Clinical and Pathologic Staging of Renal Cell Carcinoma

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KEYWORDS
RENAL CELL CARCINOMA
STAGING
PROGNOSTIC FACTORS
KIDNEY NEOPLASMS

ABSTRACT
Renal cell carcinoma (RCC), which accounts for 3% of adult malignancies, is the most lethal of the urologic cancers. It is the third most common urologic malignancy following prostate and bladder cancers; however, approximately 40% of patients eventually die of progression of their RCC, while the mortality rates for prostate and bladder carcinomas are closer to 20%. Traditionally, RCC has been staged according to anatomic staging systems, such as the tumor, node, metastasis (TNM) system. This system takes into account tumor size and extent of local disease, nodal disease, and presence of metastases when grouping patients for both prognosis and treatment. Recent advances in understanding of the pathogenesis, molecular behavior, and progression of RCC, as well as recent investigation of clinical predictive factors, have led to suggestions of new algorithms for staging RCC patients.

This chapter reviews the clinical and pathologic staging of RCC according to current practices, and provides an overview of more recently proposed, comprehensive staging systems.

CLINICAL STAGING

Clinical Factors

SIGNS AND SYMPTOMS
Due to the retroperitoneal location of the kidney, many renal masses remain asymptomatic and nonpalpable until they reach advanced stages. For this reason, the presence of clinical signs and symptoms is often indicative of advanced disease. These include
weight loss, decreased performance status, hematuria, flank pain, palpable mass, lower extremity edema, and presence of a varicocele.

The most common presenting symptom in one series of RCC patients was hematuria reported by 35%, followed by flank pain reported in 27%. Suggested etiologies of pain in the RCC patient include compression or infiltration of surrounding tissues, rapid expansion of the renal mass from acute hemorrhage, and compression and obstruction of the renal collecting system. A palpable mass is correlated with tumor size and locally advanced disease. The classic triad of RCC includes hematuria, flank pain, and palpable mass. The combination of these three signs and symptoms is now rarely seen. Renal cell carcinoma has also been associated with paraneoplastic syndromes. Systemic findings such as hypertension, erythrocytosis, and elevated liver function tests can be attributed to this.

Some specific signs on physical exam have been associated with advanced disease. The presence of bilateral lower extremity edema, new nonreducible varicocele, caput medusa, and deep venous thrombosis are indicative of venous involvement. It is also widely accepted that palpable lymphadenopathy has a negative impact on RCC stage. Bone metastasis is suggested by pain in the hip, extremity, back, and rib. Similarly, metastasis to the brain is suggested by neurologic symptoms or headache, and lung metastases are a concern in patients with respiratory symptoms. The most common sites of metastases of RCC include lung, liver, bone, and brain.

**IMAGING**

Computed tomography (CT), or in some cases magnetic resonance imaging (MRI), should be performed to assess local tumor stage. Indications for MRI include suspected venous involvement, intravenous (IV) contrast allergy, obliteration of planes between the tumor and adjacent organs on CT scan, and renal insufficiency. Additionally, a standard posteroanterior and a lateral chest x-ray are mandatory for the initial workup of RCC to rule out pulmonary metastases. Perinephric involvement can be suggested by perinephric stranding or the presence of abnormal soft tissue density within the perinephric fat. Absence of suspicious findings in the perinephric region on CT does not rule out microscopic perinephric fat involvement. Preoperative diagnosis of lymphadenopathy by CT can also alter therapeutic approach significantly. Lymph nodes of size 2 cm or greater are suspicious for malignancy, while those less than 2 cm have a high likelihood of being inflammatory reaction. Computed tomography may also illuminate the presence of venous tumor thrombus by demonstrating venous enlargement, changes in the caliber of the vessel, and intraluminal variations in contrast enhancement. If tumor thrombus is suspected based on CT findings, an MRI is indicated for better venous imaging. In addition to the presence of thrombus, the level of tumor thrombus in relation to the patient’s diaphragm will aid in operative planning.

Bone scintigraphy is an additional test that is indicated in the setting of increased alkaline phosphatase, bony pain, or the detection of other metastases in an attempt to rule out bone metastases. Computed tomography of the head is indicated only if the patient reports neurologic symptoms, or if other metastases have been discovered. If lesions are noted on chest x-ray, a CT of the chest is appropriate for further evaluation. Finally, percutaneous biopsy, though not routinely used, can be enlisted to confirm the histology of the primary tumor in patients with evidence of systemic metastases, to assess enlarged lymph nodes, or to sample metastatic lesions.