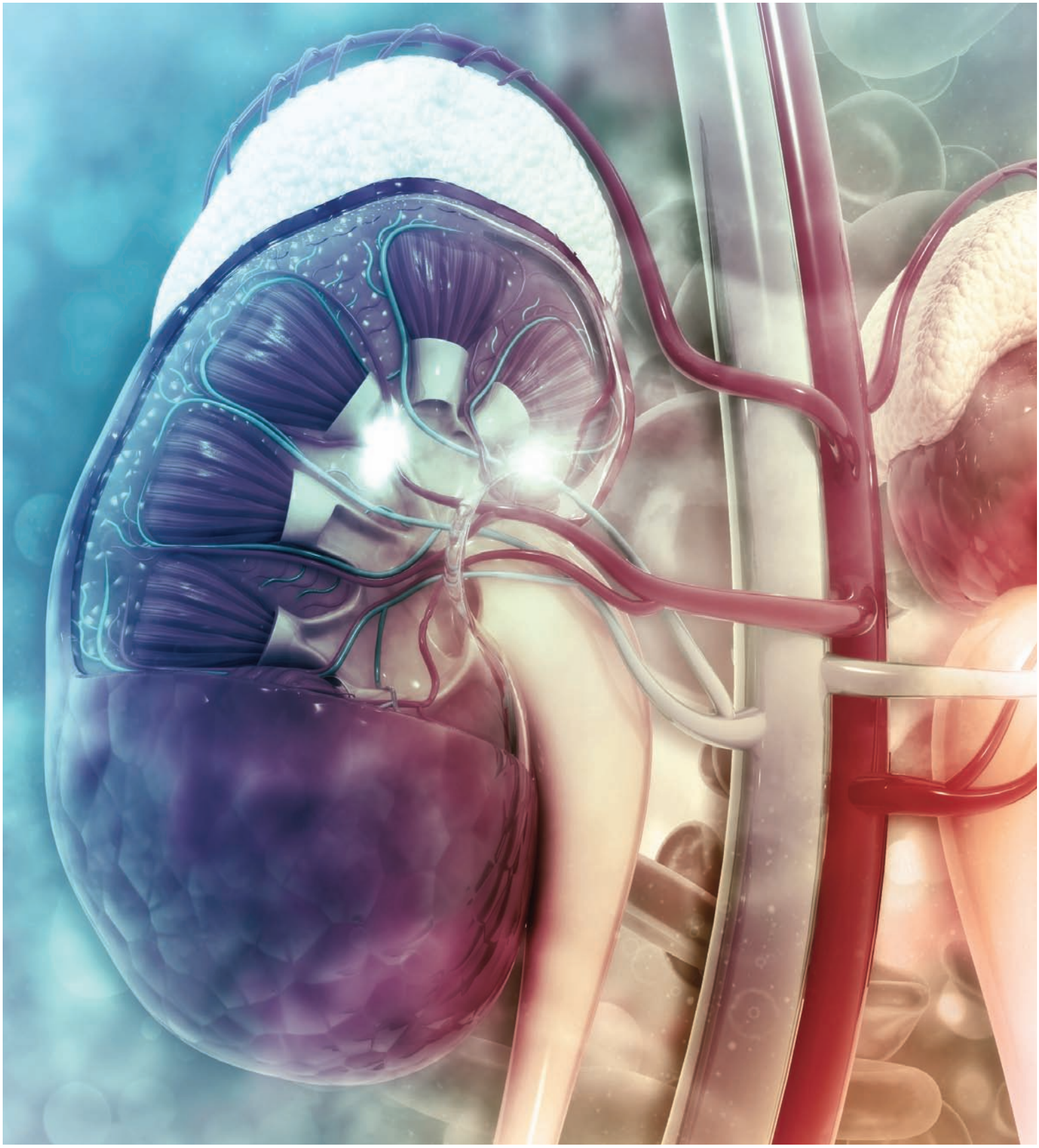

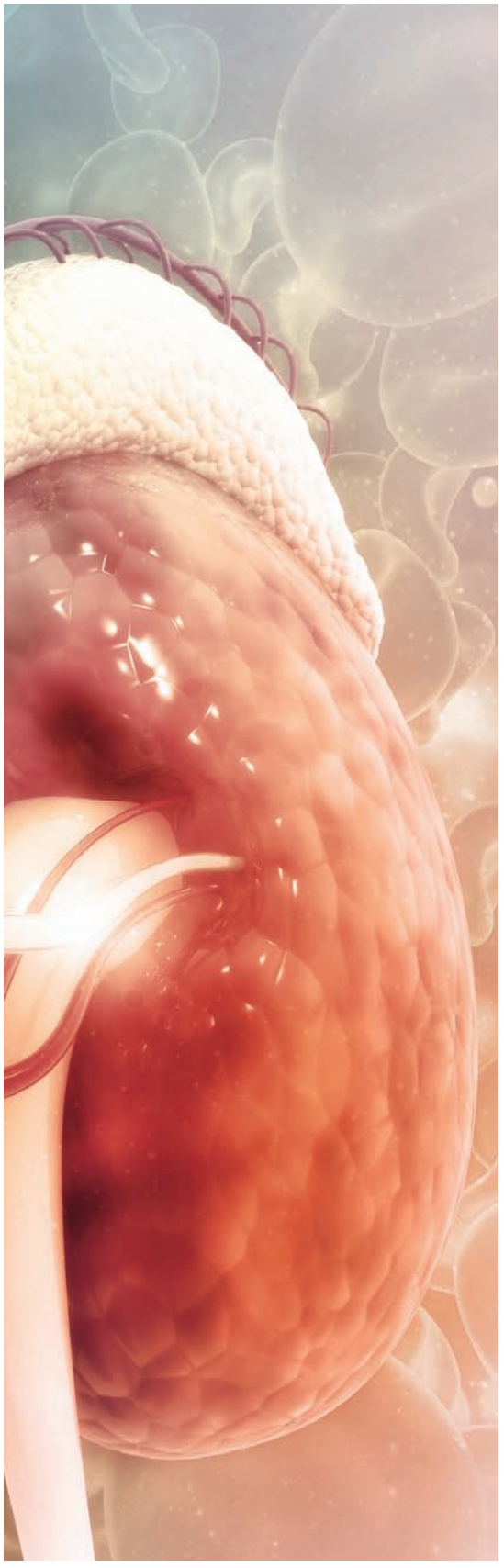

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Renal cell carcinoma, part 1

BY RICHARD L. PULLEN, Jr., EdD, MSN, RN, CMSRN, CNE-cl, CNE, ANEF

Abstract: Renal cell carcinoma (RCC) encompasses a group of malignancies that originate in the epithelium of the renal cortex, most often in the upper pole of the kidney. This article, the first of a three-part series on RCC, addresses the incidence and epidemiology of RCC along with its genetic alterations, risk factors, histologic characteristics, and imaging characteristics.

Keywords: ccRCC, chromophobe RCC, chRRC, clear cell RCC, papillary RCC, pRCC, RCC, renal cell adenocarcinoma, renal cell carcinoma, renal cell hypernephroma, VHL gene, von Hippel-Lindau gene

THE AUTHOR'S journey with chronic illness began in 1998 at age 40, with a diagnosis of systemic lupus erythematosus (SLE). SLE and medications used to treat the disease increase the risk for infection. Several years ago, computed tomography (CT) of the chest, performed to confirm a diagnosis of right lower lobe pneumonia, revealed a 3-cm mass. A diagnosis of renal cell carcinoma (RCC) followed, along with a growing acquaintance with this disease. A partial nephrectomy was performed to remove the cancer, enabling a cancer-free life for the past 2 years.

This article, the first of a three-part series on RCC, will address the incidence and epidemiology of RCC along with its genetic alterations, risk factors, histologic characteristics, and imaging characteristics. The subsequent articles will address treatment options and take a more detailed look at nursing interventions.

Incidence and epidemiology

The incidence of renal malignancy is 6 per 100,000 men and 3 per 100,000 women. Of all malignancies globally, it ranks 9th in men and 14th in women.[1] In the US, the incidence is 21 per 100,000 men and 11 per 100,000 women, representing the sixth and eighth most common malignancies in men and women, respectively.[1,2] According to the American Cancer Society, about 76,080 new cases of kidney cancer (48,780 in men and 27,300 in women) will be diagnosed in 2021, and about 13,780 people will die from this disease.[3]

Sometimes referred to as renal cell adenocarcinoma or hypernephroma, RCC accounts for at least 85% of all renal malignancies and occurs more often than benign renal masses.[3] The incidence of RCC is highest in North America, Australia, and Europe, and lowest in India, Japan, Africa, and China.[1,2,4] Morbidity and mortality associated with RCC is higher for Black Americans, Native Americans, and Hispanics than for White patients, which is likely related to socioeconomic stressors, disparities in access to healthcare, and comorbidities.[1,4,5]

Pathophysiology

RCC encompasses a group of malignancies that originate in the

epithelium of the renal cortex, most often in the upper pole of the kidney (see *Normal renal anatomy*). It is called a "silent" cancer because symptoms may not occur until tumors become large.[4,6] Most RCCs are small, low-grade tumors that are incidentally identified on imaging studies when a patient is being evaluated for another condition, as in the author's case. Approximately one-third of patients with RCC have advanced metastatic disease at the time of diagnosis. The 5-year survival rate with appropriate treatment and follow-up in RCC is best predicted by the disease stage upon diagnosis: Stage I: 94%, Stage II: 79%, Stage III: 53%, Stage IV: 12%.[4,6] Staging will be discussed in detail in the second part of this series.

Risk factors

An individual's susceptibility to developing RCC is influenced by various risk factors, including exposure to environmental chemicals, certain medications, diet and obesity, and chronic illness. While risk factors do not cause RCC, they do serve as triggers for the development of the disease in individuals who are genetically susceptible. (See *Chemical and medication risk factors*.)

Besides exposure to certain medications and chemicals, diet, lifestyle, and overall health can affect a person's risk for developing RCC.[1,2,7-9] A diet high in calories, protein (particularly red meat), and processed foods correlates with abnormally high triglyceride and cholesterol levels and increases the risk of RCC. High consumption of processed meats and sugar promotes inflammation and sodium retention. A high renal sodium load has an inflammatory effect, which promotes tumor formation in RCC.[1,2,7-9]

Overweight or obesity can also be a risk factor. Research suggests that there is a 34% and 24% increased risk of RCC in women and men, respectively, with each 5 kg/m increase in body mass index (BMI). Individuals with BMIs above 30 are three times more likely to develop RCC.[1,2,7-9]

Researchers postulate that obesity and cancer are related to the interplay of insulin resistance, sex hormones, proinflammatory cytokines, carcinogenic adipocytes including leptin and adiponectin, chronic tissue hypoxia, and increased oxidative stress. Oxidative stress creates imbalances between free radicals and antioxidants, causing inflammation and cell damage.[8,9]

Fruits and vegetables are protective in RCC, but there is no indication that the intake of water, juice, milk, tea, coffee, or soft drinks are either risk factors or protective in RCC.[9]

Alcohol is a known carcinogen. However, recent research indicates that a modest amount of alcohol consumption may be protective against RCC because small amounts improve insulin sensitivity and have antioxidant properties.[1,8,9]

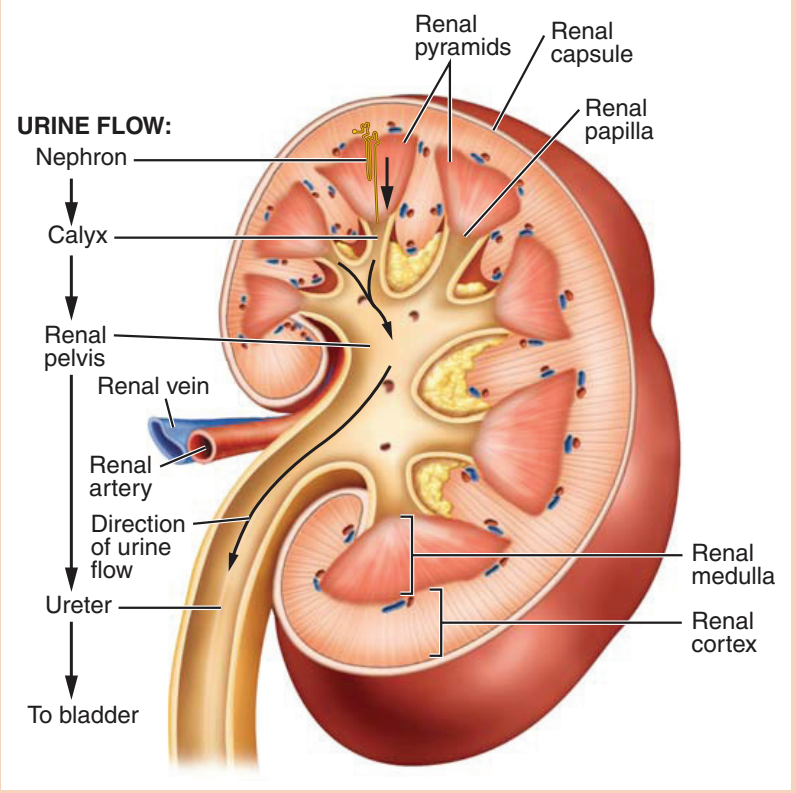
Chronic disease may also play a part

Hypertension is a major risk factor for RCC, according to the evidence. Hypertension may occur independently of specific disease processes, but it may also occur secondary to diabetes mellitus. Chronic hypertension may lead to chronic kidney disease (CKD) and renal failure.[1,2,4,7]

The renin-angiotensin system (RAS) plays an important role in regulating BP. Dysregulation of the RAS causes angiotensin II cell proliferation, inflammation, renal hypoxia, and lipid peroxidation, increasing the risk of RCC. Lipid peroxidation

Normal renal anatomy

Each kidney consists of an outer cortex and an inner medulla. Urine made by the renal tubules empties into the renal pelvis.



Source: McConnell TH, Hull KL. *Human Form, Human Function: Essentials of Anatomy & Physiology*. Philadelphia, PA: Lippincott Williams & Wilkins; 2011.

is the degradation of lipids, causing cell damage.[1,2,4,7]

Patients with ***diabetes mellitus*** are at a 17% to 21% increased risk for developing any malignancy, including RCC. Insulin resistance, proinflammatory cytokines, and oxidative stress predispose the patient to RCC.[1,2,7,10]

Patients who have ***end-stage renal disease***, receive hemodialysis, and/or undergo renal transplantation (as well as those who have cystic renal disease) are at an increased risk for RCC. Patients in end-stage renal disease have a 10 times increased risk for RCC compared with the general population.[1,2]

Individuals who are ***immunocompromised*** from antirejection medications such as azathioprine or mycophenolate postorgan transplantation, and those with autoimmune diseases face a greater risk for malignancy, including Hodgkin lymphoma, non-Hodgkin lymphoma, and nonmelanoma skin cancers.[1,2]

Research now indicates that individuals with ***SLE*** are also at a modest risk for leukemia, multiple myeloma, and malignancies in the kidneys, cervix, vulva, bladder, stomach, liver, pancreas, and thyroid.[1,2,11]

Chemical and medication risk factors[1,2,4,6,8]

Chemical

- Nicotine ingested through cigarette smoking is a major risk factor for RCC because it causes mutations and DNA damage from many carcinogens, especially n-nitrosamine and benzo[a]pyrene, and tissue hypoxia from the exposure to carbon monoxide. Patients who smoke are more likely to initially present with metastatic disease.
- Trichloroethylene (TCE) is specifically linked to RCC. This chemical is used in aerosol cleaning products, paint removers, and carpet cleaners. People may be exposed to TCE through inhalation and by consuming foods that have been cleaned with TCE-contaminated water.

  Long-term exposure to TCE causes mutations on the VHL gene through disregulation of glutathione S-transferase (GST), an antioxidant that prevents cell damage. Dysregulation of GST leads to the development of mutagens and carcinogens to initiate RCC.
- Other chemicals such as asbestos, arsenic, benzene, cadmium, and chromium are also carcinogenic risk factors for RCC.

Medications

- Long-term use of nonsteroidal anti-inflammatory drugs is highly implicated in RCC because of the inhibition of prostaglandin synthesis, uncontrolled cell proliferation, and damage to DNA causing renal injury.

  Aspirin may have a protective effect in the development of RCC with intermittent use by decreasing inflammation, inhibiting cell proliferation, and inducing apoptosis of cancer cells. However, the research also indicates that aspirin may cause renal injury with long-term regular use at higher doses and pose a modest risk for RCC through the development of chronic interstitial nephritis.
- Long-term regular use of acetaminophen at higher doses poses a modest risk for RCC because this drug has carcinogenic effects on the renal parenchyma through depletion of GST.
- Chemotherapeutic agents such as cisplatin and cyclophosphamide may also damage DNA and raise the risk of RCC.
- Antihypertensive medications and diuretics may increase the risk of RCC because of potentially carcinogenic effects on the renal endothelium, although the research in this area is inconclusive.

Genetic alterations in RCC

Researchers postulate that as many as 16 genes may be implicated in the various forms of renal malignancies, including RCC.[4,6,12-14] Most RCCs are ***clear cell RCC (ccRCC)***, sometimes referred to as conventional RCC. These are genetically linked to mutations on the short arm of chromosome 3 (3p).[4,6,12-14]

The primary gene implicated in ccRCC is the von Hippel-Lindau (VHL) gene, known as pVHL.[4,6,12-14] VHL helps to control cell growth and division in all body tissues. pVHL is a suppressor protein that undergoes mutation leading to an increase in insulin-like growth factor-1, upregulation of hypoxia-inducible factor and vascular endothelial growth factor (VEGF), creation of VEGF receptors, and angiogenesis, which results in tumor formation.[4,6,12-14]

Most ccRCCs occur sporadically as a solitary tumor subsequent to medical, physical, environmental, and occupational triggers. They are often found in older men who smoke.[4,6]

A pathogenic variant in the VHL gene is linked to *VHL disease*, which is an autosomal dominant syndrome that predisposes a person to ccRCC in one or both kidneys, renal cysts, pheochromocytoma, and tumors in the brain, spinal cord, retina, pancreas, adrenal glands, and endolymphatic sacs. The syndrome occurs in 2% to 4% of patients with ccRCC, and more frequently in younger men and women.[4,6,12-15]

Papillary RCC (pRCC), the second most common form of RCC, is genetically linked to alterations in chromosomes 7 and 17 and a loss of chromosome Y. ***Chromophobe RCC (chRCC)***, the third most common form of RCC, is genetically linked to alterations in chromosomes 1, 2, 6, 10, 13, and 17.[4,6,12-14]

Hereditary papillary RCC (HPRCC), leiomyomatosis and RCC (HLRCC-Reeds syndrome), Birt-Hogg-Dube syndrome (BHDS), and tuberous sclerosis (TSC) are among the hereditary disorders that should also be considered as pathogenic mechanisms that make an individual susceptible to a unique type of RCC.[4,6,12-14] For example, HPRCC

may cause pRCC, BHDS may cause chRCC, and TSC may cause a variety of RCCs. Hereditary susceptibility also predisposes a person to nonmalignant renal masses such as angiomyolipoma and oncocytoma.[4,6,12-14]

Histologic features of RCC

Histologic characteristics of renal tissue are determined from a biopsy specimen. Various malignant and benign renal masses should be considered in the differential diagnosis (see *Selected malignant and benign renal masses*).[1] The types of RCCs have histologic and imaging similarities and differences. A composite of various imaging studies may be necessary for an accurate diagnosis of RCC. Correlation of histologic and imaging findings with the patient's clinical status is crucial.

The three major types of RCC usually occur sporadically, or they may be a part of inherited syndromes.[4,6,14]

- Approximately 80% of RCCs are ccRCC, which occur primarily in older men, usually in the sixth and seventh decades of life.[4,6,16,17] Histologically, ccRCC presents as a round, well-circumscribed mass with rich vasculature, a fibrous capsule, polygonal epithelial cells with centrally located small nuclei surrounded by clear cytoplasm from carbohydrates and lipids, and cystic degeneration. It is hemorrhagic with possible necrosis.[4,6,16,17] See *Clear cell RCC* for a microscopic view of ccRCC.

ccRCC has a yellow appearance from the presence of lipids and tends to infiltrate the venous system causing metastasis, particularly to the bone and lungs initially.[4,6,16,17] The rich vasculature of the tumor provides a mechanism for metastasis. At least 90% of patients with sporadic ccRCC have alterations on chromosome 3p, including chromosome 3p 25-26 on the VHL gene.[4,6,13,16,17]

- Approximately 10% of patients with RCC have pRCC (Type 1 pRCC or Type 2 pRCC).[4,6,16,17] Gender and age demographics are similar to those for patients with ccRCC.[4,6] pRCC usually presents as a well-circumscribed yellow-tan mass, which tends to be less vascular than ccRCC and chRCC and can mimic cysts.[4,6,16,17]

The papillae in the mass have fragile vasculature infiltrated by histiocytes that causes inflammation.[4,6,16,17] Larger pRCC may lead to hemorrhage and necrosis and may initially present as completely necrotic. Type 2 pRCC has larger nuclei and a more abundant cytoplasm than Type 1 pRCC. pRCC and ccRCC may occur together.[4,6]

- Approximately 5% of patients with RCC have chRCC, which occurs equally in men and women.[4,6] Under the microscope, chRCC presents as a well-circumscribed nonencapsulated mass that originates from the epithelial cells of the distal tubules in the nephron.[4,6,16,17] These tubules help to filter waste products from the serum and facilitate urine production. Hemorrhagic and necrotic features are not common in chRCC.[4,6]

The cytoplasm is granular with irregular nuclei.[4,6,16,17] Most of the nuclei are surrounded by clear halos. Cells are surrounded by thick cell membranes that have a plant-like appearance. chRCC usually grows more slowly and is less likely to metastasize than ccRCC and pRCC.[4,6]

- Collecting duct RCC is a very rare and aggressive form of RCC that arises from the collecting ducts. It may initially present as ccRCC or transitional cell carcinoma, and occurs more often in Black men.[4,6] An aggressive, non-RCC malignancy known as *medullary renal carcinoma* should be explored in young men with sickle cell trait.[4,6]
- *Unclassified RCC* is the term used when a renal mass has features of RCC, but does not fit the criteria for ccRCC, pRCC, or chRCC. This type occurs in less than 1% of patients with RCC.[18] Unclassified RCC may contain a combination of the well-recognized subtypes and have sarcomatoid features, which means the malignancy involves the connective tissues and grows and metastasizes quickly.[18]

Imaging characteristics

Imaging studies such as ultrasound, CT, and MRI of the abdomen and pelvis play a major role in identifying RCC and nonmalignant masses.[19,20] Imaging studies help to determine

Selected malignant and benign renal masses[1]

Malignant	Benign
RCC	angiomyolipoma
clear cell RCC	oncocytoma
papillary RCC	simple cyst
chromophobe RCC	hemorrhagic cyst
collecting duct RCC (very rare)	infected cyst
Other renal malignancies	renal adenoma
transitional cell carcinoma	hemangioma
renal medullary carcinoma (associated with sickle cell trait)	vascular malformation
squamous cell carcinoma	pseudo-tumor
Wilms tumor (children)	inflammatory mass
lymphoma	infarction
leiomyosarcoma	abscess
liposarcoma	focal pyelonephritis
rhabdomyosarcoma	rheumatic granuloma
metastasis (from primary site to kidneys)	

if a mass is a simple or hemorrhagic cyst, contains fat, inflammation, infection, infarction, lymphoma, sarcoma, Wilms tumor, or metastatic disease from the lungs, breasts, gastrointestinal tract, or melanoma.[18,19] CT with and without contrast is the predominant imaging study used to diagnose RCC.[4,6,19,20]

From a radiologic perspective, a suspicious renal mass on an imaging study is assumed to be malignant until tissue examination proves otherwise.[19,20] Tissue examination may be in the form of a preoperative percutaneous renal mass biopsy (RMB) using ultrasound or CT guidance or from a mass excised during surgery. Preoperative RMB is not always routinely performed in contemporary practice.[21]

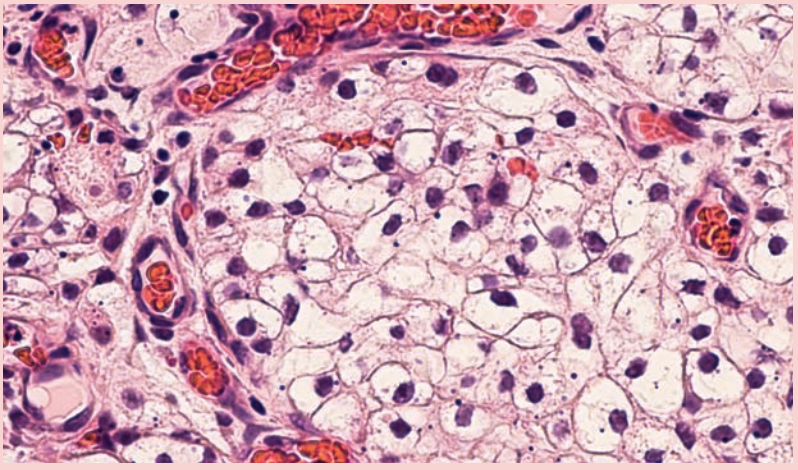
On imaging, a solid renal mass may have a ball or bean shape.[18,19,21,22] Ball-type masses are characteristic of RCC and tend to expand and distort the renal contour, whereas bean-shaped masses are not as prominent and do not distort the renal contour on imaging studies.[19,20,22,23]

Ultrasonography is among the most common imaging studies of the abdomen and pelvis. Ultrasound can clearly differentiate renal cystic masses from solid masses and may be the initial step in determining whether a renal mass is benign or malignant.[19,20] This test may identify the hypervascularity around the periphery of a round mass that is hypoechoic (dense tissue) in RCC.[19,20]

Renal masses must be assessed for enhancement on CT.[18,19,21,22] Contrast enhancement is the degree of blood flow through a mass and is a reliable predictor of malignancy.[4,6,19-23] For example, the vasculature of abnormal blood vessels in renal malignancy is different than normal blood vessels, making the attenuation (intensity) of the mass more pronounced on CT.[19-23] Small renal masses may enhance homogenously, whereas larger masses may have irregular enhancement (heterogenous). RCC, especially ccRCC, often shows strong enhancement.[19-23]

Clear cell RCC

Microscopic image of ccRCC, the most common type of RCC. It is characterized by cytoplasmic clearing and a pattern of small branching blood vessels.



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The density of a renal mass is also assessed on CT using Hounsfield Units (HU), which is a measure of density in body tissues.[19-23] For example, RCC generally has an HU of +20 to +70, which reflects the extent of vascularity and density of a renal mass. An HU of 0.00, showing no density, is characteristic of a simple cyst consisting of water. An HU of -20 or less is characteristic of a renal mass containing significant fat.[19-23]

MRI is an effective modality used to identify the hypervascularity and dysregulation in angiogenesis in RCC.[19-23] T1 and T2 are specific identifiers that radiologists use to classify images. For example, T1 tissue appears as a bright white color on the MRI that may signify fat. Conversely, T2 tissue with fat in the presence of water content may appear dark in color.[24]

T2 images show a high intensity in ccRCC, whereas T2 images in pRCC are of lower intensity.[19-23] Additionally, low intensity on T1 images may indicate intracellular fat, which is a feature of RCC on MRI.[19-23] High intensity on T1-weighted images may indicate the extensiveness of the fat-rich components of an angiomyolipoma.[23,25]

The most common benign renal mass, angiomyolipoma must be ruled out during the diagnostic workup. This type of mass is composed of blood vessels, smooth muscle, and fat. Imaging studies identify fat as a diagnostic feature of the mass.[4,23,25]

Oncocytoma, the second most common benign renal mass, must also be considered in the differential diagnosis.[4] Oncocytoma is a sharply demarcated mass that has a central scar and resembles the central scar with necrosis in RCC on CT.[4] Differentiating between the two masses on imaging studies is challenging.[16,20,24] Angiomyolipoma and oncocytoma may show enhancement on CT.[17,21,26]

A chest CT should be considered when a chest X-ray raises suspicion for metastasis and the patient has pulmonary symptoms.[19,20] A nuclear bone scan may be necessary when patients have bone pain or elevated alkaline phosphatase. Positron emission tomography (PET) is a powerful nuclear medicine modality that may be used to stage glucose-seeking tumors in metastatic RCC. Most PET modalities combine with CT in contemporary practice.[19,20]

Putting the picture together

To develop a plan of care with the interprofessional team, nurses need to correlate the patient's health history and head-to-toe assessment with an understanding of the pathophysiology of RCC and histologic and imaging findings as discussed here. Part 2 in this series will discuss the classification of renal masses, staging and grading of RCC, and signs and symptoms. It will also introduce medical management strategies and nursing care. ■

REFERENCES

1. Siddiqui SN, Haas CR, McKiernan JM. Epidemiology, screening, and clinical staging. In: Libertino JA, Gee JR, eds. *Renal Cancer: Contemporary Management*. 2nd ed. Cham, Switzerland: Springer; 2020.
2. Harris RE. Epidemiology of kidney cancer. In: *Harris Epidemiology of Chronic Disease: Global Perspectives*. 2nd ed. Burlington, MA: Jones and Bartlett Learning; 2020.
3. American Cancer Society. Key statistics about kidney cancer. 2021. www.cancer.org/cancer/kidney-cancer/about.html.
4. Mikami S, Kuroda N, Nagashima Y. Pathology of renal cell carcinoma. In: Oya M, ed. *Renal Cell Carcinoma: Molecular Features and Treatment Updates*. Tokyo, Japan: Springer; 2017.
5. Batai K, Harb-De la Rosa A, Lwin A, et al. Racial and ethnic disparities in renal cell carcinoma: an analysis of clinical characteristics. *Clin Genitourin Cancer*. 2019;17(1):e195-e202.
6. Francis F, Zhou M. Pathology of renal cell carcinoma. In: Libertino JA, Gee JR, eds. *Renal Cancer: Contemporary Management*. 2nd ed. Cham, Switzerland: Springer; 2020.
7. Wu X, Shu X. Epidemiology of renal cell carcinoma. In: Oya M, ed. *Renal Cell Carcinoma: Molecular Features and Treatment Updates*. Tokyo, Japan: Springer; 2017.
8. Al-Bayati O, Hasan A, Pruthi D, Kaushik D, Liss MA. Systematic review of modifiable risk factors for kidney cancer. *Urol Oncol*. 2019;37(6):359-371.
9. Zhang S, Jia Z, Yan Z, Yang J. Consumption of fruits and vegetables and risk of renal cell carcinoma: a meta-analysis of observational studies. *Oncotarget*. 2017;8(17):27892-27903.
10. The Johns Hopkins Lupus Center. Lupus and cancer. www.hopkinslupus.org/lupus-info/lifestyle-additional-information/lupus-cancer.
11. Song L, Wang Y, Zhang J, Song N, Xu X, Lu Y. The risks of cancer development in systemic lupus erythematosus (SLE) patients: a systematic review and meta-analysis. *Arthritis Res Ther*. 2018;20(1):270.
12. Ball MW, Pinto PA. Familial and hereditary syndromes in renal cell carcinoma. In: Libertino JA, Gee JR, eds. *Renal Cancer: Contemporary Management*. 2nd ed. Cham, Switzerland: Springer; 2020.
13. Quddus MB, Pratt N, Nabi G. Chromosomal aberrations in renal cell carcinoma: an overview with implications for clinical practice. *Urol Ann*. 2019;11(1):6-14.
14. Maher ER. Hereditary renal cell carcinoma syndromes: diagnosis, surveillance and management. *World J Urol*. 2018;36(12):1891-1898.
15. Plon SE, Jonasch E. Clinical features, diagnostics, and management of von Hippel-Lindau disease. UpToDate. 2020. www.uptodate.com.
16. Warren AY, Harrison D. WHO/ISUP classification, grading and pathological staging of renal cell carcinoma: standards and controversies. *World J Urol*. 2018;36(12):1913-1926.
17. Williamson SR, Gill AJ, Argani P, et al. Report from the International Society of Urological Pathology (ISUP) consultation conference on molecular pathology of urogenital cancers: III: molecular pathology of kidney cancer. *Am J Surg Pathol*. 2020;44(7):e47-e65.
18. Sirohi D, Smith SC, Agarwal N, Maughan BL. Unclassified renal cell carcinoma: diagnostic difficulties and treatment modalities. *Res Rep Urol*. 2018;10:205-217.
19. Afnan J, Therrien JA, Wald C. Imaging of renal cancer. In: Libertino JA, Gee JR, eds. *Renal Cancer: Contemporary Management*. 2nd ed. Cham, Switzerland: Springer; 2020.
20. van Oostenbrugge TJ, Fütterer JJ, Mulders PFA. Diagnostic imaging for solid renal tumors: a pictorial review. *Kidney Cancer*. 2018;2(2):79-93.
21. Patel HD, Nichols PE, Su ZT, et al. Renal mass biopsy is associated with reduction in surgery for early-stage kidney cancer. *Urology*. 2020;135:76-81.
22. de Leon AD, Pedrosa I. Imaging and screening of kidney cancer. *Radiol Clin North Am*. 2017;55(6):1235-1250.
23. Reinhard R, van der Zon-Conijn M, Smithuis R. Kidney—solid masses. Radiology Assistant. https://radiologyassistant.nl/abdomen/kidney-solid-masses.
24. MRI interpretation. T1 v T2 images. Radiology Master Class. 2017. www.radiologymasterclass.co.uk/tutorials/mri/t1_and_t2_images.
25. Vos N, Oyen R. Renal angiomyolipoma: the good, the bad, and the ugly. *J Belg Soc Radiol*. 2018;102(1):41.
26. American Urological Association. Renal mass and localized renal cancer: AUA guideline. 2017. www.auanet.org/guidelines/renal-cancer-renal-mass-and-localized-renal-cancer-guideline.

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