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Renal cell carcinoma, part 2

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

Abstract: Renal cell carcinoma (RCC) accounts for most renal malignancies. This article, the second in a three-part series, addresses how renal masses are classified, signs and symptoms of RCC, medical treatments for RCC, and priority nursing interventions for patients with RCC.

Keywords: Bosniak classification system of renal cystic masses, Fuhrman grading system, International Society of Urological Pathology grading system, ISUP grading system, nephrectomy, paraneoplastic syndromes, partial nephrectomy, radical nephrectomy, RCC, renal cell carcinoma, simple nephrectomy

RENAL CELL CARCINOMA (RCC) accounts for most renal malignancies. Part 1 of this three-part series discussed the incidence and epidemiology, genetic alterations, risk factors, histologic characteristics, and imaging characteristics of RCC.¹ This article addresses how renal masses are classified, signs and symptoms of RCC, an overview of medical treatments for RCC, and priority nursing interventions.

Classifying renal masses

The Bosniak classification system of renal cystic masses standardizes the management of complex cystic renal masses that are identified on contrast-enhanced CT.²⁻⁴ Each of the categories describes the incremental complexities of renal masses and the probability of malignancy. The Bosniak classification system helps radiologists and providers categorize masses according to specific characteristics, determine if surgery is necessary, and develop a monitoring or treatment plan.²⁻⁴

- Bosniak I describes a simple benign cyst with a thin wall. The cyst has no calcifications, solid components, or enhancement. A Bosniak I cyst has a malignancy risk of 0% and does not require monitoring or follow-up.

- Bosniak II describes a mildly complex benign cyst with calcifications. The cyst is well-marginated with no enhancement. A Bosniak II cyst has a malignancy risk of 0% and does not require treatment.

- Bosniak II-F describes a minimally complex cyst with calcifications, some septal wall thickening, and no measurable enhancement. Bosniak II-F cysts have a 5% chance of being malignant and should be monitored.

- Bosniak III describes a cystic mass that has a thickened, smooth or irregular wall and measurable enhancement; it is generally referred to as indeterminate in nature. Most Bosniak III masses are malignant (estimates range from 55% to 90%).^{2,5} The recommended treatment is generally surgical excision.

- Bosniak IV describes a distinctly enhanced soft tissue mass independent of the wall or septa. The incidence of malignancy is nearly 100%. The treatment for a Bosniak IV mass is surgical excision.

Staging RCC

The pathologic stage of a tumor, which combines clinical staging with surgical pathology results, is the most reliable prognostic indicator

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for patients with RCC and provides a direction for treatment approaches.⁶⁻⁹ Macroscopic and microscopic analysis of tissue quantifies tumor size and determines the absence or presence of tumor invasion into the perinephric fat, renal vein, inferior vena cava, adrenal glands, and lymph nodes.⁶⁻⁹

The American Joint Committee on Cancer (AJCC) has developed a standardized TNM staging scheme based on characteristics of the primary tumor (T), regional lymph node involvement (N), and distant metastasis (M).¹⁰ (See *Abbreviated AJCC TNM staging of RCC*.) In RCC, tumors are staged as follows:^{3,6-9}

- Stage I malignancies are tumors measuring 7 cm or less that are contained within the kidney with no lymph node involvement or distant metastasis.
- Stage II malignancies are tumors measuring more than 7 cm but are still contained in the kidney with no lymph node involvement or distant metastasis.
- Stage III malignancies may be locally invasive and/or involve nearby lymph nodes. There is no distant

lymph node involvement and no spread to other organs.

- Stage IV malignancies extend from the kidney to adjacent body organs and/or have metastasized to distant lymph nodes and/or other organs.

As an example, a tumor that is 6 cm and contained in the kidney is Stage 1. However, if imaging reveals lymph node involvement (N1), that 6-cm tumor is then considered Stage 3. It becomes Stage 4 if distant metastasis (M1) is present.^{3,6-10}

Grading RCC

The grading of tumor cells by physical appearance can also be a helpful prognostic indicator. The Fuhrman grading system, which evaluates nuclear characteristics of cancer cells, has been a widely used system for grading RCC. The International Society of Urological Pathology (ISUP) and the World Health Organization (WHO) developed a standardized system to grade RCC that complements the Fuhrman grading system and includes a more definitive measure of nuclear characteristics of RCC.^{1,3-6} Each criterion in the WHO/ISUP classification system

provides a prognostic indicator of the tumor. For example, Grades 1 and 2 are considered the least aggressive tumors, and Grades 3 and 4 are considered high-grade aggressive tumors.⁹ Tumor grade should be correlated with tumor stage and the patient's clinical status.^{3,6-9}

Signs and symptoms of RCC

Many cases of RCC are identified incidentally at an early stage of disease because of the availability of imaging modalities used in evaluation of a variety of symptoms and disorders.^{6,7} For example, patients may have imaging studies of the abdomen and pelvis because of symptoms related to the appendix, gallbladder, or colon. This imaging may reveal a renal mass in one or both kidneys. Most often, a solitary, round mass is noted in one kidney.^{6,7} Similarly, a chest CT may also image a portion of the kidneys and reveal a suspicious mass.

Most patients are asymptomatic in the early stages of RCC when renal masses are incidentally identified on imaging studies for other conditions. Only approximately 10% of

Abbreviated AJCC TNM staging of RCC^{6,10,19}

Stage	Tumor (T)	Node (N)*	Metastasis (M)*	Explanation
I	T1	N0	M0	Tumor is ≤ 7 cm. No regional lymph node involvement or distant metastasis.
II	T2	N0	M0	Tumor is > 7 cm. No regional lymph node involvement or distant metastasis.
III	T3	N0	M0	Tumor is regionally invasive. No regional lymph node involvement or distant metastasis.
	T3	N1	M0	Tumor is regionally invasive. Regional lymph node involvement is present, but no distant metastasis.
	T1 or T2	N1	M0	Meets T1 or T2 criteria for tumor size. Regional lymph node involvement is present but no distant metastasis.
IV	T4	N0-N1	M0	Tumor invades beyond the renal fascia and ipsilateral adrenal gland. Regional lymph node involvement may or may not be present. No distant metastasis.
	T1, T2, T3, T4	N0-N1	M1	Meets criteria for any tumor. Regional lymph node involvement may or may not be present. Distant metastasis is present.

***N0**: no regional lymph node involvement. **N1**: regional lymph node involvement is present.
M0: no metastasis to distant lymph nodes/organs. **M1**: metastasis to distant lymph nodes/organs is present.

patients with RCC initially manifest with the classic triad of symptoms: hematuria, pain in the flank, and a palpable mass in the abdomen. The classic triad of symptoms accompanied with fever, fatigue, and weight loss may indicate metastasis and the development of paraneoplastic syndrome, which will be discussed later in this article.^{3,6,7,11}

Tumors release inflammatory cytokines causing fever, fatigue, and a decrease in appetite and weight.^{6,7,11,12} Chronic inflammation may also cause anemia and elevations in the erythrocyte sedimentation rate and in c-reactive protein.

Large RCCs in the left kidney may create pressure on the left renal vein and diminish normal venous drainage in the left testicle, resulting in dilation of testicular veins and the creation of a varicocele.^{6,7,11-13} Because the right testicular vein drains into the right inferior vena cava, a blockage in the right renal vein by a large tumor does not usually cause the same problem.^{6,7,11-13}

RCC has a tendency to invade the renal vein, where it grows rapidly and reaches the inferior vena cava, which provides a mechanism for malignant cells to spread to other body organs.^{6,7,11-14} Indicators of metastasis to the lungs, bone, and liver include pulmonary signs and symptoms, bone pain, ascites, jaundice, and elevated levels of alkaline phosphatase, alanine aminotransferase, aspartate aminotransferase, and bilirubin.^{6,7,11-14}

It is common for patients with RCC to develop a *paraneoplastic syndrome*, in which malignant cells stimulate abnormal hormone production or create other abnormal responses, resulting in various signs, symptoms, and complications.^{7,11,12,15}

- Increased erythropoietin production causes an abnormally elevated red blood cell count that may lead to polycythemia, which slows blood flow and predisposes the patient to thromboembolism.

Resources for patients

- **American Cancer Society: Kidney cancer**
www.cancer.org/cancer/kidney-cancer.html
- **KCCure: Kidney cancer support communities**
<https://kccure.org/kidney-cancer-patient-support-communities>
- **Kidney Cancer Association**
www.kidneycancer.org
- **Renal cell carcinoma support group (Log-in to Facebook required)**
www.facebook.com/groups/279630142502937/members
- **Smart Patients (kidney cancer support group)**
www.smartpatients.com/forums/kidney-cancer

- The release of renin by the renin-angiotensin-aldosterone system causes problems maintaining normal BP.

- The release of parathyroid peptide may lead to hypercalcemia with the patient experiencing bone pain, muscle weakness and cramps, tingling in the lips and fingers, increased thirst and urination, and changes in mental status.

- The release of adrenocorticotrophic hormone stimulates the stress hormone cortisol, causing Cushing syndrome. Signs and symptoms include sodium and water retention, weight gain, increased serum sodium, increased BP, acceleration of atherosclerotic heart disease, and mental status changes.

Treatment options: An overview

Surgical intervention is the standard treatment for all stages of RCC, although the approach and techniques vary depending on the stage and the patient's clinical condition.^{14,16,17}

However, active surveillance (AS) is an option for patients for whom the risks of aggressive treatment outweigh the benefits. Excluded from AS are patients who are reasonable candidates for aggressive treatment if the size and infiltrative characteristics, internal growth, or pathology of the renal mass suggest progression of the malignancy.^{14,16}

The mean growth rate of RCC is generally slow at 0.1 to 0.3 cm per year, although the rate may vary

significantly among individuals based on the tumor's aggressiveness.^{3,14,16} Because the growth rate of RCC is relatively slow, older adults may elect AS rather than aggressive treatment because they are more likely to die of non-RCC causes.^{3,14}

The treatment options summarized below will be discussed in greater detail in part 3 of this series.

- **Partial nephrectomy (PN)**, which involves removing the tumor and tissue immediately surrounding it, is an option for treating small tumors. A priority goal of PN is to preserve renal function through a nephron-sparing approach, especially in young patients and in those with comorbidities that are likely to compromise renal function in the future, such as diabetes mellitus, hypertension, recurrent urolithiasis, and obesity. The surgeon may elect to perform PN as an open procedure or through a laparoscopic, robot-assisted approach.^{14,16,17}

- **Radiofrequency ablation** (application of heat) and **cryoablation** (application of cold/freezing) are options in patients with Stage I RCCs smaller than 3 cm. An important advantage for radiofrequency ablation and cryoablation techniques compared with PN is their superior ability to preserve renal tissue.¹⁸

- A radical nephrectomy (RN) involves removal of the entire kidney, fatty tissue surrounding the kidney, connective tissue that encloses and supports the kidney (Gerota's fascia),

and adrenal glands.^{3,4,8,9,11} On rare occasions, the surgeon may elect to remove only the kidney and leave the adrenal gland in place (simple nephrectomy). RN is generally considered when a PN cannot be accomplished because of a tumor's anatomic location, size, or complexity.^{14,16,17}

An RN may be performed laparoscopically or as an open procedure. A laparoscopic approach is preferred if feasible because it is associated with less blood loss and a shorter hospital stay. An evaluation of the contralateral kidney should be performed prior to RN.^{14,16,17}

Interventions for advanced disease

Advanced metastatic RCC does not generally respond sufficiently to traditional chemotherapy.^{14,16,17} However, because RCC sometimes regresses when a person's immune system attacks a tumor, immunotherapy may be prescribed to prime a person's immune system to recognize and destroy malignant cells.^{14,16} Consequently, immunomodulating drugs are the mainstay of systemic therapy in metastatic RCC. These drugs include selected monoclonal antibodies and cytokines, which will be addressed in detail in part 3 of this series.^{14,16}

Taking the lead with wellness programs

To reduce morbidity and mortality associated with RCC and comorbid conditions, nurses can develop community wellness programs that focus on nutrition, exercise, and mental health. Mental health education helps people achieve an enhanced self-image so they are better able to make healthier lifestyle choices through the lifespan. For example, individuals with an enhanced self-image may be more likely to avoid smoking, have healthy eating habits, and value the importance of being physically active.

Community wellness programs should start with children, perhaps in prekindergarten, and be fused through elementary, middle school, and high school. Colleges and universities should have wellness programs for students, staff, and community members. Partnerships between colleges, universities, schools of nursing, public and private school systems, and clinical agencies should be explored, and sources for funding wellness programs identified. Nurses, school counselors, social workers, dietitians, exercise and kinesiology instructors, licensed professional counselors, psychologists, physicians, students, and lay community members should be included on the interprofessional team to develop wellness programs. A focus on disease prevention is key to promoting health and wellness in the community.

Priority patient teaching

By providing patient education, nurses can help patients maintain their health and reduce risk factors for RCC. Nurses can:

- teach patients that a lifelong pattern of eating a well-balanced diet of proteins, fats, and carbohydrates reduces the risk of RCC. Encourage patients to include plenty of fruits and vegetables in their diet because they are an important source of minerals and vitamins; they also help to reduce cholesterol and maintain normal blood glucose levels.
- educate patients on the importance of maintaining a healthy weight through good nutrition and physical activity.
- advise patients to avoid tobacco and to limit alcohol intake.
- warn patients about the risks of exposure to carcinogenic chemicals and toxins in the workplace and home. Recommend that they wear gloves and masks as indicated and practice good hand hygiene.
- recommend that patients discuss any use of over-the-counter analgesics with their healthcare provider. Recommend that they balance pain relief with these medications with nonpharmacologic pain management strategies.
- encourage periodic visits with their primary care provider for regular health screenings and to ensure that chronic diseases such as hypertension are appropriately managed.
- encourage patients with a family history of RCC to consider genetic counseling.

Priority nursing interventions

Nurses caring for a patient with known or suspected RCC should correlate the patient's health history and assessment findings with signs, symptoms, imaging studies, and lab data suggesting RCC. The patient history should include a thorough analysis of RCC risk factors and comorbidities.

Patients who have had a PN or RN are usually hospitalized for a few days. It is crucial for the nurse to monitor surgical incision(s) for any

erythema, edema, drainage, or bleeding and teach patients to report any of those findings promptly. To reduce risk of atelectasis and pneumonia after surgery, nurses can teach patients to use an incentive spirometer regularly.

Patients who have had laparoscopic surgery will have carbon dioxide (CO₂) placed into the abdominal cavity to displace body organs so that the surgeon can access the affected kidney. CO₂ irritates the phrenic nerve and may cause mild-to-severe shoulder pain on the side of the affected kidney when the patient moves from a lying to sitting position after surgery. Tell patients that the discomfort will resolve after the CO₂ absorbs over a day or two.

To prevent constipation after a PN or RN, patients should consume high-fiber foods, increase fluid intake, and take a stool softener as directed by the healthcare provider.

Patients will need follow-up with imaging studies after PN and RN to monitor for disease recurrence and any progression of metastatic disease. Nurses play an important role in educating patients about the importance of regular follow-up care (see *Priority patient teaching*). Patients with

advanced metastatic disease who are receiving immunotherapy should be educated to recognize and report signs and symptoms of infection.

The interprofessional team, which includes the patient and loved ones, should explore end-of-life care options when the prognosis is poor. Nurses should assess patients for their understanding of RCC and of their prognosis and encourage the patient and family to verbalize the fear, anxiety, and feelings of uncertainty that are likely to accompany an RCC diagnosis. These emotions will vary among individuals and according to the stage of the disease and prognosis. Counselors, psychologists, and support groups are often helpful (see *Resources for patients*).

Reducing risks and promoting wellness

Nurses can take leadership roles in the community to reduce the morbidity and mortality associated with RCC (see *Taking the lead with wellness programs*). Along with patient teaching, these interventions can help reduce modifiable risk factors for RCC.

Nurses need both clinical knowledge and critical thinking skills to

support and educate patients being treated for RCC. A detailed analysis of treatment options and nursing care for these patients will be discussed in the third part of this series. ■

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Richard L. Pullen is a professor of nursing at Texas Tech University Health Sciences Center School of Nursing in Lubbock, Tex., and a member of the *Nursing2021* editorial board.

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