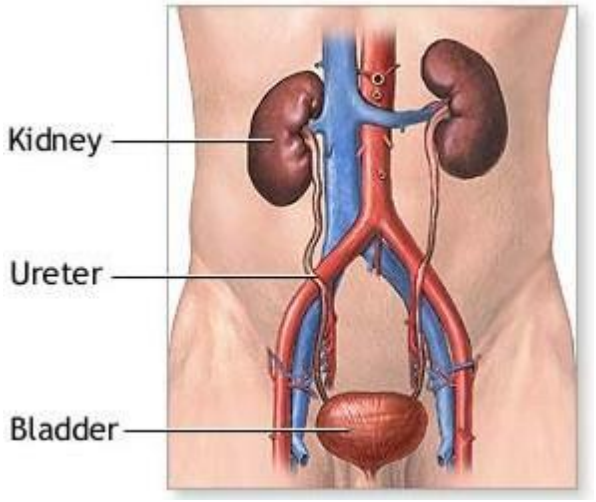
Cancer Association of South Africa (CANSA)

Fact Sheet
on
Kidney Cancer

Introduction

The kidneys are two organs that serve several essential regulatory roles in man. They form an essential part of the urinary system and also serve homeostatic functions such as the regulation of electrolytes, maintenance of acid–base balance and regulation of blood pressure (by maintaining salt and water balance). They serve the body as a natural filter of the blood and remove wastes which are diverted to the urinary bladder. In the process of producing urine, the kidneys excrete wastes such as urea and ammonia. They are also responsible for the reabsorption of water, glucose, and amino acids. The kidneys also produce hormones including calcitriol, erythropoietin, and the enzyme renin.



[Picture Credit: Urinary Tract Anatomy].

Bergerot, C.D., Battle, D., Bergerot, P.G., Dizman, N., Jonasch, E., Hammers, H.J., George, D.J., Bex, A., Ljungberg, B., Pal, S.K. & Staehler, M.D. 2019.

"Despite numerous therapeutic advances in renal cell carcinoma (RCC), little is known about patients' perspectives on cancer care. An international survey was conducted to identify points of frustration associated with cancer care reported by patients with RCC. Data were obtained from an online survey, conducted from April 1 to June 15, 2017, through social media and patient networking platforms. This survey obtained baseline demographic, clinicopathologic, and treatment-related information. Open-ended questions accessed sources of frustration in cancer-related care and patients' suggestions for amelioration. Responses were categorized and reviewed by independent reviewers. A qualitative analysis was performed and the Kruskal-Wallis test was used to define associations between baseline characteristics and sources of frustration. Among 450 patients surveyed, 71.5% reported sources of frustration, classified as either emotional (48.4%) or practical (23.1%). The most common were fear of recurrence/progression (15.8%), distrust of their cancer care system (12.9%), and lack of appropriate information (9.8%). Female gender and non-clear cell histology were associated with both types of frustration, and older age was linked to practical sources of frustration. Patients suggested solutions included greater compassion among health care practitioners (20.7%), better access to information (15.1%) and research to improve their chances of being cured (14.7%). Sources of frustration related to emotional and practical causes were identified amongst patients with RCC. Certain demographic and clinical characteristics were associated with

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more sources of frustration. This study provides the first characterization of specific ways to improve the patient experience by addressing common frustrations."

Motzer, R.J., Jonasch, E., Michaelson, M.D., Nandagopal, L., Gore, J.L., George, S., Alva, A., Haas, N., Harrison, M.R., Plimack, E.R., Sosman, J., Agarwal, N., Bhayani, S., Choueiri, T.K., Costello, B.A., Derweesh, I.H., Gallagher, T.H., Hancock, S.L., Kyriakopoulos, C., LaGrange, C., Lam, E.T., Lau, C., Lewis, B., Manley, B., McCreery, B., McDonald, A., Mortazavi, A., Pierorazio, P.M., Ponsky, L., Redman, B.G., Somer, B., Wile, G., Dwyer, M.A., Hammond, L.J. & Zuccarino-Catania, G. 2020.
"The NCCN Guidelines for Kidney Cancer provide multidisciplinary recommendations for the clinical management of patients with clear cell and non-clear cell renal cell carcinoma, and are intended to assist with clinical decision-making. These NCCN Guidelines Insights summarize the NCCN Kidney Cancer Panel discussions for the 2020 update to the guidelines regarding initial management and first-line systemic therapy options for patients with advanced clear cell renal cell carcinoma."

Cancer of the Kidneys
Kidney cancer is the uncontrolled growth of abnormal cells in the kidneys. Cancerous cells are also called malignant cells.

Possible Early Signs and Symptoms of Kidney Cancer
Early kidney cancers do not usually cause any signs or symptoms. Some possible signs and symptoms of kidney cancer include:

- Blood in the urine (haematuria)
- Low back pain on one side (not caused by injury)
- A mass (lump) on the side or lower back
- Fatigue (tiredness)
- Loss of appetite
- Weight loss not caused by dieting
- Fever that is not caused by an infection and that doesn't go away
- Anaemia (low red blood cell counts)

These signs and symptoms can be caused by kidney cancer (or another type of cancer), but more often they are caused by other, benign, diseases. For example, blood in the urine is most often caused by a bladder or urinary tract infection or a kidney stone. Still, if one has any of these symptoms, one must see a doctor so that the cause can be found and treated.

Incidence of Kidney Cancer in South Africa
According to the outdated National Cancer Registry (2017), known for under reporting, the following number of Kidney Cancer cases was histologically diagnosed in South Africa during 2016. "Histologically diagnosed means that a tissue sample (biopsy) was forwarded to an approved laboratory where a specially trained pathologist confirmed a cancer diagnosis.

Group - Males 2017	Actual No of Cases	Estimated Lifetime Risk	Percentage of All Cancers
All males	462	1:362	1,16%
Asian males	24	1:331	2,47%
Black males	146	1:884	1,09%
Coloured males	67	1:259	1,43%
White males	225	1:137	1,06%

Group - Females 2017	Actual No of Cases	Estimated Lifetime Risk	Percentage of All Cancers
All females	304	1:849	0,73%
Asian females	19	1:466	1,48%
Black females	132	1:1 817	0,68%
Coloured females	43	1:565	0,95%
White females	110	1:310	0,64%

The frequency of histologically diagnosed cases of Kidney Cancer in South Africa for 2017 was as follows (National Cancer Registry, 2017):

Group - Males 2017	0 – 19 Years	20 – 29 Years	30 – 39 Years	40 – 49 Years	50 – 59 Years	60 – 69 Years	70 – 79 Years	80+ Years
All males	49	6	15	51	116	126	79	20
Asian males	2	2	0	3	6	5	6	0
Black males	35	1	9	18	44	23	14	2
Coloured males	4	1	2	10	16	22	10	2
White males	4	2	8	29	59	58	52	5

Group - Females 2017	0 – 19 Years	20 – 29 Years	30 – 39 Years	40 – 49 Years	50 – 59 Years	60 – 69 Years	70 – 79 Years	80+ Years
All females	56	13	20	35	72	54	49	13
Asian females	1	3	1	3	8	1	1	1
Black females	46	7	15	15	26	17	5	2
Coloured females	1	0	1	10	13	11	5	1
White females	8	3	3	7	25	25	30	9

N.B. In the event that the totals in any of the above tables do not tally, this may be the result of uncertainties as to the age, race or sex of the individual. The totals for 'all males' and 'all females', however, always reflect the correct totals.

Risk Factors for Kidney Cancer

A risk factor is anything that affects one's chance of getting a disease such as cancer. Different cancers have different risk factors. Having a risk factor, or even several risk factors, does not mean that one will get the disease. Several risk factors that may make one more likely to develop kidney cancer have been identified.

Huang, W.C., Donin, N.M., Levey, A.S. & Campbell, S.C. 2020.

Purpose: We sought to provide a contemporary understanding of chronic kidney disease and its relevance to kidney cancer surgery. Another purpose was to resolve points of discrepancy regarding the survival benefits of partial vs radical nephrectomy by critically evaluating the results of prospective and retrospective studies in the urological literature.

Materials and methods: We performed a comprehensive literature search for relevant articles listed in MEDLINE® from 2002 to 2018 using the key words radical nephrectomy, partial nephrectomy, glomerular filtration rate, kidney function and chronic kidney disease. We also assessed select review articles and society guidelines about chronic kidney disease pertinent to urology and nephrology.

Results: Complete evaluation of the potential consequences of chronic kidney disease involves assessment of the cause, the glomerular filtration rate level and the degree of albuminuria. Chronic kidney disease is commonly defined in the urological literature solely as a glomerular filtration rate less than 60 ml/minute/1.73 m^2. This ignores the significance of the cause of chronic kidney disease, and the presence and degree of albuminuria. Although this glomerular filtration rate is relevant for preoperative assessment of patients who undergo surgery of kidney tumors, recent studies suggest that a glomerular filtration rate less than 45 ml/minute/1.73 m^2 represents a more discerning postoperative prognostic threshold. Reported survival benefits of partial over radical nephrectomy in retrospective studies were likely influenced by selection bias. The lack of survival benefit in the partial nephrectomy cohort in the only randomized trial of partial vs radical nephrectomy was consistent with data demonstrating that patients in each study arm were at relatively low risk for mortality due to chronic kidney disease when accounting for the chronic kidney disease etiology and the postoperative glomerular filtration rate.

Conclusions: The prognostic risk of chronic kidney disease in patients with kidney cancer is increased when the preoperative glomerular filtration rate is less than 60 ml/minute/1.73 m^2 or the postoperative rate is less than 45 ml/minute/1.73 m^2. Additional factors, including nonsurgical causes of chronic kidney disease and the degree of albuminuria, can also dramatically alter the consequences of chronic kidney disease after kidney cancer surgery. Urologists must have a comprehensive knowledge of chronic kidney disease to assess the risks and benefits of partial vs radical nephrectomy when managing tumors with increased complexity and/or oncologic aggressiveness.

Lifestyle- and Work-related Risk Factors

Smoking - Smoking increases the risk of developing renal cell carcinoma. Smoking has been shown to double the risk of kidney cancer and contributes to as many as one-third of the cases. The increased risk seems to be related to how much one smokes. The risk increases the longer one smokes and decreases after one quits, although it takes years to reach the same risk level as someone who has never smoked.

Obesity - People who are overweight or obese have a higher risk of developing renal cell cancer. Some doctors think obesity is a factor in about 2 out of 10 people who get this cancer. Obesity may cause changes in certain hormones that can lead to renal cell carcinoma.

Workplace exposures - Many studies have suggested that workplace exposure to certain substances increases the risk for renal cell carcinoma. Some of these are petroleum products, asbestos, cadmium (a metal), some herbicides, benzene, and organic solvents, particularly trichloroethylene.

Genetic and Hereditary Risk Factors

Genetic factors have been linked to an increased risk of kidney cancer. Some people inherit a tendency to develop certain types of cancer. It is important that people who have hereditary causes of renal cell cancer see their doctors frequently, particularly if they have already had a renal cell

cancer diagnosed. Some doctors recommend regular imaging tests (such as CT scans) for such individuals.

People who have the conditions listed below also have a much higher risk for getting kidney cancer, although they account for only a small portion of cases overall:

von Hippel-Lindau (VHL) disease - People with this hereditary disorder often develop several kinds of tumours and cysts (fluid-filled sacs) in different parts of the body. They have an increased risk for developing clear cell renal cell carcinoma, especially at a younger age. They may also have benign tumours in their eyes, brain, spinal cord, pancreas and other organs; and a type of adrenal gland tumour called pheochromocytoma. This condition is caused by mutations (changes) in the VHL gene.

Hereditary papillary renal cell carcinoma - People with this condition have inherited a tendency to develop one or more papillary renal cell carcinomas, but they do not have tumours in other parts of the body, as is the case with the other inherited conditions listed here. This disorder is linked to changes in many genes, most often the MET gene.

Hereditary leiomyoma-renal cell carcinoma - People with this syndrome develop smooth muscle tumours called leiomyomas or fibroids of the skin and uterus (in women) and have a higher risk for developing papillary renal cell cancers. It has been linked to changes in the fumarate hydratase (FH) gene.

Birt-Hogg-Dube (BHD) syndrome - People with this syndrome, which is characterised by the development of small benign skin tumours, have an increased risk of developing different kinds of kidney tumours, including renal cell cancers and oncocytomas. They may also have benign or malignant tumours of several other tissues. The gene linked to BHD is officially known as folliculin (FLCN).

Hereditary renal oncocytoma - Some people inherit the tendency to develop a kidney tumour called oncocytoma, which has a very low potential for being malignant.

Other risk factors

Other risk factors include:

Family history of kidney cancer - People with a strong family history of renal cell cancer (without one of the known inherited conditions listed previously) also have a 2 to 4 times higher chance of developing this cancer. This risk is highest in brothers or sisters of those with the cancer. It is not clear whether this is due to shared genes or something that both people were exposed to in the environment - or both.

High blood pressure - The risk of kidney cancer is higher in people with high blood pressure. Some studies have suggested that certain medicines used to treat high blood pressure may raise the risk of kidney cancer, but it is hard to tell if it is the condition or the medicine (or both) that may be the cause of the increased risk.

Certain medicines - Phenacetin, once a popular non-prescription pain reliever, has been linked to renal cell cancer in the past. Because this medicine has not been available for over 20 years, this no longer appears to be a major risk factor.

Over-The-Counter Pain Relievers - many over the counter pain relievers are somewhat toxic to the kidney. These non-steroidal anti-inflammatory drugs include aspirin, ibuprofen, and naproxen. Trade names for ibuprofen and naproxen include Motrin, Advil, and Aleve. Long term use of acetaminophen (Tylenol) has also been associated with kidney failure.

Diuretics - Some studies have suggested that diuretics (water pills) may be linked to a small increase in the risk of renal cell carcinoma. It is not clear whether the cause is the drugs or the high blood pressure it treats.

Advanced kidney disease - People with advanced kidney disease, especially those needing dialysis, have a higher risk of renal cell carcinoma. Dialysis is a treatment used to remove toxins from your body if the kidneys do not work properly.

Sex - Renal cell carcinoma is about twice as common in men as in women. Men are more likely to be smokers and are more likely to be exposed to cancer-causing chemicals at work, which may account for some of the difference.

Physical activity - An active lifestyle has many positive healthy benefits including decreasing high blood pressure, strengthening bones, helping to maintain a healthy weight, and reducing the risk of kidney cancer. It is important to discuss an exercise or physical activity regimen with your doctor - most physicians suggest getting at least 30 minutes a day of exercise.

Alcohol consumption - Alcohol use is a cause of cancer. Any level of alcohol consumption increases the risk of developing an alcohol-related cancer; the level of risk increases in line with the level of consumption. There is *convincing* evidence that alcohol use increases the risk of cancers of the mouth, pharynx, larynx, oesophagus, kidney, bowel (in men) and breast (in women), and *probable* evidence that it increases the risk of bowel cancer (in women) and liver cancer.

Age - According to the international literature, the risk of renal cell carcinoma significantly increases with age, most kidney cancers occur in people over 45 years of age; with the highest incidences between the ages of 55 and 84. Kidney cancer is mostly a disease seen in adults aged over 55, and is rare in children. In South Africa, according to the National Cancer Registry of 2014, there is a high incidence of kidney cancer in the 0 to 9 year age group with a peak in the 45 to 69 year age group in both males and females.

Dialysis - People who receive long-term dialysis for treatment of chronic renal failure are at greater risk of developing kidney cancer, possibly because renal failure depresses the immune system. People who have a kidney transplant and receive immunosuppressant drugs also are more likely to develop kidney cancer.

Radiation - In some cases, exposure to radiation may increase the risk of kidney cancer.

Obesity – Being overweight among adults has been linked with renal cell carcinoma (RCC) risk.

Landberg, A., Fäly, A., Montgomery, S., Sundqvist, P. & Fall, K. 2019.
"While overweight among adults has been linked with renal cell carcinoma (RCC) risk, little is known about the potential influence of overweight and obesity during adolescence. To ascertain if adolescent body mass index is associated with subsequent risk of RCC, we identified a cohort of 238,788 Swedish men who underwent mandatory military conscription assessment between 1969 and 1976 at a mean age of 18.5 years. At the time of conscription assessment, physical and psychological tests were performed including measurements of height and weight. Participants were followed through linkage to the Swedish Cancer Registry to identify incident diagnoses of RCC. The association between body mass index (BMI, kg/m^2) at conscription assessment and subsequent RCC was evaluated using multivariable Cox regression. During a follow-up of up to 37 years, 266 men were diagnosed with RCC. We observed a trend for higher RCC risk with increasing BMI during adolescence, where one-unit increase in BMI conferred a 6% increased risk of RCC (95% CI 1.01-1.10). compared to normal weight men (BMI 18.5- < 25), men with overweight (BMI 25- < 30) or obesity (BMI ≥30) had hazard ratios for RCC of 1.76 (95% CI 1.16-2.67) and 2.87 (95% CI 1.26-6.25), respectively. The link between overweight/obesity and RCC appear to be already established during late adolescence. Prevention of unhealthy weight gain during childhood and adolescence may thus be a target in efforts to decrease the burden of RCC in the adult population."

Diagnosis of Kidney Cancer
Early kidney cancer does not usually cause any signs or symptoms. Most kidney tumours are found incidentally - during an evaluation with radiologic imaging studies for other nonspecific abdominal complaints (gallbladder pain, for example), or during follow-up for other previously treated malignancies. These 'incidental cancers' are often found early, before any symptoms have occurred. Because such cancers are usually detected before they have spread, patients with incidental kidney tumours are often cured of their disease, commonly by surgery alone. As many as 30% of kidney masses represent a benign condition.

Some of the earliest signs and symptoms of kidney cancer include:
- Blood in the urine (haematuria)
- Low back pain on one side (not caused by injury)
- A mass (lump) on the side or lower back
- Fatigue (tiredness)
- Weight loss not caused by dieting
- Fever that is not caused by an infection and that does not go away after a few weeks
- Swelling of the ankles and legs (oedema)

None of these symptoms are positively indicative of kidney cancer. For example, blood in the urine may be a sign of kidney, bladder or prostate cancer, but can also be an indication of a bladder infection or a kidney stone.

Kim, T.H., Kang, Y.T., Cho, Y.H., Kim, J.H., Jeong, B.C., Seo, S.I., Jeon, S.S. & Lee, H.M. 2019.
INTRODUCTION: The aim of this study was to detect circulating tumour cells (CTCs) in patients with advanced renal cell carcinoma (RCC) using a novel CTC detection platform. Furthermore, we evaluated the clinical outcomes associated with a CTC-positive status.
METHODS: A total of 34 patients with advanced RCC (stage III or IV) were prospectively enrolled, and 104 peripheral blood samples were analyzed for the presence of CTCs at various time points.

CTCs were isolated using a tapered-slit filter, which captures CTCs based on size and deformability. The presence of CTCs was confirmed using both staining and morphological criteria. CTC status was then correlated with clinical characteristics and survival outcomes.
RESULTS: CTCs were detected in 62% of patients during the pre-treatment period, and the median CTC count was 2 (interquartile range 1-3). During the followup period, CTCs were detected in 56% (18/32), 65% (20/31), and 41% (7/17) of patients at one week, one month, and three months after treatment, respectively. Overall, CTCs were found in 57.9% (66/114) of blood samples in the range of 1-7 cells. Although no statistical significance was found, CTC detection in patients with stage IV disease was more common than in patients with stage III disease (68.4% vs. 53.3%). Two-year progression-free survival and cancer-specific survival tended to be lower in CTC-positive patients compared with CTC-negative patients.

The following tests and procedures may be used to diagnose kidney cancer:

Blood and urine tests - tests of blood and urine may give the doctor clues about what is causing the signs and symptoms.

Urinary aquaporin-I (AQP-1) and adipose differentiation-related protein (ADFP) as biomarkers of kidney cancer. This is a new process for:

- early and non-invasive detection of renal cancer
- population screening for renal cancer
- post-treatment surveillance for recurrence of renal cancer
- progression, regression or time-course of disease in untreated, partially treated, and definitively treated patients with renal cancer

Imaging tests - imaging tests allow a doctor to visualise a kidney tumour or abnormality. Imaging tests may include ultrasound, computerised tomography (CT) or magnetic resonance imaging (MRI).

Removing a sample of kidney tissue (biopsy) - in some selected cases, the doctor may recommend a procedure to remove a small sample of cells (biopsy) from a suspicious area of a kidney. Because surgery is usually the first line treatment for kidney cancer and a kidney biopsy carries the risk of a "false-negative," doctors usually forgo kidney biopsy. Kidney biopsy is typically reserved for cases that are most likely to be noncancerous or for people who can't undergo an operation.

Fine needle aspiration (FNA) - are sometimes used to obtain a biopsy of the kidney. This involves the insertion of a long, thin needle into the kidney to take a tiny sample of tissue for examination under a microscope. With modern biopsy methods, there is virtually no risk of 'spreading cancer'.

Cystoscopy and retrograde pyelography - if a doctor suspects that a kidney tumour is arising from the collecting system in the kidney, he/she may examine the patient using cystoscopy and retrograde pyelography. Using a cystoscope (an instrument consisting of a slender tube with a lens and light that is placed into the kidney through the urethra), the doctor can pass a small catheter into the opening of the ureter (the tube that carries urine form the kidney to the bladder), inject dye, and take X-ray pictures of the entire collecting system of the affected kidney to check for possible cancers.

Intravenous Pyelogram (IVP) – the doctor performs this examination by injecting a dye into the bloodstream, which travels to the kidneys, ureters, and bladder to more clearly outline these organs on x-ray. IVP has been largely replaced by CT scans because the CT scan creates a computer enhanced reconstruction of the entire urinary tract and more accurately identifies small tumours.

Types of Kidney Cancer

Renal Cell Carcinoma (RCC) **-** Renal Cell Carcinoma (RCC) is the most common type of kidney cancer, accounting for approximately 85% of all malignant kidney tumours. In RCC, cancerous (malignant) cells develop in the lining of the kidney tubules and grow into a mass called a tumour. Like many other cancers, the growth begins small and grows larger over time. RCC typically grows as a single mass. However, there are cases where a kidney may contain more than one tumour, or tumours are found in both kidneys at the same time.

Blas, L., Roberti, J., Petroni, J., Reniero, L. & Cicora, F. 2019.

PURPOSE OF THE REVIEW: We present an updated report of renal medullary carcinoma (RMC), a rare and aggressive condition.

RECENT FINDINGS: There is a majority of male patients, of African descent, in the second or third decade of life. In differential diagnosis, other tumors, such as malignant rhabdoid tumor (MRT), vinculin-anaplastic lymphoma kinase (VCL-ALK) translocation renal cell carcinoma, and collecting duct carcinoma, may present difficulties. Abnormalities of tumor suppressor gene SMARCB1 have been found in RMC. Reported symptoms were hematuria, pain, weight loss, respiratory distress, palpable mass, cough, and fever. Most patients present with metastases at diagnosis. There is no definite recommended treatment, and protocols are extrapolated from other malignancies, with nephrectomy and systemic therapies being most frequently used. Response to treatment and prognosis remain very poor. RMC is a rare and aggressive tumor. Definitive diagnosis requires histological assessment and the presence of sickle-cell hemoglobinopathies.

Types of Renal Cell Carcinoma (RCC)

There are five main types of renal cell carcinoma that are identified by examining the tumour under a microscope: clear cell, papillary, chromophobe, collecting duct and 'unclassified'.

Clear Cell RCC - Clear Cell RCC is the most common form of renal cell carcinoma, accounting for about 80% of people with kidney cancer. When viewed under a microscope, the individual cells that make up *clear cell* renal cell carcinoma appear very pale or clear.

Papillary RCC - Papillary RCC is the second most common type - about 10% to 15% of people have this form. These cancers form little finger-like projections (called papillae).

Chromophobe RCC - The third most common form of renal carcinoma is chromophobe RCC, accounting for about 5% of cases. Like clear cell carcinoma, the cells of these cancers are also pale, but are much larger and have certain other distinctive features.

Collecting Duct RCC - The rarest form of RCC is collecting duct renal carcinoma. The major characteristic of collecting duct RCC is that the cancer cells can form irregular tubes.

Unclassified RCC - About 5% of renal cancers are *unclassified* because their appearance does not fit into any of the other categories.

Recent data suggests that clear cell RCC has a slightly worse prognosis as compared to papillary or chromophobe cell RCC. However, the majority of low stage tumours, regardless of cell type, can be cured with surgical resection. Oncocytoma is usually a benign lesion with an extremely low chance of spreading. Spindle cell types, or sarcomas, tend to grow and spread more quickly than the other kinds of renal cell carcinoma. It can be associated with any of the subtypes mentioned, and this subtype is a sign of a poor prognosis.

Other Types of Cancerous Kidney Tumours

RCC accounts for about 90% of malignant kidney tumours. Less common types of cancerous tumours include transitional cell carcinomas, Wilms tumours and renal sarcomas.

Transitional Cell Carcinoma: About 5% to 10% of all kidney tumours are transitional cell carcinomas, also known as *urothelial carcinomas*. Transitional cell carcinomas begin in the renal pelvis (the junction of ureter and kidney). Under the microscope, transitional cell carcinomas look like bladder cancer cells and act very much like bladder cancer. Studies have shown that, like bladder cancer, these cancers are linked to cigarette smoking and occupational exposures to certain cancer-causing chemicals.

The signs and symptoms of transitional cell carcinoma are typically the same as with renal cell carcinoma - blood in the urine and, sometimes, back pain.

Transitional cell carcinomas are usually treated by surgically removing the entire kidney and the ureter, as well as the section of the bladder where the ureter is attached. Chemotherapy and radiation therapy are often used in addition to surgery, depending on how much cancer is found. As with RCC, with early stage transitional cell carinomas, there are several treatments. If a patient has early transitional cell carcinoma, there are several treatment options available. There are different ways to surgically treat early disease. Newer surgical techniques are also being studied. Patients should talk with their surgeon and be aware of their options and the benefits and risks of those options.

About 90% of transitional cell carcinomas of the kidney are curable if they are found early enough. The chances for cure drop dramatically if the tumour has grown into the ureter wall, or if it has a more aggressive (high-grade) appearance when viewed under the microscope.

Wilms Tumour - About 5% to 6% of all kidney cancers are Wilms' tumours. This type of cancer is almost always found in children and is extremely rare among adults. It has a female predominance and a higher incidence in black children. Seventy eight per cent of children are diagnosed at 1 - 5 years of age, with a peak incidence at 3 - 4 years. Wilms' tumour usually occurs sporadically, but in 1% of cases it is familial.

Zou, X.P., Jiang, Y.Y., Liao, Y., Dang, Y.W., Chen, G., Feng, Z.B. & Ma, Y. 2019.
"A combination of a Wilms' tumor (WT) and renal cell carcinoma (RCC) is an extremely rare pediatric renal neoplasm. Its prognosis and clinicopathological features remain unclarified. Herein, we describe a case of the coexistence of a WT and an RCC in a male child aged 5 years and 10 months.

The child had symptoms of hematuria for more than 1 month. Although his irises were clear, medical imaging revealed a potential malignant tumor in the left kidney. The patient underwent resection of the left kidney. The pathological diagnosis was the coexistence of a WT and papillary RCC. Negative surgical margins were examined. One month following the resection, chemotherapy with vincristine plus dactinomycin (EE-4A regimen) was commenced. At the 69-month follow-up, there was no recurrence or metastasis. The coexistence of a WT and an RCC in the pediatric population is considered a rare pathological event. At present, there is no standard treatment for these renal neoplasms. In this study, the RCC treatment, which was the same as that applied in cases of WTs, was reasonable."

Renal Sarcoma - Renal sarcomas are a rare type of kidney cancer (less than 1% of all kidney tumours) that begins within the kidney's connective tissue.

Doroudinia, A., Ahmadi, S., Mehrian, P. & Pourabdollah, M. 2019.
"Primary Ewing sarcoma (ES) or primitive neuroectodermal tumour (PNET) is a rare tumour in adults and primary renal involvement is extremely rare. Patients with renal ES or PNET respond to and would benefit from conventional ES treatment according to ES study protocols. Here, we report a case of a young woman, presenting with right flank pain and haematuria. After ultrasound and CT evaluation, a right middle pole renal mass was detected. The patient underwent radical right nephrectomy, and a grade 4 ES with peritoneal involvement was documented. Subsequently, the patient underwent adjuvant chemotherapy for 5 months. Follow-up 18F-fluorodeoxyglucose (FDG) positron emission tomography (PET)/CT scan demonstrated bilateral cervical, hilar, mediastinal and retroperitoneal FDG-avid adenopathies associated with mild right-sided pleural effusion with no metabolic activity, signifying the role of PET/CT scan in tumour restaging."

Benign (Non-Cancerous) Kidney Tumours
Some types of kidney tumours (including renal cell adenomas, renal oncocytomas and angiomyolipomas) do not usually spread (metastasize) to other parts of the body, although they can still grow and cause problems.

Renal Adenoma - Renal adenomas are very small, slow growing, benign tumours that, under a microscope, look a lot like low-grade renal cell carcinomas. In rare cases, tumours first thought to be renal adenomas may turn out to be small renal cell carcinomas.

Oncocytoma **-** Oncocytomas are a type of benign kidney tumour that can sometimes grow quite large. Because oncocytomas do not normally metastasize to other organs, removing the kidney can often produce a cure.

Angiomyolipoma - Angiomyolipomas are another rare benign kidney tumour. They often develop in people with tuberous sclerosis (a disease charachterized by several bumps on the skin, seizures, mental retardation, and cysts in the kidneys, liver and pancreas).

Stages of Kidney Cancer

A staging system is a standardised way in which the cancer care team describes the extent of the cancer. Staging assists the treating physician to better plan a treatment regimen for each patient. Use is often made of the TNM system of staging.

How Kidney Cancer Spreads Through the Body

In the event of kidney cancer spreading to other parts of the body, it would most probably spread as indicated below:

Cancer Type:	Main Sites of Metastasis (Spread)
Bladder	Bone, liver, lung
Breast	Bone, brain, liver, lung
Colon	Liver, lung
Colorectal	Liver, lung, peritoneum (lining of abdomen)
Kidney	Adrenal gland, bone, brain, liver, lung
Lung	Adrenal gland, bone, brain, liver, other lung
Melanoma	Bone, brain, liver, lung, skin, muscle
Ovary	Liver, lung, peritoneum (lining of abdomen)
Pancreas	Liver, lung, peritoneum (lining of abdomen)
Prostate	Adrenal gland, bone, liver, lung
Stomach	Liver, lung, peritoneum (lining of abdomen), ovaries
Thyroid	Bone, liver, lung
Uterus	Boner, liver, lung, peritoneum (lining of abdomen), vagina
Non-melanoma skin cancer	Very rare: lymph nodes, lung, bone (if in head/neck region)

Treatment of Kidney Cancer

Common treatment options for people with kidney cancer usually include surgery, targeted therapy, and biological therapy. A patient may receive more than one type of treatment.

Treatment depends mainly on the following:

- The size of the tumour
- Whether the tumour has invaded tissues outside the kidney
- Whether the tumour has spread to other parts of the body
- Age and general health

At any stage of disease, supportive care is available to control pain and other symptoms, to relieve the side effects of treatment and to ease emotional concerns. For example, some people with kidney cancer may need to have radiation therapy to relieve pain or certain other problems.

According to *Cancer Therapy Advisor*, Cabozantinib, Sunitinib, Pazopanib, and Tivozanib show similar efficacy for the treatment of metastatic renal cell carcinoma (mRCC), but Tivozanib's safety profile is superior to the profiles of the other 3 tyrosine kinase inhibitor (TKI) drugs, according to the results of a network meta-analysis published in the journal *Advances in Therapy*.

Xu, W., Atkins, M.B. & McDermott, D.F. 2020.
"Kidney cancer has unique features that make this malignancy attractive for therapeutic approaches that target components of the immune system. Immune checkpoint inhibition is a well-established part of kidney cancer treatment, and rapid advances continue to be made in this field. Initial preclinical studies that elucidated the biology of the programmed cell death 1 (PD-1), programmed cell death 1 ligand 1 (PD-L1) and cytotoxic T lymphocyte antigen 4 (CTLA-4) immune checkpoints led to a series of clinical trials that resulted in regulatory approval of nivolumab and the combination of ipilimumab plus nivolumab for the treatment of advanced renal cell carcinoma. Subsequent data led to approvals of combination strategies of immune checkpoint inhibition plus agents that target the vascular endothelial growth factor receptor and a shift in the current standard of renal cell carcinoma care. However, controversies remain regarding the optimal therapy selection and treatment strategy for individual patients, which might be eventually overcome by current intensive efforts in biomarker research. That work includes evaluation of tumour cell PD-L1 expression, gene expression signatures, $CD8^+$ T cell density and others. In the future, further advances in the understanding of immune checkpoint biology might reveal new therapeutic targets beyond PD-1, PD-L1 and CTLA-4, as well as new combination approaches."

Nayan, M., Punjani, N., Juurlink, D.N., Finelli, A., Austin, P.C., Kulkarni, G.S., Uleryk, E. & Hamilton, R.J. 2019.
OBJECTIVES: Metformin has been associated with improved survival outcomes in various malignancies. However, studies in kidney cancer are conflicting. We performed a systematic review and meta-analysis to evaluate the association between metformin and kidney cancer survival.
MATERIALS AND METHODS: We searched Medline and EMBASE databases from inception to June 2017 to identify studies evaluating the association between metformin use and kidney cancer survival outcomes. We evaluated risk of bias with the Newcastle-Ottawa scale. We pooled hazard ratios (HRs) for recurrence-free, progression-free, cancer-specific, and overall survival using random effects models, and explored heterogeneity with metaregression. We evaluated publication bias through Begg's and Egger's tests, and the trim and fill procedure.
RESULTS: We identified 9 studies meeting inclusion criteria, collectively involving 7426 patients. Five studies were at low risk of bias. The direction of association for metformin use was toward benefit for recurrence-free survival (HR, 0.99; 95% confidence interval [CI], 0.36-2.74), progression-free survival (pooled HR, 0.84; 95% CI, 0.66-1.07), cancer-specific (pooled HR, 0.72; 95% CI, 0.48-1.09), and overall survival (pooled HR, 0.73; 95% CI, 0.50-1.09), though none reached statistical significance. Metaregression found no study-level characteristic to be associated with the effect size, and there was no strong evidence of publication bias for any outcome.
CONCLUSIONS: There is no evidence of a statistically significant association between metformin use and any survival outcome in kidney cancer.

Surgery
Surgery is the most common treatment for people with kidney cancer. The type of surgery depends on the size and stage of the cancer, whether the patient has two kidneys, and whether cancer was found in both kidneys.

Assi, T., El Rassy, E., Farhat, F. & Kattan, J. 2020.
"The advent of molecular therapy through targeted kinase inhibitors (TKI) has revolutionized the management of renal cell carcinoma. Although surgical resection remains the cornerstone of any therapeutic plan, an increased risk of morbidity and mortality can be of concern in large and complex bulky tumors. Preoperative therapy with TKIs is hypothesized to facilitate resectability,

reduce surgical morbidity and allow nephron-sparing surgery. Many concerns on the safety, efficacy and tolerability of these agents before surgery have halted the progress in this setting. In this paper, we will review the indications and safety of preoperative TKIs in RCC as well as the future approaches."

The patient and his/her surgeon can talk about the types of surgery and which may be right:

Removing all of the kidney (radical nephrectomy): The surgeon removes the entire kidney along with the adrenal gland and some tissue around the kidney. Some lymph nodes in the area may also be removed.

Removing part of the kidney (partial nephrectomy): The surgeon removes only the part of the kidney that contains the tumour. People with a kidney tumour that is smaller than a tennis ball may choose this type of surgery.

There are two approaches for removing the kidney. The surgeon may remove the tumour by making a large incision into the body (open surgery). Or the surgeon may remove the tumour by making small incisions (laparoscopic surgery). The surgeon sees inside the abdomen with a thin, lighted tube (a laparoscope) placed inside a small incision. Sometimes a robot is used. The surgeon uses handles below a computer display to control the robot's arms.

The surgeon may use other methods of destroying the cancer in the kidney. For people who have a tumour smaller than 4cm and who can't have surgery to remove part of the kidney because of other health problems, the surgeon may suggest:

Cryosurgery: The surgeon inserts a tool through a small incision or directly through the skin into the tumour. The tool freezes and kills the kidney tumour.

Radiofrequency ablation: The surgeon inserts a special probe directly through the skin or through a small incision into the tumour. The probe contains tiny electrodes that kill the kidney cancer cells with heat.

It takes time to heal after surgery, and the time needed to recover is different for each person. It is common to feel weak or tired for a while.

Pain or discomfort may be felt for the first few days. Medicine can help control the pain. Before surgery, there should be discussions about a plan for pain relief with the doctor or nurse. After surgery, the doctor can adjust the plan if the patient needs more pain control.
The health care team will watch for signs of bleeding, infection, or other problems. They will keep track of how much fluid the patient takes in and how much urine passes out of his/her body.

If one kidney is removed, the remaining kidney is usually able to do the work of both kidneys. However, if the remaining kidney is not doing a good job cleaning the blood, the patient may need dialysis. Some people may need a transplant with a healthy kidney from a donor.

Arterial Embolisation for Kidney Cancer

Arterial embolisation for kidney cancer is a treatment that may be used when surgery to remove the tumour is not an option. This treatment is meant to shrink the tumour and relieve the symptoms of kidney cancer by blocking the flow of blood to the tumour. After undergoing an arterial embolization for kidney cancer, some people may experience back pain or develop a fever. Other side effects of arterial embolization can include nausea and vomiting.

Targeted Therapy

People with kidney cancer that has spread may receive a type of drug called targeted therapy. Many kinds of targeted therapy are used for kidney cancer. This treatment may shrink a kidney tumour or slow its growth.

Usually, the targeted therapy is taken by mouth. Patients may feel very tired while taking targeted therapy for kidney cancer. Other side effects may include diarrhoea, nausea, vomiting, sores on the lips or in the mouth and high blood pressure.

Pérez-Gracia, J.L., Castellano, D., Climent, M.Á., Mellado, B. & Suárez, C. 2019.

"The introduction of targeted therapy for the treatment of advanced renal cell carcinoma (RCC) has improved the outcome of these patients in the last decade. However, many patients still relapse. The aim of this consensus study was to establish common recommendations about the best treatment options in patients with RCC. A two-round Delphi methodology was used. A total of 25 statements were submitted to a panel of 30 specialists. If consensus was not obtained in the first round a second and last round was performed. Agreement was achieved for 19 of the proposed 25 statements (76%). When making a decision about the treatment option, considering the efficiency and response rate to previous treatment, drug's toxicity and the patients' clinical features are very relevant."

Biological Therapy

People with kidney cancer that has spread may receive biological therapy. Biological therapy for kidney cancer is a treatment that may improve the body's natural defence (the immune system response) against cancer. The treatments used for kidney cancer can slow the growth of tumours or shrink them. The biological therapy is injected intravenously or under the skin. The treatment may be given at the hospital or a doctor's office.

Immunotherapy, also called biologic therapy, is a type of cancer treatment that boosts the body's natural defenses to fight cancer. It uses substances made by the body or in a laboratory to improve or restore immune system function. Immunotherapy may work by stopping or slowing the growth of cancer cells.

Cortellini, A., Buti, S., Santini, D., Perrone, F., Giusti, R., Tiseo, M., Bersanelli, M., Michiara, M., Grassadonia, A., Brocco, D., Tinari, N., De Tursi, M., Zoratto, F., Veltri, E., Marconcini, R., Malorgio, F., Garufi, C., Russano, M., Anesi, C., Zeppola, T., Filetti, M., Marchetti, P., Botticelli, A., Antonini Cappellini, G.C., De Galitiis, F., Vitale, M.G., Sabbatini, R., Bracarda, S., Berardi, R., Rinaldi, S., Tudini, M., Silva, R.R., Pireddu, A., Atzori, F., Chiari, R., Ricciuti, B., Iacono, D., Migliorino, M.R., Rossi, A., Porzio, G., Cannita, K., Ciciarelli, V., Fargnoli, M.C., Ascierto, P.A. & Ficorella, C. 2019.

BACKGROUND: Patients with a history of autoimmune diseases (AIDs) have not usually been included in clinical trials with immune checkpoint inhibitors.

MATERIALS AND METHODS: Consecutive patients with advanced cancer, treated with anti-programmed death-1 (PD-1) agents, were evaluated according to the presence of pre-existing AIDs. The incidence of immune-related adverse events (irAEs) and clinical outcomes were compared among subgroups.
RESULTS: A total of 751 patients were enrolled; median age was 69 years. Primary tumors were as follows: non-small cell lung cancer, 492 (65.5%); melanoma, 159 (21.2%); kidney cancer, 94 (12.5%); and others, 6 (0.8%). Male/female ratio was 499/252. Eighty-five patients (11.3%) had pre-existing AIDs, further differentiated in clinically active (17.6%) and inactive (82.4%). Among patients with pre-existing AIDs, incidence of irAEs of any grade was significantly higher when compared with patients without AIDs (65.9% vs. 39.9%). At multivariate analysis, both inactive (p = .0005) and active pre-existing AIDs (p = .0162), female sex (p = .0004), and Eastern Cooperative Oncology Group Performance Status <2 (p = .0030) were significantly related to a higher incidence of irAEs of any grade. No significant differences were observed regarding grade 3/4 irAEs and objective response rate among subgroups. Pre-existing AIDs were not significantly related with progression-free survival and overall survival.
CONCLUSION: This study quantifies the increased risk of developing irAEs in patients with pre-existing AIDs who had to be treated with anti-PD-1 immunotherapy. Nevertheless, the incidence of grade 3/4 irAEs is not significantly higher when compared with control population. The finding of a greater incidence of irAEs among female patients ranks among the "hot topics" in gender-related differences in immuno-oncology.
IMPLICATIONS FOR PRACTICE: Patients with a history of autoimmune diseases (AIDs) have not usually been included in clinical trials with immune checkpoint inhibitors but are frequent in clinical practice. This study quantifies the increased risk of developing immune-related adverse events (irAEs) in patients with pre-existing AIDs who had to be treated with anti-programmed death-1 immunotherapy. Nevertheless, their toxicities are mild and the incidence of grade 3/4 irAEs is not significantly higher compared with those of controls. These results will help clinicians in everyday practice, improving their ability to offer a proper counselling to patients, in order to offer an immunotherapy treatment even to patients with pre-existing autoimmune disease.

Adjuvant Therapy
Until recently there was no adjuvant therapy for kidney cancer treatment.

Spek, A., Szabados, B., Casuscelli, J. Stief, C. & Staehler, M. 2019.
BACKGROUND: Until recently, there was no approved adjuvant therapy (AT) for renal cell carcinoma (RCC) unless sunitinib was approved in the US. We evaluated clinical opinion and estimated use regarding different treatment options and patient selection of AT in RCC patients based on current scientific data and individual experience in Germany.
METHODS: We conducted an anonymous survey during a national urology conference in 01/2017. Answers of 157 urologists treating RCC patients could be included. Questions were related to practice setting, treatment of RCC, follow-up strategy, physicians' personal opinion and individually different important parameters regarding S-TRAC and ASSURE-trial.
RESULTS: 82% were office based. 67% were located in larger cities. 83% reported that nephron-sparing surgery (NSS) was performed in tumors with diameter < 4 cm. Follow-up was done mainly in concordance with guideline recommendations. 68% treated an average of 2.9 patients/year with systemic therapy. Therapy was predominantly advocated using sunitinib (94%). Urologists were informed about S-TRAC and ASSURE-trial. For 47%, reported hazard ratio is the most important

parameter to understand trial results followed by overall survival (OS) in 46%, disease-free survival in 38%, and results of other trials in 34%. The most convincing parameter to decide on AT is OS (69%). 62% placed their confidence in ASSURE over STRAC-trial. 44% would use AT for 12 months. Nodal involvement was the most common denominator for use of AT. 82% favor sunitinib as AT.
CONCLUSIONS: A minority of urologists would use AT and are more confident in ASSURE-trial. Reluctance of prescribing AT mainly is based on lack of OS data and conflicting trial results.

Radiotherapy

Renal-cell carcinoma is considered to be radio-resistant, but it was recently found that this notion might be wrong. During Recent research De Meerleer, *et al*. (2014) found that if given in a few (even single) fractions, but at a high fraction dose, steriotactic body radiotherapy becomes increasingly important in the management of renal-cell carcinoma, both in primary settings and in treatment of oligometastatic disease.

There is an established biological rationale for the radio-sensitivity of renal-cell carcinoma to stereotactic body radiotherapy based on the ceramide pathway, which is activated only when a high dose per fraction is given. Apart from the direct effect of stereotactic body radiotherapy on renal-cell carcinoma, stereotactic body radiotherapy can also induce an abscopal effect (an abscopal effect is a phenomenon in the treatment of metastatic cancer where localised irradiation of a tumour causes not only a shrinking of the irradiated tumour but also a shrinking of tumours far from the irradiated area), This effect, caused by immunological processes, might be enhanced when targeted drugs and stereotactic body radiotherapy are combined. Therefore, rigorous, prospective randomised trials involving a multidisciplinary scientific panel are needed urgently, according to De Meerleer, *et al*.

Second Opinion

Before starting treatment, patients may want a second opinion about the diagnosis, stage of cancer, and treatment plan. Some people worry that the doctor will be offended if they ask for a second opinion. Usually the opposite is true. Most doctors welcome a second opinion.

If a patient gets a second opinion, the second doctor may agree with the first doctor's diagnosis and treatment plan. Or the second doctor may suggest another approach. Either way, the patient has more information and perhaps a greater sense of control. Patients can also feel more confident about the decisions they make, knowing that they have looked at all of their options.

It may take some time and effort to gather the medical records and see another doctor. In most cases, it's not a problem to take several weeks to get a second opinion. The delay in starting treatment usually will not make treatment less effective. To make sure, patients should discuss this delay with their doctor.

Side Effects of Treatment

Because treatment may damage healthy cells and tissues, unwanted side effects are common. These side effects depend mainly on the type and extent of the treatment. Side effects may not be the

same for each person, and they may change from one treatment session to the next. Before treatment starts, the health care team will explain possible side effects and suggest ways to help the patient manage them.

Surgery - It takes time to heal after surgery, and the time needed to recover is different for each person. Patients are often uncomfortable during the first few days. However, medicine can usually control their pain. Before surgery, patients should discuss the plan for pain relief with the doctor or nurse. After surgery, the doctor can adjust the plan if more pain relief is needed.

It is common to feel tired or weak for a while. The health care team watches the patient for signs of kidney problems by monitoring the amount of fluid the patient takes in and the amount of urine produced. They also watch for signs of bleeding, infection, or other problems requiring immediate treatment. Lab tests help the health care team monitor for signs of problems.

If one kidney is removed, the remaining kidney generally is able to perform the work of both kidneys. However, if the remaining kidney is not working well or if both kidneys are removed, dialysis is needed to clean the blood. For a few patients, kidney transplantation may be an option. For this procedure, the transplant surgeon replaces the patient's kidney with a healthy kidney from a donor.

Ventimiglia, E., Larcher, A., Trevisani, F., Muttin, F., Cianflone, F., Montorsi, F., Salonia, A., Bertini, R. & Capitanio, U. 2019. Post-operative complications increase the risk of long-term chronic kidney disease after nephron sparing surgery in renal cancer patients with normal preoperative renal function. BJU Int. 2019 Feb 15. doi: 10.1111/bju.14712. [Epub ahead of print]
OBJECTIVES: To investigate whether post-operative complications may affect long-term functional outcomes of renal patients treated with nephron sparing surgery (NSS).
MATERIALS AND METHODS: We performed an observational study enrolling 596 patients with pre-operative normal renal function treated with NSS for clinical T1abN0M0 renal mass. Cox regression models estimated hazard ratios (HR) and 95% confidence intervals (CI) for CKD including as covariates age, comorbidity (scored as for the Charlson comorbidity index), hypertension, tumor size, pre-operative eGFR, eGFR<60 ml/min/1.73m^2 at discharge, and ischemia time.
RESUTLS: Of all, 137 (23%) patients developed post-operative complications. At a median follow-up of 53 (26-91) months, CKD risk was 19% for patients with post-operative complications and 11% for those without complications. Patients experiencing post-operative complications (HR 1.90, 95% CI 1.26-2.86) were at increased risk of developing CKD during the follow up at multivariable analysis, after accounting for confounders.
CONCLUSIONS: Our data outline how post-operative complications might have a detrimental impact on post-operative renal function in patients submitted to NSS. Improper patient selection, increasing the risk of post-operative complications, could limit the benefit in terms of renal function brought by NSS. This article is protected by copyright.

Arterial Embolisation - After arterial embolization, some patients have back pain or develop a fever. Other side effects are nausea and vomiting. These problems will usually go away soon.

Radiation Therapy - The side effects of radiation therapy depend mainly on the amount of radiation given and the part of the body that is treated. Patients are likely to become very tired during

radiation therapy, especially in the later weeks of treatment. Resting is important, but doctors usually advise patients to try to stay as active as they can.

Radiation therapy to the kidney and nearby areas may cause nausea, vomiting, diarrhoea, or urinary discomfort. Radiation therapy also may cause a decrease in the number of healthy white blood cells, which help protect the body against infection. In addition, the skin in the treated area may sometimes become red, dry, and tender. Although the side effects of radiation therapy can be distressing, the doctor can usually treat or control them.

Biological Therapy - Biological therapy may cause flu-like symptoms, such as chills, fever, muscle aches, weakness, loss of appetite, nausea, vomiting, and diarrhoea. Patients also may get a skin rash. These problems can be severe, but they go away after treatment stops.

Chemotherapy - Kidney cancer does not respond well to chemotherapy drugs.

The side effects of chemotherapy depend mainly on the specific drugs and the amount received at one time. In general anticancer drugs affect cells that divide rapidly, especially:

Blood cells: These cells fight infection, help the blood to clot, and carry oxygen to all parts of the body. When drugs affect blood cells, patients are more likely to get infections, may bruise or bleed easily, and may feel very weak and tired.

Cells in hair roots: Chemotherapy can cause hair loss. The hair grows back, but sometimes the new hair is somewhat different in colour and texture.

Cells that line the digestive tract: Chemotherapy can cause poor appetite, nausea and vomiting, diarrhoea, or mouth and lip sores. Many of these side effects can be controlled with drugs.

Reducing the Risk for Kidney Cancer

Taking steps to improve one's health may help reduce the risk of kidney cancer. To reduce the risk:

- Quit smoking. If smoking, quit. Many options for quitting exist, including support programs, medications and nicotine replacement products. Contact CANSA to join CANSA's e-KickButt programme
- Eat at least five portions of vegetables and fresh fruit (in season). A variety of fruits and vegetables helps ensure getting all the nutrients one needs. Replace some snacks and side dishes with fruits and vegetables – this may help one lose weight as well
- Maintain a healthy weight. Work to maintain a healthy weight. If overweight or obese, reduce the number of calories consumed each day and try to exercise most days of the week
- Control high blood pressure
- Reduce or avoid exposure to environmental toxins (Mayo Clinic).

Tahbaz, R., Schmid, M. & Merseburger, A.S. 2018. Prevention of kidney cancer incidence and recurrence: lifestyle, medication and nutrition. *Curr Opin Urol*. 2018 Jan;28(1):62-79. doi: 10.1097/MOU.0000000000000454.

PURPOSE OF REVIEW: The incidence of kidney cancer rises globally with the highest rates in developed countries. This demonstrates the impact of advanced diagnostic imaging but also rising prevalence of modifiable risk factors such as smoking, obesity and hypertension. A literature search was performed with focus on recent studies on risk factors related to lifestyle, medication and nutrition. Further we searched for the effect of cancer prevention strategies.

RECENT FINDINGS: Overall, we included 76 studies of the past 5 years. Based on current evidence smoking tobacco, obesity and hypertension remain established risk factors for kidney cancer. Certain analgesics and consumption of processed meat have been linked to increase development of renal cell carcinoma, although data are limited. Fruits, fiber-rich vegetables, coffee and physical activity may have a protective effect against kidney cancer but causal conclusions are not yet supported. Significantly, there is an increasing evidence of inverse association between moderate alcohol consumption.

SUMMARY: Overall evidence confirms an effective way to prevent the risk of kidney cancer is maintaining a healthy weight and avoid smoking. State policies should further ensure strategies to raise public awareness and support to adopt healthy lifestyles.

Complications of Kidney Cancer

Complications that have been mentioned in various sources for Kidney Cancer includes:

- Metastases (cancer that has spread) to:
  - Lungs
  - Bones
  - Brain
- Paraneoplastic syndrome
- Blood clots
- Congestive heart failure
- Polycythaemia
- Pyrexia (fever) of unknown origin
- AA amyloidosis
- Renal cysts
- Malignant hepatopathy
- Haematuria
- Cutaneous metastasis
- Renal enlargement

Follow-up Care

After surgery for early or locally advanced kidney cancer, the patient will have regular check-ups. The first appointment is usually 4 to 6 weeks after going home from hospital. This is to make sure the patient is recovering well from the operation. After this, if the risk of cancer coming back is

thought to be low, they patient may only need follow up for 5 years. They might have a chest X-ray every 3 months for the first 2 years, and then every 6 months until they reach 5 years.

If the risk of cancer coming back is higher patients are usually ordered to undergo regular CT scans for the first 3 years. Things that increase the risk of the cancer coming back include:

- Having a tumour larger than 5cm across
- Changes in the tumour cells called sarcomatoid de-differentiation
- Tumour cells at the edge of the tissue that the surgeon removed – doctors call this a positive margin
- Raised levels in the blood of a chemical called alkaline phosphatase
- Raised levels in the blood of a chemical called lactate dehydrogenase

If all is well after 3 years, the patient is advised to have X-rays every 6 months. But this follow up may continue for life to check for any sign of the cancer coming back.

After surgery for kidney cancer, the more time that passes with no sign of it, the smaller the risk of the cancer ever coming back. But there is still a small risk, even after 10 years.

What happens at follow-up appointments

The treating doctor will conduct a physical examination and may order one or more of the following tests:

- Blood tests
- Chest X-ray
- CT scan
- Ultrasound scan

Follow-up after cryotherapy or radiofrequency ablation

In the event of a small kidney cancer treated by cryotherapy or radiofrequency ablation, the patient will be advised to attend appointments and scans every 3 to 6 months. These are to see whether the cancer has come back or is growing.

Appointments during biological therapy treatment for advanced kidney cancer

In the case of advanced cancer and while on treatment with biological therapy, the patient will be advised to attend regular appointments and scans every 3 to 6 months. The scans check how well the treatment is working.

Between appointments

Patients who have any concerns or who are worried or notice any new symptoms between appointments, must contact their doctor as soon as possible (CancerHelp UK).

About Clinical Trials

Clinical trials are research studies that involve people. They are conducted under controlled conditions. Only about 10% of all drugs started in human clinical trials become an approved drug.

Clinical trials include:

- Trials to test effectiveness of new treatments
- Trials to test new ways of using current treatments
- Tests new interventions that may lower the risk of developing certain types of cancers
- Tests to find new ways of screening for cancer

The South African National Clinical Trials Register provides the public with updated information on clinical trials on human participants being conducted in South Africa. The Register provides information on the purpose of the clinical trial; who can participate, where the trial is located, and contact details.

For additional information, please visit: www.sanctr.gov.za/

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This Fact Sheet is intended to provide general information only and, as such, should not be considered as a substitute for advice, medically or otherwise, covering any specific situation. Users should seek appropriate advice before taking or refraining from taking any action in reliance on any information contained in this Fact Sheet. So far as permissible by law, the Cancer Association of South Africa (CANSA) does not accept any liability to any person (or his/her dependants/ estate/heirs) relating to the use of any information contained in this Fact Sheet.

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Beetroot family
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