light is passed through the ureteroscope and directed onto the tumour to destroy it. Sometimes a stent might be needed to temporarily keep the ureter open. This treatment is not used often, because there is a high risk of the tumour coming back after treatment.

Percutaneous endoscopic surgery

During this operation the tumour is removed using an endoscope (a small camera on the end of a thin, flexible tube). The surgeon makes a small cut in the skin on the side of the body. Ultrasound or CT is then used to guide the endoscope into the kidney. The



surgeon then uses specialist instruments to remove the tumour from the kidney. This operation is usually only done for patients who have one kidney. However, it is not done often, because there is a high risk of the tumour coming back.

Laparoscopic surgery

For laparoscopic (or keyhole) surgery, the surgeon makes several small cuts and uses a thin tube with a light and a magnifier at one end (called a laparoscope) to see inside your tummy and perform the operation. This type of surgery results in less scarring and faster recovering times than traditional open surgery. Surgeons need special training before they are competent to do laparoscopic surgery.

Robot-assisted laparoscopic surgery

Sometimes a robot is used to help with laparoscopic surgery (robot-assisted laparoscopic surgery). The surgeon uses a robotic system to perform the operation. Robotic tools need very small cuts, provide better 3-D images during the operation, and can make fine or complex motions that are similar to what a surgeon's hand can do in open surgery.

Surgery to remove the kidney and ureter is generally very safe. However, as with any operation, there can be some risks, such as infection, bleeding that continues for more than a few days, or damage to the bladder during surgery. If you are concerned by any of these, or if you have any symptoms of an infection (fever, feeling generally unwell, smelly or cloudy urine) or blood or blood clots in your urine, please see your GP.

After radical nephroureterectomy, the remaining healthy kidney can usually do all the work so patients can live a normal life. Blood and urine tests can be used to monitor the function of the remaining kidney, if necessary.

What to expect after surgery?

After your surgery, your ward nurse or physiotherapist will encourage you to start walking about as soon as possible. If you are not able to walk, they will encourage you to do deep breathing exercises and leg movements in the bed. Getting active helps recovery.

You may have a drip to put fluid into your blood stream, a catheter to drain urine from your bladder and drains to remove any excess fluid or blood from your wound when you return to the ward. The catheter and drains are usually only needed for a couple of days and the drip can be removed as soon as you are able to eat and drink normally.

You will be given pain relief while you recover from your operation. At first you will require strong painkillers such as opiates (e.g., morphine). These can be given as injections from the ward nurse or by a patient-controlled pump attached to your arm. Some people have an epidural method of pain relief instead. This uses a local anaesthetic to numb the area where the operation took place and uses a tube into your back to deliver the local anaesthetic to the area.

You should expect to be in hospital for between 4 and 10 days after your operation. Ask your surgeon or ward nurse how long you should rest at home before getting back to daily activities, such as

shopping, exercise, gardening, housework and returning to work.

You should get a follow-up outpatient appointment to check your recovery six weeks after your operation. During this visit your oncologist should discuss your outlook (prognosis) and/or further treatment options and follow-up schedule with you.

Depending on the grade of your cancer, you may need further treatment. TCC is different to renal cell carcinoma (RCC) in that treatments such as chemotherapy and radiotherapy are effective against TCC but not RCC (see below). Your oncologist or specialist nurse will discuss this with you.

Chemotherapy

Chemotherapy may be used to reduce the risk of the cancer coming back after your operation or when your cancer has spread to other parts of the body and surgery is not possible anymore. Your oncologist might also recommend chemotherapy if you are not able to have surgery for other health reasons.

Chemotherapy is the use of toxic drugs to kill cancer cells (cytotoxic drugs). The chemotherapy drugs are given by an injection into a vein (intravenous) in the arm. They circulate around the body in the blood stream (systemic drugs) and act by disrupting the growth of cancer cells.

Intravenous chemotherapy is given in hospital, usually in the outpatient clinic. Chemotherapy may be given before surgery to shrink the cancer and reduce the risk of it coming back. This is called neo-adjuvant chemotherapy. Chemotherapy may also be given after surgery to prevent the cancer from coming back. This is called adjuvant chemotherapy.

TCC of the ureter and renal pelvis is commonly treated with chemotherapy drugs, which are given over a few days; this is called a cycle of chemotherapy. A number of cycles will be repeated every few weeks over a period of several months; this is called a course of chemotherapy.

Common chemotherapy drugs used for the treatment of

advanced TCC of the ureter and renal pelvis are listed in the following table:

Side effects to chemotherapy depend on the drug used and the patient, and may include fatigue, anaemia, nausea, vomiting, diarrhoea, sore mouth, loss of appetite, hair loss and risk of infection. However, most side effects can be treated effectively and usually go away when treatment with the drug stops.

The effectiveness of some chemotherapy drugs might be reduced by dietary or herbal supplements, such as fish oil preparations and grapefruit. It is therefore important to let your oncologist or specialist nurse know if you are taking any dietary supplements or complementary therapies before you start treatment.

It is also dangerous to become pregnant or to father a child while taking chemotherapy drugs, as they may harm the developing baby. It is therefore important to use effective contraception during treatment and for a few months after

treatment. Please discuss this issue your oncologist or specialist nurse.

Immunotherapy

Immunotherapy is a type of biological therapy that stimulates the body's own immune system to attack the cancer cells.

Bacillus Calmette-Guerin or BCG is the most common immunotherapy for treating early-stage TCC of the ureter and renal pelvis. It is used to help keep the cancer from growing and spreading into nearby tissues, and to help keep it from coming back. BCG is a germ that's related to the one that causes tuberculosis (TB), but it doesn't usually cause serious disease. It is thought that BCG triggers the cells of the immune system in the lining of the ureter to destroy the cancer cells.

BCG is put into the ureter and renal pelvis through a thin tube or catheter via the urethra. For BCG to work effectively it must meet the cancer cells.

Side effects to BCG treatment include inflammation of the bladder

Chemotherapy drugs	How does it work?	Administration
Cisplatin	Destroys quickly dividing cells, such as cancer cells. Used to stop the cancer coming back after surgery or to shrink the cancer before surgery. Used to treat cancer that has spread	Intravenous through a short tube into a vein in your arm
Gemcitabine	Gemcitabine is a so-called antimetabolite which interfere with the DNA of cells and stops cells working properly	Intravenous through a short tube into a vein in your arm
Methotrexate	Stops cancer cells making and repairing DNA so that they cannot grow and multiply. Methotrexate stops the cancer cells working properly	Intravenous through a short tube into a vein in your arm
Vinblastine	Stops cancer cells from multiplying and growing	Intravenous through a short tube into a vein in your arm or through a long tube into a large vein in the chest (a central line)
Doxorubicin	Slows or stops the growth of cancer cells by blocking an enzyme that is needed for the cells to divide and grow	Intravenous through a short tube into a vein in your arm or through a long tube into a large vein in the chest (a central line)
Carboplatin	Interferes with the genetic material in a cell, the DNA, and stops the cells from dividing and growing	Intravenous through a short tube into a vein in your arm or through a long tube into a large vein in the chest (a central line)
Mitomycin C	Interferes with the genetic material in a cell, the DNA, and stops the cells from dividing and growing	Intravenous through a short tube into a vein in your arm or through a long tube into a large vein in the chest (a central line). Can be administered directly into your ureter or kidney through a thin tube called a catheter inserted through your urethra. Only used for people unable to have an operation



lining (cystitis) causing a need to pass urine more often, pain or stinging when you pass urine, and blood in the urine. This will settle down in a day or two and drinking plenty of fluid will help to ease the irritation. Some people may also get a urinary tract infection, flu-like symptoms for 1-2 days after each treatment and painful joints; please let your oncologist or specialist nurse know immediately if you have any of these side effects.

There is also a very small chance that some of the tuberculosis bacteria could get into your system causing fever and chills, joint pain, cough, feeling sick or vomiting, skin rash and feeling extremely tired. If you have any of these symptoms or have a high temperature for more than 2 days, you must see your GP immediately for treatment.

Another immunotherapy used for the treatment of TCC are antibodies targeting proteins called immune checkpoint inhibitors (PD-1 or PD-L1). Experience of the use of immune checkpoint inhibitors comes from the treatment of bladder cancer. They are used when chemotherapy doesn't work or when you are not well enough to have chemotherapy.

Immune checkpoint inhibitors are given through a vein (intravenous). Most patients can tolerate the treatment well, but some have serious side effects where the immune system is triggered to attack the patient's own body. This can lead to inflammation in the bowel causing diarrhoea, skin rashes, problems with hormones, and more dangerous side effects involving the heart and the lungs. Before treatment with an immune checkpoint inhibitor these potential side effects will be explained to you in more detail so that you can recognise them early and have them treated. Many side effects caused by immune checkpoint inhibitors can be treated with steroids and are well managed.

Radiotherapy

Radiotherapy is the use of high-energy X-rays to kill cancer cells. These X-rays are directed at the tumour to avoid harm to normal healthy tissue. Radiotherapy may be recommended if you are not well enough to have an operation or to treat TCC that has spread to nearby tissues. Sometimes radiotherapy is given after surgery to reduce the risk of the cancer growing back.

Radiotherapy is given in the hospital radiotherapy department. It is given as a series of short treatments for a few minutes each weekday, with a break at the weekend. The length of treatment depends on the stage of the cancer. Usually, you will have a CT scan to show the radiotherapist (a doctor specialising in radiotherapy treatment for cancer) where the cancer is located and to enable the radiotherapy beam to be directed precisely at the cancer. Your skin might be tattooed (with your permission) with tiny marks that act as reference points to help plan your treatment each day.

Stereotactic body radiotherapy (SBRT) can be used to treat metastases found in the liver and lungs. In SBRT, radiotherapy is directed at the area of the body containing the tumour so as to kill the cancer cells and avoid as much healthy tissue as possible.

Side effects to radiotherapy can include tiredness, nausea and vomiting, and sore or red skin (a bit like sunburn), pubic hair loss, bladder irritation, diarrhoea and risk of infection. They take a while

to build up and usually last for a few days after the treatment has finished. Your radiographer will be able to tell you what to expect and how to cope.

Long-term side effects to radiotherapy include infertility in both men and women, impotence (inability to have an erection) in men, narrowing of the vagina in women, more frequent bowel motions or diarrhoea, shrinkage of the bladder, early menopause in women and a small chance of developing a second cancer later in life. If you are concerned by any of these, please talk to your oncologist or specialist nurse.

What happens if my cancer comes back?

When your treatment has been completed and you are in remission (your symptoms have gone away), talk with your oncologist about what happens next and how you will be monitored for recurrence of the cancer. Many patients feel worried or anxious that the cancer will return.

If the cancer does return, you will undergo further tests to learn as much as possible about the recurrence. You and your oncologist will then talk about your treatment options, such as further surgery or drug treatment.

People with recurrent cancer often experience emotions such as disbelief, confusion and fear. Patients are encouraged to talk with their healthcare team about these feelings and ask about support services to help them cope. Side effects to radiotherapy can include fatigue, nausea and vomiting, and sore or red skin. They take a while to build up and usually persist for a few days after the treatment has finished. Your radiographer will be able to tell you what to expect and how to cope.

What if my cancer has already spread?

In advanced cases, TCC may spread to the lymph nodes, liver, lungs, and bones. If your cancer has already spread to other

parts of the body, surgery may still be useful to relieve symptoms such as pain and bleeding, or to help control the chemical balance in the blood. Surgery after the cancer has spread does not usually cure the cancer, so it is important to think carefully about the risks and benefits it may bring.

Sometimes, if there is metastatic spread to just the lymph nodes, lung or liver, this can be removed by surgery as well. Removing as many of the metastatic tumours from, for example, the lung or liver may improve your overall survival.

Other treatments for patients with metastatic cancer include chemotherapy, radiotherapy or immunotherapy, depending on the location and extent of cancer spread. Patients are encouraged to talk through the treatment options with their oncologist. At this stage, patients may also be recommended to consider participation in a clinical trial.

Survival

The outcome (prognosis) of TCC of the ureter and renal pelvis depends on the size and spread (the stage) of the tumour and how quickly the tumour is growing and spreading (the grade). About 90% of TCCs of the renal pelvis and ureter can be cured if found

early, before the tumour has grown into the wall of the ureter or the main part of the kidney. For early-stage tumours more than 90% of people can survive for 5 years or more. This drops to less than a quarter of people surviving 5 years or more for late-stage tumours (see staging system).

Cancer survival statistics should be interpreted with caution. Any estimates are based on data from many people with this type of cancer, but the actual risk for a particular individual may differ. It is not possible to tell a person how long he or she will live with TCC. Because survival statistics are often measured over a number of years, advances in the treatment or diagnosis of this cancer may not show in the numbers.

Further reading

- **Cancer Research UK:**
<https://www.cancerresearchuk.org/about-cancer/kidney-cancer/stages-types-grades/types-grades/transitional-cell>
- **Macmillan Cancer Support:**
<https://www.macmillan.org.uk/cancer-information-and-support/ureter-and-renal-pelvis-cancer>
- **National Cancer Institute:**
<https://www.cancer.gov/types/kidney/patient/transitional-cell-treatment-pdq>
- **Fight Bladder Cancer:**
<https://fightbladdercancer.co.uk/>

Acknowledgements

Medical reviewer: Dr Andreas Schmitt, Royal Marsden Hospital

Patient reviewer: Rose Woodward, Founder

Patient reviewer: Julia Black, Charity Operations

Medical writer: Sharon Deveson Kell BSc PhD MBA, Medical Affairs



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Factsheet Updated: April 2021

Next Review: April 2023