Title	Basics of Kidney Cancer
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Course No	KC4020708
Contact Hours	4

Purpose

The goal of this course is to help health care professionals learn about kidney cancer, the different types, treatments, and answers to frequently asked questions.

Objectives

1. Discuss how cancer develops.
2. Describe four types of kidney cancer.
3. Identify three common symptoms of kidney cancer.
4. Differentiate between Stages I, II, III, and IV kidney cancer.
5. List the two most important prognostic factors for kidney cancer.
6. State the most prominent risk of kidney cancer.

Kidney Cancer

Cancer develops when cells in the body start to grow out of control. There are many kinds of cancer and all are from out of control cells. Normal body cells grow, divide, and die. When a person is young, normal cells divide more rapidly until the person becomes an adult. Then most cells divide only to replace worn out or dying cells and to repair injuries. Because cancer cells continue to grow and divide, they are different from normal cells. Instead of dying, they outlive normal cells and continue to form new abnormal cells.

Damage to DNA causes cancer cells to develop. DNA is in all cells and directs all activities. When DNA becomes damaged the body is able to repair it most of the time. In cancer cells, the damaged DNA is not repaired. People can inherit damaged DNA, which accounts for inherited cancers. More often a person's DNA becomes damaged by exposure to something in the environment like smoking. Cancer usually forms as a tumor. Some cancers do not form tumors, like leukemia. These cancer cells involve the blood and blood-forming organs and circulate through other tissues where they grow. Metastasis is when cancer cells travel to other parts of the body where they begin to grow and replace normal tissue. No matter where a cancer may spread, it is always named for the place it began. Breast cancer that spreads to the lungs is still called breast cancer, not lung cancer.

Tumors that form and are not cancerous are called benign tumors and they do not spread (metastasize) to other parts of the body. With very rare exceptions, they are not life threatening. Different types of cancer can behave very differently. Lung cancer and breast cancer are very different diseases and they grow at different rates and respond to different treatments. That is why people with cancer need treatment that is aimed at their particular kind of cancer. Cancer is the second leading cause of death in the United States. In the U.S., 1/2 of all men and 1/3 of all women will develop cancer during their lifetimes. Millions of people today have had cancer or are living with cancer. Quitting smoking is one lifestyle change a person can

make that will reduce the chance of getting cancer. (1)

The Kidneys

The kidneys are part of the urinary tract. The kidneys are a pair of organs on either side of the spine in the lower abdomen, each one about the size of a fist. The kidneys can be divided into two main functional parts. The outer region of the kidneys is called the cortex, which is responsible for the filtration of blood. It consists of a series of collecting tubules. The inner region of the kidneys contain medullary pyramids that collect the filtrate (urine) from these collecting tubules and send it to the urinary bladder via the ureters. This inner region is called the renal pelvis. Different types of cancers develop from the two different regions of the kidneys. On top of each kidney is an adrenal gland. The kidneys and adrenal glands are enclosed by a mass of fatty tissue and a layer of fibrous tissue. The kidneys make urine by removing wastes and extra water from the blood. The urethra is a tube that drains the urine from the body. The kidneys make substances that help control blood pressure. They produce erythropoetin, a hormone responsible for the production of the oxygen carrying red blood cells. They also ensure that the electrolytes within the blood are correct.

Several types of cancer can start in the kidney, but the most common type in adults is renal cell cancer. It is sometimes called renal adenocarcinoma or hypernephroma. It accounts for more than 90% of malignant kidney tumors. Like all cancers, renal cell carcinoma begins small and grows larger over time. Although renal cell carcinoma usually grows as a single mass within the kidney, a kidney may contain more than one tumor. Sometimes tumors may be found in both kidneys at the same time. Some renal cell carcinomas are noticed only after they have become quite large. Most are found before they metastasize to other organs through the bloodstream or lymph vessels. Like most cancers, renal cell carcinoma is difficult to treat once it has metastasized. There are five main types of renal cell carcinoma that are identified by examining the tumor under a microscope: clear cell, papillary, chromophobe, collecting duct, and "unclassified".

When viewed under a microscope, the individual cells that make up clear cell renal cell carcinoma appear very pale or clear. This is the most common form of renal cell carcinoma. About 80% of people with renal cell carcinoma have this kind of cancer. Papillary renal cell carcinoma is the second most common type. About 10-15% of people have this kind. These cancers form little finger-like projections (called papillae) in some, if not most, of the tumor. Some doctors call these cancers chromophilic because the cells take up certain dyes used in preparing the tissue to be viewed under the microscope, causing them to appear pink. Chromophobe renal carcinoma is the third most common type. It accounts for about 5% of cases. The cells of these cancers are also pale, like the clear cells, but are much larger and have certain other features that can be recognized. The fourth type, collecting duct renal carcinoma, is very rare. The major feature is that the cancer cells can form irregular tubes. About 5% of renal cancers are unclassified because their appearance doesn't fit into any of the other categories.

Another aspect of a renal cell carcinoma is its Fuhrman grade (named after the pathologist who developed the system). This refers to how closely the cancer cellsA' nuclei (part of a cell in which DNA is stored) look like normal kidney cellsA' nuclei. Renal cell cancers are usually graded on a scale of 1-4. Grade 1 renal cell cancers have cell nuclei that differ very little from normal kidney cell nuclei. These cancers usually grow and spread slowly and tend to have a good outlook (prognosis). At the other extreme, grade 4 renal cell cancer nuclei look quite different from normal kidney cell nuclei and have a worse prognosis. Although the cell type and grade are sometimes helpful in predicting a prognosis, the cancer's stage is by far the best predictor of survival. The stage describes the cancer's size and how far it has spread beyond the kidney.

Transitional cell carcinoma is another type that affects the renal pelvis. It is similar to bladder cancer and is often treated like bladder cancer. Cancers are described by the types of cells from which they arise. When discussing kidney cancer, the cortex and the renal pelvis must be mentioned separately. In the kidney cortex, the majority of cancers arise from the cells that line the collecting tubules, the proximal tubules. Cancers of the renal pelvis, or medulla, are uncommon. Over 90% of cancers that develop in the renal pelvis are called transitional cell carcinomas. About 5-10% of all kidney tumors are transitional cell carcinomas, also known as urothelial carcinomas. They are so named because they develop from cells that line the renal pelvis and upper ureters. Kidney cancer rarely causes signs or symptoms in its early stages. In the later stages, the most common sign of both renal cell and transitional cell cancers is blood in the urine (hematuria). These cancers are usually treated by surgically removing the whole kidney and the ureter, as well as that portion of the bladder where the ureter attaches. Chemotherapy and radiation therapy are often used in addition to surgery, depending on how much cancer is found. If you have early transitional cell carcinoma, you have several treatment options available. There are different ways to surgically treat early disease. Newer surgical techniques are also being studied. 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 tumor has grown into the ureter wall or kidney or if it has a more aggressive (high-grade) appearance when viewed under the microscope. Because of the inaccessibility of ureteral and pelvic anatomy, accurate staging requires pathologic analysis of the surgically excised specimen. After surgery, follow-up visits for monitoring with x-rays and cystoscopies (looking into the bladder) are extremely important because transitional cell carcinoma can come back in the bladder, as well as other places in the body.

Wilms' tumor is the most common type of childhood kidney cancer and is different from adult kidney cancer so it requires different treatment. About 5-6% of all kidney cancers are Wilms' tumors. Wilms' tumors are extremely rare among adults.

Renal sarcomas are a rare type of kidney cancer that begin within the kidney's connective tissue. This accounts for less that 1% of all kidney tumors.

Cancer cells are often found in nearby lymph nodes when kidney cancer spreads outside the kidney. Kidney cancer may spread to the lungs, bones, and liver or from one kidney to another. When cancer spreads from its original place to another part of the body, the new tumor has the same kind of abnormal cells. If kidney cancer spread to the lungs, the cancer cells in the lungs are actually kidney cancer cells. The disease is metastatic kidney cancer, not lung cancer and is treated as such. Doctors sometimes call the new tumor metastatic or "distant" disease.

Kidney cancer presents as signs and symptoms of either the local tumor in the kidney or as signs and symptoms resulting from spread of disease to other locations in the body. Symptoms resulting from local tumor extension include hematuria (blood in the urine), abdominal pain, and a flank mass. Hematuria is the most common symptom and present as either gross hematuria, where the blood is visible in the urine, or as microscopic hematuria, where the blood is only detected by laboratory testing. Any presence of blood in the urine that is detected in a urine sample should be investigated. Only about 10% of kidney cancer patients actually have all three symptoms at diagnosis.

Symptoms caused by metastatic disease include fever, weight loss, and night sweats (drenching sweats that require changing of clothes or bedsheets). Other symptoms include hypertension, increased calcium in the blood, and liver problems. These more unique symptoms are thought to be caused by chemical signals released by the tumor cells into the bloodstream and the body's reaction to them. Using CT scans and ultrasounds, 25-40% of kidney cancers are now detected incidentally during the work up of a different problem. These tumors are more likely to be smaller (causing no symptoms), and more likely to result in a cure.

Common symptoms of kidney cancer include:

- Blood in the urine. Since blood in the urine must come from one of the organs involved in making or transporting the urine, the evaluation of hematuria requires consideration of the entire urinary tract. This organ system includes the kidneys, ureter (the tube that carries urine from the kidney to the bladder), bladder, prostate, or urethra (tube leading out of the bladder). Even a single episode of hematuria requires evaluation, even if it resolves spontaneously. There are multiple causes of blood in urine. Some are serious, including cancers, trauma, stones, infections, and obstructions of the urinary tract. Others are less important, and may require no treatment. These may include viral infections, nonspecific inflammations of the kidney, medications that thin the blood's clotting ability, and benign prostate enlargement.
- Pain in the side that does not go away.
- A lump or mass in the side or the abdomen.
- Weight loss
- Fever
- Feeling very tired or having a general feeling of poor health.

Often these symptoms do not mean cancer. An infection, a cyst, or another problem can cause the same symptoms. A person with any of these symptoms should see a doctor so that any problem can be diagnosed and treated as early as possible.

If a patient has symptoms that suggest kidney cancer, the doctor may perform one or more of the following procedures:

- Physical exam: The doctor checks general signs of health and tests for fever and high blood pressure. The doctor also feels the abdomen and side for tumors.
- Urine tests: Urine is checked for blood and other signs of disease. A urine cytology test checks for abnormal cancer cells in the urine.
- Blood tests: The lab checks the blood to see how well the kidneys are working. The lab may check the level of several substances, such as creatinine. A high level of creatinine may mean the kidneys are not doing their job.
- Intravenous pyelogram (IVP): The doctor injects dye into a vein in the arm and it travels through the body and collects in the kidneys. The dye makes them show up on x-rays. A series of x-rays then tracks the dye as it moves through the kidneys to the ureters and bladder. The x-rays can show a kidney tumor or other problems.
- CT scan (CAT scan): A computerized axial tomography scan is more commonly known by its abbreviated name, CAT scan or CT scan. It is a x-ray procedure which combines many x-ray images with the aid of a computer to generate cross-sectional views and, if needed, three-dimensional images of the internal organs and structures of the body. A CAT scan is used to define normal and abnormal structures in the body and/or assist in procedures by helping to accurately guide the placement of instruments or treatments. A large donut-shaped x-ray machine takes x-ray images at many different angles around the body. These images are processed by a computer to produce cross-sectional pictures of the body. In each of these pictures the body is seen as a x-ray "slice" of the body, which is recorded on a film. This recorded imagine is called a tomogram. This can show a kidney tumor. The patient may receive an injection of dye so the kidneys show up clearly in the pictures. A CAT scan is a very low-risk procedure. The most common problem is an adverse reaction to intravenous contrast material. CAT scanning is painless.
- Ultrasound test: The ultrasound device uses sound waves that people cannot hear. The waves bounce off the kidneys, and a computer uses the echoes to create a picture called a sonogram. A solid tumor or cyst shows up on a sonogram.
- Biopsy: A biopsy is the removal of tissue to look for cancer cells using a microscope. A pathologist does this. The doctor inserts a thin needle through the skin into the kidney to remove a small amount of tissue. The doctor may use ultrasound or x-rays to guide the

needle.
- Surgery: The doctor has enough information to recommend surgery to remove part or all of the kidney based on the results of the CT scan, ultrasound and x-rays. A pathologist makes the final diagnosis by examining the tissue under a microscope.

The doctor needs to know the stage of the disease in order to plan treatment. The stage is based on the size of the tumor, whether the cancer has spread and if so, to what parts of the body. Staging may involve imagining tests such as an ultrasound or a CT scan. The doctor also may use a MRI.

Doctors describe kidney cancer by the following stages:

- Stage I is an early stage of kidney cancer. The tumor measures up to 2-3/4 inches (7 centimeters). It is not bigger than a tennis ball. The cancer cells are found only in the kidney.
- Stage II is also an early stage of kidney cancer, but the tumor measures more than 2-3/4 inches. The cancer cells are found only in the kidney.
- Stage III is one of the following: The tumor does not extend beyond the kidney, but cancer cells have spread through the lymphatic system to one nearby lymph node; or the tumor has invaded the adrenal gland or the layers of fat and fibrous tissue that surround the kidney, but cancer cells have not spread beyond the fibrous tissue. Cancer cells may be found in one nearby lymph node; or the cancer cells have spread from the kidney to a nearby large blood vessel. Cancer cells may be found in one nearby lymph node.
- Stage IV is one of the following: The tumor extends beyond the fibrous tissue that surrounds the kidney; or cancer cells are found in more than one nearby lymph node; or the cancer has spread to other places in the body such as the lungs.
- Recurrent cancer is cancer that has come back (recurred) after treatment. It may come back in the kidney or in another part of the body.

While more kidney cancers are being diagnosed and treated early, the number of deaths from the disease continues to increase. The fact that the number of cases has been growing is largely due to the detection of small, presumably curable, tumors, so scientists are not exactly sure why so many patients are still dying. The trend might be explained by the lack of effective chemotherapy drugs to give kidney cancer patients once they have had surgery to remove tumors. From 1983 to 2002, the incidence of kidney cancer increased 52%. The biggest increase was seen in the number of people with small tumors, roughly 2-4 cm in size. Death rates went up mostly among those with tumors larger than 7 cm. Deaths from kidney cancer rose from 1.2 to 3.2 per 100,000 people. These findings are partly explained by the increasing incidence of larger, more lethal tumors. While more small, detectable kidney tumors are being treated, the number of patients with larger, lethal masses has not decreased. It is these larger, lethal masses that seem to mainly affect mortality. There aren't any good drugs for kidney cancer. It is not a tumor that is very responsive.

Some types of kidney tumors do not usually spread to other parts of the body, although they can still grow and cause problems. These include renal cell adenomas, renal oncocytomas, and angiomyolipomas. Renal adenomas are very small, slow growing, benign tumors that, under a microscope, look a lot like low-grade renal cell carcinomas. In rare cases, tumors first thought to be renal adenomas may turn out to be small renal cell carcinomas. Oncocytomas are a type of benign kidney tumor that can sometimes grow quite large. Because oncocytomas do not normally metastasize to other organs, removing the kidney can often produce a cure. Angiomyolipomas are another rare benign kidney tumor. They often develop in people with tuberous sclerosis. (2)

Staging

The staging of cancer basically describes how much it has grown before the diagnosis has been made, documenting the extent of the disease. This is important in terms of what treatment is offered to each individual patient. Cancers cause problems because they spread and can disrupt the functioning of normal organs. One way kidney cancer can spread is by local extension to invade through the normal structures. This initially includes the kidney and gives the symptoms of hematuria, a mass and abdominal pain. If more growth occurs, it could grow to involve the main vein that leaves the kidney (the renal vein), the large vein that returns blood from the bottom half of the body to the heart (the inferior vena cava), or into other organs, most commonly the adrenal glands. Kidney cancer can also spread by accessing the lymphatic system. The lymphatic circulation is a complete circulation system in the body, somewhat like the blood circulatory system, that drains into various lymph nodes. When cancer cells access this lymphatic circulation, they can travel to lymph nodes and start new sites of cancer. This is called lymphatic spread. Kidney cancer can spread into the lymph nodes surrounding the kidney, called the perirenal lymph nodes.

Kidney cancers can also spread through the bloodstream. Cancer cells gain access to distant organs via the bloodstream. Cancers of the kidney generally spread locally into the fat surrounding the kidney, the adrenal glands, or the veins prior to spreading via the lymphatic system or the bloodstream. Larger tumors can access the bloodstream and spread to the lungs and bones, most commonly. Kidney tumors have also been known to spread to the testis and ovaries through the testicular or ovarian veins that are in close proximity to the kidney.

The staging system used today in kidney cancer is designed to describe the extent of disease within the area of the kidney, in the surrounding lymph nodes, and distantly. The staging system most commonly used today to describe kidney tumors is the "TNM system", as described by the American Joint Committee on Cancer. This replaced the "Robson Modification of the Flocks and Kadesky Staging System" because of its superiority in describing the local extent and lymph node involvement. The TNM systems are used to describe many types of cancers. They have three components: T - describing the extent of the "primary" tumor; N - describing the spread to the lymph nodes; M –describing the spread to other organs (metastasis).

The "T" stage is as follows:

For Kidney (cortex) tumors:

- T1 – tumor size of 7 cm or less and confined to the kidney
- T2 – tumor size more than 7 cm, but still confined to the kidney
- T3a – tumor invading into the adrenal gland or just outside of the kidney
- T3b – tumor invading into the renal vein or inferior vena cava, but contained below the diaphragm
- T3c – tumor invading into the renal vein or inferior vena cava, but extending above the diaphragm
- T4 – tumor invades outside of these areas

For collecting system tumors:

- T1 – tumor contained within the collecting system
- T2 – tumor invades into the muscular layer of the wall of the collecting system
- T3 – tumor invades into the fat surrounding the collecting system
- T4 – tumor invades into other organs

The "N" stage is as follows for any subsite:

- N0 – no spread to lymph nodes
- N1 – tumor spread to a single lymph node
- N2 – tumor spread to multiple lymph nodes or for collecting system tumors, lymph node spread that is between 2 - 5 cm
- N3 – for collecting system tumors only, those lymph nodes that are > 5 cm

The "M" stage is as follows:

- M0 – no tumor spread to other organs
- M1 – tumor spread to other organs

The overall stage is based on a combination of these T, N, and M parameters:

For kidney cortex tumors

- Stage I: T1N0M0
- Stage II: T2N0M0
- Stage III:
  - T1-2N1M0
  - T3N0-1M0
- Stage IV: any T4, any N2 or M1

For collecting system tumors

- Stage I: T1N0M0
- Stage II: T2N0M0
- Stage III: T3N0M0
- Stage IV: any T4, any N1-3, any M1

Though complicated, these staging systems help physicians determine the extent of the cancer, and make treatment decisions regarding a patient's cancer. (3)

Being at Risk

Cancer of the renal pelvis occurs in about 3,000 – 4,000 Americans each year, while kidney cancer occurs in about 35,000 Americans each year. The American Cancer Society estimates that there will be about 38,890 new cases of kidney cancer (24,650 in men and 14,240 in women) in the U.S. in 2006. About 12,840 people (8,130 men and 4,710 women) will die from this disease. These statistics include both adults and children and include renal cell carcinomas and transitional cell carcinomas of the renal pelvis. Most patients are diagnosed between the ages of 50 and 70. It is very uncommon under age 45, and its incidence is highest between the ages of 55 and 84. It is more common in men than women and being equally common in Caucasians and African Americans. A number of risk factors are associated with an increased chance of renal cell cancer, but the most prominent risk is cigarette smoking. People who smoke have twice the risk of developing kidney cancer, and smoking is directly responsible for up to one out of every three cancers. The risk for kidney cancer also increases fourfold in persons with a first-degree relative who had kidney cancer. Other, less-proven risk factors include obesity (especially in women), analgesic abuse, high blood pressure, and several uncommon hereditary diseases, including von Hippel-Lindau disease and polycystic disease.

As cigarette smoking doubles the risk of kidney cancer, the best way to decrease your risk of developing kidney cancer is to discontinue smoking. Other than smoking, the only substantial risk factors for the development of kidney cancer are related to family pedigree. No one can

change the family they are born into, so the risk factor of having someone in the family with a history of kidney cancer, or rare genetic diseases such as von Hippel Lindau and polycystic disease cannot be prevented.

For reasons that are not clear, the rate of people developing kidney cancer has been increasing at about 1.5% per year. This is probably because the cancer is discovered during other tests such as abdominal CT scans. Although our kidneys are important, we actually need less than 1 complete kidney to do all of the important functions they do. Tens of thousands of people in the U.S. are living normal healthy lives with just one kidney. Some people may not have any working kidneys at all, and survive with the help of a medical procedure called dialysis. Dialysis uses a specially designed machine that acts like a real kidney to filter the blood. (4)

Transitional Cell Carcinoma, Renal

Renal urothelial (transitional cell) carcinoma is a malignant tumor arising from the transitional (urothelial) epithelium lining of the renal pelvis. Urothelial carcinoma (UC) is the most common tumor of the renal pelvis. Upper urinary tract urothelial tumors may be bilateral in 2-10% of cases. Patients with primary bladder cancer develop upper tract UC in 2-4% of cases, with a mean interval of 17-170 months. The incidence is higher and the interval is shorter in patients who are treated with bacillus Calmette-Guerin (BCG) for bladder cancer, in patients with bladder carcinoma in situ (CIS) (upper tract UC in these cases may reach 21%) and in those with certain occupational exposures. Patients with upper tract urothelial tumors are at risk of developing bladder tumors, with an estimated occurrence of 20-48%. Bladder cancer usually appears within 5 years. Urothelial cancer accounts for more than 90% of renal pelvic tumors. Squamous cell carcinomas (SCCs) account for 0.7-7% of upper tract cancers. The vast majority of urothelial tumors arise in the bladder. Urothelial tumors of the renal pelvis and ureter are rare, comprising approximately 5-6% of all urothelial tumors and 5-9% of approximately 35,000 renal cancers diagnosed annually. Worldwide statistics vary and are inaccurate since renal pelvis tumors are not reported separately. The highest incidence is found in Balkan countries (Bulgaria, Greece, Yugoslavia, and Romania), where urothelial cancers account for 40% of all renal cancers and are bilateral in 10% of cases.

Upper-tract urothelial tumors are twice as common in Caucasians as in African Americans. Men are affected 2-3 times more frequently than women. Symptoms are significant enough to suggest the diagnosis in a relatively short time after disease development. Gross hematuria is the most common presenting symptom (75-95%). Microscopic hematuria occurs in 3-11% of patients. Approximately 14-37% of patients report pain. Pain is usually dull and is caused by the gradual obstruction of the collecting system. Renal colic also may occur with the passage of blood clots. Patients are rarely asymptomatic (1-2%). Physical examination usually is not informative or specific, especially in early stage disease. A palpable flank mass may be noted in less than 20% of patients. The classic clinical triad of hematuria, pain, and mass is also rare (15%), and is usually an indicator of advanced disease. Patients with SCC usually present with advanced disease. Renal calculi are present in 14-50% of patients with SCC. Primary adenocarcinoma of the renal pelvis constitutes less than 1% of upper tract urothelial tumors. It is associated with chronic urolithiasis, hydronephrosis, and pyelonephritis. A metastatic lesion must be ruled out before a diagnosis of primary disease can be made.

The exact cause of upper tract transitional cell carcinoma (TCC) is not known. Several risk factors have been identified. Workers in the chemical, petrochemical, aniline dye, and plastics industries, and those exposed to coal, coke, tar, and asphalt, are at increased risk for renal pelvis and ureteral tumors. Cigarette smoking appears to be the most significant acquired risk factor for upper tract urothelial cancer. It is suggested that 70% of upper tract urothelial tumors in men and 40% in women can be attributable to smoking. The chemotherapy drugs cyclophosphamide and ifosfamide are implicated in the development of upper tract and lower

tract urothelial cancers, particularly following drug-induced hemorrhagic cystitis.

Surgery is mandatory for upper tract TCC after making the diagnosis. Surgical intervention is the main form of radical treatment for localized disease. In choosing a treatment, the following should be considerations. Patients with low-stage, low-grade tumors respond well to either radical or conservative treatment. Patients with high-stage, high-grade tumors respond poorly to either radical surgery or conservative surgery. Patients with positive cytologic findings but normal radiographic and endoscopic examinations are not treated, but are monitored closely by periodic intravenous urography or retrograde pyelography. Traditional radical surgery for renal UC consists of total nephroureterectomy with excision of a bladder cuff around the ureteral orifice. Otherwise, 30-75% of patients develop tumor recurrence in the ureteral stump or around the ipsilateral ureteral orifice. Transection of the ureter must be avoided because of the high risk of tumor spillage in the retroperitoneum. Laparoscopic or hand-assisted laparoscopic nephroureterectomy is as effective oncologically as an open technique for localized disease. In general, the laparoscopic approach is accompanied by less blood loss, less pain and discomfort, faster recovery, and shorter hospital stay. Patients with poorly differentiated tumors or high-stage disease (especially those with microscopic lymph node involvement) may benefit from extensive retroperitoneal lymphadenectomy. The benefit is marginal and appropriate candidates must be chosen carefully.

Because of the high risk of local and bladder recurrences, long term follow-up care for these patients is mandatory. The follow-up care should include ureteroscopy, cystoscopy and either IVU or RPG in the routine follow-up procedures. Urine markers are used more and more frequently in the follow-up of patients with UCs. Specificity of these tests is acceptable for follow-up, and their sensitivity is much better than that or urine cytology.

Perforation (0-10%) and stricture formation (5-13%) are the major complications of ureteroscopic treatment. Use of lasers may decrease the rate of stricture formation. Seeding through the nephrostomy tract is a concern during percutaneous management. Other serious complications of percutaneous treatment include perforation (5.5%) and uretero-pelvic-junction stricture (1.4%). Frequency of stricture is much less than after ureteroscopy.

Tumor stage is the most important prognostic factor for upper tract UC. Survival correlates closely with tumor stage. The TNM staging system for upper tract carcinomas is the most comprehensive. Tumor grade is another predictor of prognosis. Tumor grade usually follows tumor stage, and patients with high-grade carcinomas have more advanced (i.e., high-stage) disease. Stage and grade correlate in up to 83% of cases, although stage remains a more accurate predictor of prognosis. Stage T3 renal tumors have a better prognosis than ureteral tumors. Five-year survival rate after radical surgery depends on disease stage.

- Stages T1: 91%
- Stage T2: 43%
- Stage T3, T4, N1, or N2: 23%
- Stages N3 or M1: 0%

Tumors recur in the contralateral kidney after radical nephroureterectomy in 2% of cases. The 5-year survival rate in selected patients after conservative surgery is reported to be 70-90%. Recurrences in the remaining urothelium after conservative treatment are relatively frequent because of the multifocal nature of transitional cell carcinomas. Most low-grade recurrences can be treated with repeat conservative excision. Five-year survival rates in these patients with low-grade low-stage disease can approach 100%. The prognosis is poor for patients with advanced squamous cell carcinoma. (5)

Treatments

Before starting treatment, a person with kidney cancer might want a second opinion about the diagnosis and the treatment plan. Some insurance companies require a second opinion. Others may cover a second opinion if the patient or doctor request it. There are a number of ways to find a doctor for a second opinion.

- The patient's doctor may refer the patient to one or more specialists. At cancer centers, several specialists often work together as a team.
- The Cancer Information Service at 1-800-4-CANCER can tell callers about nearby treatment centers.
- A local or state medical society, a nearby hospital, or a medical school can usually provide the names of specialists.
- The American Board of Medical Specialties (ABMS) offers a list of doctors who have met specific education and training requirements and have passed a specialty examination. Their directory lists doctors' names along with their specialty and their educational background. The directory is available in most public libraries. The ABMS offers this information by telephone and on the Internet. The toll-free number is 1-866-275-2267. The Internet address is http://www.abms.org.
- A helpful fact sheet on how to find a doctor called "How To Find a Doctor or Treatment Facility If You Have Cancer" is available on the Internet at http://cancer.gov/publications.

Treatment depends mainly on the stage of disease and the patient's general health and age. The doctor can describe treatment choices and discuss the expected results. The doctor and patient can work together to develop a treatment plan that fits the patient's needs. People may want to ask the doctor these questions before treatment begins:

- What is the stage of the disease? Has the cancer spread? If so, where?
- What are my treatment choices? Which do you recommend for me? Will I have more than one kind of treatment?
- What are the expected benefits of each kind of treatment? Will it cure or control the disease?
- What are the risks and possible side effects of each treatment? Will I be given anything to control side effects?
- How long will treatments last?
- Will I have to stay in the hospital?
- What is the treatment likely to cost? Is this treatment covered by my insurance plan?
- How will treatment affect my normal activities?
- How often should I have checkups?
- Would a clinical trial (research study) be appropriate for me?

People do not need to ask all their questions or understand all the answers at once. They have other chances to ask the doctor to explain things that are not clear and to ask for more information.

Treatments for renal cell carcinoma include:

- Surgical removal. Until recently, the standard treatment for cancer that was confined to the kidney was surgical removal of the entire kidney (radical or simple nephrectomy), In a radical nephrectomy, surgeons remove the kidney along with the adrenal gland that sits atop the kidney, a border of normal tissue and adjacent lymph nodes. A simple nephrectomy involves removing the entire kidney, although not the adrenal gland or lymph nodes. But studies show that removing just the tumor (nephron-sparing surgery), rather than the whole kidney, results in survival rates similar to those of more radical procedures. In addition, people who have nephron-sparing surgery appear less likely to develop chronic kidney failure and are more likely to enjoy a better quality of life than do

those who have the whole kidney removed. Sometimes surgeons may choose to remove the entire kidney because of the extent and the location of the tumor. In that case, laparoscopic nephrectomy may offer advantages over traditional open surgery because it typically results in less postoperative pain, faster recovery time and less scarring. In a laparoscopic procedure, a tiny camera is inserted into the body through a small incision. The camera transmits video images that allow the surgeon to see the kidney in great detail. The surgeon inserts surgical instruments through 2 or 3 additional small incisions and performs the operation. The recovery time and side effects of any type of kidney surgery will vary, but it is likely the patient would feel tired and weak for a time, even with laparoscopic nephrectomy.

- Arterial embolization. In this procedure, a radiologist injects a special material into the main blood vessel leading to the kidney. By clogging this vessel, the tumor is deprived of oxygen and other nutrients. Arterial embolization may be used before an operation or to relieve pain and bleeding when an operation is not possible. Side effects may include temporary nausea, vomiting or pain.
- Radiation therapy. This makes the use of high energy x-rays to kill cancer cells. It does this by damaging the DNA in tumor cells. Normal cells in our body can repair radiation damage much quicker than tumor cells, so while tumor cells are killed by radiation, many normal cells are not. This is the basis for the use of radiation therapy in cancer treatment. Radiation is delivered using large machines that produce the high energy x-rays. Radiation therapy is not routinely used in the initial treatment of kidney cancer. As the local failure in patients with complete removal of tumor is 5%, adding local radiation, which is done to improve local control of a tumor, would do little to improve results. In patients without a complete removal of tumor, there could be a role for postoperative radiation therapy, though it should only be done as part of an investigational trial.
- Chemotherapy. This is defined as drugs that are used to kill tumor cells. Up to this point, there is no chemotherapy regimen that has been consistently shown to be efficacious in the treatment of curative or metastatic kidney cancer. New modalities are constantly being investigated, including interferon, anti-angiogenesis agents (which inhibit the tumor from growing more blood vessels), and molecular agents that target specific genes that may be essential for the tumor cells' survivals.
- Immunotherapy. This treatment uses your body's immune system to fight cancer. An oncologist may administer a substance known as a biological response modifier, such as interferon or interleukin-2. Normally produced by the body, these substances are also made in laboratories. Studies show that people may do better when they are treated with both interferon and surgery, rather than with interferon alone. Biological response modifiers can have serious side effects, including chills, fever, nausea, vomiting and loss of appetite. You may bruise easily after treatment and feel extremely tired. Interleukin-2 and interferon therapies can also affect liver and kidney function. These side effects are often severe, but usually disappear once treatment is stopped.

To treat transitional cell cancer in its early stages, surgeons remove an area surrounding the tumor while trying to save the kidney itself. If the tumor is too large or too centrally located, the kidney and ureter may need to be removed along with the portion of the bladder that is connected to the ureter. This helps decrease the risk of cancer cells spreading to the bladder. Chemotherapy is often used to treat transitional cell cancer that has spread.

Treatment for children with Wilms' tumor depends on the child's age and overall health, the type of tumor and whether the cancer has spread. In many cases, treatment may include surgical removal of the tumor followed by chemotherapy or radiation.

If kidney cancer has spread, standard treatments are seldom effective. For that reason, a patient may choose to participate in a clinical trial. These trials test the effectiveness and side effects of new treatments. Doctors all over the country are conducting many types of clinical trials. Researchers are studying surgery, biological therapy, chemotherapy, and combinations of

these types of treatment. They also are combining chemotherapy with new treatments, like stem cell transplantation. A stem cell transplant allows a patient to be treated with high doses of drugs. The high doses destroy both cancer cells and normal blood cells in the bone marrow. Later, the patient receives healthy stem cells from a donor. New blood cells develop from the transplanted stem cells. Other approaches are also under study. Researchers are studying cancer vaccines that help the immune system to find and attack kidney cancer cells. Those who take part have a chance to receive a treatment that may be promising but not yet widely available. If a person is interested in clinical trials, he should talk to his doctor. The patient can also contact the National Cancer Institute for detailed information, or visit the clinical trial page on its Web site. The Cancer Information Service at 1-800-4-CANCER or at LiveHelp can answer questions and provide information about clinical trials. (6)

Dialysis

Dialysis is a method of removing toxic substances (impurities or wastes) from the blood when the kidneys are unable to do so. Dialysis is most frequently used for patients who have kidney failure, but may also be used to quickly remove drugs or poisons in acute situations. This technique can be life saving in people with acute or chronic kidney failure. Dialysis can be performed using several different methods.

Peritoneal dialysis works by using the body's peritoneal membrane, which is inside the abdomen, as a semi-permeable membrane. Special solutions that help remove toxins are infused in, remain in the abdomen for a time, and then are drained out. This form of dialysis can be performed at home, but must be done every day.

Hemodialysis works by circulating the blood through special filters outside the body. The blood flows across a semi-permeable membrane (the dialyzer or filter), along with solutions that help remove toxins. Hemodialysis requires a blood flow of 400-500 milliliters per minute (ml/min). A normal IV tube in an arm or leg will not support that volume of blood flow, so dialysis uses special ways of accessing the blood in the blood vessels. The access can be temporary or permanent. Temporary access takes the form of dialysis catheters. These are large-size catheters placed in large veins that can support acceptable blood flows. Most catheters are used in emergency situations, for short periods of time. Catheters called tunneled catheters can be used for prolonged periods of time, often weeks to months.

Permanent access is created by surgically joining an artery to a vein. This allows the vein to receive blood at high pressure, leading to thickening of the vein's wall. Now this "arterialized vein" can sustain repeated puncture and also provides excellent blood flow rates. The connection between an artery and a vein can be made using blood vessels (an arteriovenous fistula, or AVF) or a synthetic bridge (arteriovenous graft, or AVG). The AVF is more desirable, because rates of infection are very low and it is quite durable. It may take many months for the AVF to mature, so careful planning is required. The AVG can be accessed a few weeks after creation. It provides good flows but has a high complication rate. It should be attempted only if the AVF is not feasible. Blood is diverted from the access point in the patient's body to a dialysis machine. Here, the blood flows counter-current to a special solution called the dialysate. The chemical imbalances and impurities of the blood are corrected and the blood is then returned to the body. Typically, most patients undergo hemodialysis for three sessions every week. Each session lasts 3-4 hours.

It is important to adhere to the diet and medicines prescribed by the dialysis staff and the nephrologist. Just before the health care provider begins the hemodialysis procedure, the following assessments will be made:

- Blood pressure

- Temperature
- Heart rate
- Breathing rate
- Weight
- Chest assessment
- Examination of venous access

Since dialysis takes several hours, it may become tedious for the patient. With children, it is especially important to have games, something to read, or other distractions. This procedure removes contaminants from the blood that could, and eventually would, result in death if the kidneys were not functioning. The kidneys function as filters for the blood, removing products of amino acid breakdown. More than that, they serve to reclaim and regulate body water, maintain electrolyte balance, and ensure that the blood pH remains between 7.35 and 7.45. Without the function of the kidney, life is not possible. Dialysis serves to replace some of the functions of the kidney. Since dialysis is not a constant ongoing process, it cannot serve as a constant monitor as do normal functioning kidneys, but it can eliminate waste products and restore electrolyte and pH levels on an as-needed basis.

The immediate risks are:

- Hypotension (low blood pressure)
- Infection
- Electrolyte imbalance
- Bleeding from the access site
- Nausea and vomiting
- Cramps
- Dialyzer reaction
- Air embolism
- Cardiac ischemia or arrhythmia (irregular heart beats)

Long-term risks include:

- Dialysis-associated amyloidosis
- Dialysis dementia (uncommon now that aluminum levels are closely monitored)
- Cardiovascular disease
- Autonomic neuropathy
- Blood loss leading to iron deficiency (requiring regular iron replacement)

The following precautions need to be taken if a patient has an AVF or AVG:

- When the patient sleeps, avoid placing pressure on an arm with the access.
- Do not allow anyone to take a blood pressure reading on an arm with the access.
- Observe the access site after dialysis, watching for swelling, infection, or bleeding.
- Do not wear tight clothing around the access site.
- Routinely check the access site for the “thrill”, indicating that the AV site is still functioning. (If the thrill disappears, the patient needs to call his doctor immediately).
- Do not use creams or lotions over the access site.

If a patient has an external access, these additional precautions need to be taken:

- Avoid physical activity that might dislodge the access, which could result in excessive bleeding and air entering the circulatory system. (If this happens, call 911 and get immediate medical attention).
- If the color in the tubes changes color and becomes a dark red, call the doctor

immediately. (The blood may be clotting).
- Call the doctor immediately if the patient has a fever or any other signs of infection. (7)

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Course Exam

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1. From 1983 to 2002, the incidence of kidney cancer increased 52%.

   ◯ True ◯ False

2. A CT scan is used to define normal and abnormal structures in the body.

   ◯ True ◯ False

3. There are not any good drugs for kidney cancer as the tumor is not very responsive.

   ◯ True ◯ False

4. While more kidney cancers are being diagnosed, the number of deaths from the disease continues to decrease.

   ◯ True ◯ False

5. The urinary tract includes the kidneys, ureter, bladder, prostate, and urethra.

   ◯ True ◯ False

6. In Stage III of kidney cancer, the tumor extends beyond the kidney.

   ◯ True ◯ False

7. Transitional cell cancer rarely comes back once the kidney is removed.

   ◯ True ◯ False

8. Wilm's tumors are extremely rare among children.

   ◯ True ◯ False

9. In the later stages, the most common sign of both renal cell and transitional cell cancers is blood in the urine (hematuria).

   ○ True ○ False

10. Transitional cell carcinomas are also known as urothelial carcinomas.

    ○ True ○ False

11. The most common type of kidney cancer in adults is renal cell cancer.

    ○ True ○ False

12. Renal cell cancer accounts for more than 90% of malignant kidney tumors.

    ○ True ○ False

13. There are five main types of renal cell carcinoma.

    ○ True ○ False

14. Papillary is the most common form of renal cell carcinoma.

    ○ True ○ False

15. Chromophobe renal carcinoma is the third most common type of kidney cancer.

    ○ True ○ False

16. About 15% of renal cancers are unclassified because their appearance does not fit into any of the other categories.

    ○ True ○ False

17. Renal cell cancers are usually graded on a scale of 1-5.

    ○ True ○ False

18. The cancer's grade is by far the best predictor of survival.

    ○ True ○ False

19. Transitional cell carcinoma is a type of kidney cancer that affects the renal pelvis.

    ○ True ○ False

20. Transitional cell carcinoma is very similar to bladder cancer.

    ○ True ○ False

21. When discussing kidney cancer, the cortex and the renal pelvis must be mentioned separately.

    ○ True ○ False

22. Over 90% of cancers that develop in the renal pelvis are called transitional cell carcinomas.

    ○ True ○ False

23. The kidneys ensure that the electrolytes within the blood are correct.

    ○ True ○ False

24. Kidney cancer often causes pain in its early stages.

○ True ○ False

25. The kidneys make substances that help control blood pressure.

○ True ○ False

26. Accurate staging of transitional cell cancer can be done after a CT scan and biopsy.

○ True ○ False

27. The ureter is a tube that drains the urine from the body.

○ True ○ False

28. The inner region of the kidney is called the cortex.

○ True ○ False

29. Renal sarcoma are a rare type of kidney cancer that begin within the kidney's connective tissue.

○ True ○ False

30. Renal sarcomas account for less than 1% of all kidney tumors.

○ True ○ False

31. Kidney cancer may spread to the lungs, bones, and liver or from one kidney to another.

○ True ○ False

32. Symptoms caused by metastatic disease include fever, weight loss, and night sweats.

○ True ○ False

33. In the United States, one-half of all men and one-third of all women will develop cancer during their lifetimes.

○ True ○ False

34. A low level of creatinine may mean the kidneys are not doing their job.

○ True ○ False

35. Damage to DNA causes cancer cells to develop.

○ True ○ False

36. In Stage I of kidney cancer, the tumor measures up to 9 centimeters.

○ True ○ False

37. The kidneys can be divided into three main functional parts.

○ True ○ False

38. Cancer is the third leading cause of death in the United States.

○ True ○ False

39. All kinds of cancer are from out of control cells.

True False

40. Metastasis is when cancer cells travel to other parts of the body where they begin to grow and replace normal tissue.

True False