AJR FOCUS ON:

Renal Cell Carcinoma: What the Surgeon and Treating Physician Need to Know

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OBJECTIVE. The multimodality approach to treating both localized and metastatic renal cell carcinoma has led to a demand for improved imaging evaluation. We review the information needed from the radiologic studies used to determine treatment strategies.

CONCLUSION. Adequate preoperative radiologic assessment provides the treating physician with information critical in determining the sequence of treatments, role of nephron-sparing surgery, surgical approach, and timing of systemic therapy for metastatic disease.

Reevaluation of historical treatments of renal cell carcinoma (RCC) has led to refinements in surgical technique, the use of ablative techniques, and the increased use of nephron-sparing surgery. One of the most notable achievements has been the development of systemic therapies, which have increased survival among patients with metastatic RCC [1]. Patients with metastatic disease are treated with a multimodality approach that incorporates surgical and systemic therapies. This approach to treatment of RCC has led to a demand for improved imaging evaluation, including tumor subtype differentiation, accurate staging and detection of metastatic disease, evaluation for local and systemic recurrence after extirpative therapy, and measuring response to systemic treatments. The information provided by radiologists is paramount in guiding decisions regarding therapy for both localized and systemic disease. The focus of this review is a clinical perspective on how the results from imaging studies are used to determine appropriate strategies for the surgical and systemic treatment of RCC.

Guidelines for Preoperative Radiologic Assessment of Renal Cell Carcinoma

Several leading organizations, including the European Association of Urology, National Comprehensive Cancer Network, and American College of Radiology, have published recommendations based on reviews of the published data on evaluation of patients with RCC. These guidelines contain similar conclusions about the preoperative studies needed for adequate staging of RCC. Brain imaging and bone scanning are recommended only if the history or physical examination findings suggest they are necessary. PET is not recommended as a routine study in the evaluation of RCC [2–4]. Contrast-enhanced CT or MRI of the abdomen is recommended to evaluate the primary lesion. Chest imaging is recommended: chest radiography for patients at low risk and chest CT for those at in higher risk, risk being based on the size of the primary lesion (American College of Radiology guidelines) or determined by the clinician (European Association of Urology and National Comprehensive Cancer Network). Although most urologists are facile in reviewing renal images, subtle findings by the radiologist often alter therapeutic strategies.

Clinical Staging

Accurate clinical staging is essential in surgical planning. The American Joint Committee on Cancer released a new staging system for renal cancer in January 2010. The details of the system are shown in Table 1 [5]. Size of the primary tumor and evidence of venous involvement (T3b or T3c), adjacent organ invasion (T4), nodal metastasis (N1), and distant metastatic disease are critical in determining the surgical plan or need for systemic therapy. The following sections describe the extent to which radiologic findings are used to determine stage and how these findings affect the surgical management of RCC.

Keywords: imaging, renal cell carcinoma, surgery, treatment, urologist

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TABLE 1: TNM Classification of Renal Cell Carcinoma (American Joint Committee on Cancer, 2010)

Category	Characteristic
T	
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
T1a	Tumor 4 cm in greatest dimension, limited to kidney
T1b	Tumor > 4 mm but ≤ 7 cm in greatest dimension, limited to kidney
T2a	Tumor > 7 cm but ≤ 10 cm in greatest dimension, limited to kidney
T2b	Tumor > 10 cm, limited to kidney
T3a	Tumor grossly extends into the renal vein or its segmental (muscle-containing) branches, or tumor invades perirenal or renal sinus fat but not beyond Gerota fascia
T3b	Tumor grossly extends into the vena cava below the diaphragm
T3c	Tumor grossly extends into the vena cava above the diaphragm or invades the wall of the vena cava
T4	Tumor invades beyond Gerota fascia (including contiguous extension into the ipsilateral adrenal gland)
N	
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Regional lymph node metastasis
M	
M0	No distant metastasis
M1	Distant metastasis

Note—Adapted with permission from [5].

Surgical Treatment of Localized (T1–2) Disease

The paradigm shift has been toward nephron-sparing surgery through the use of partial nephrectomy. This change in management is based on evidence of an increase in the numbers of hospitalizations, cardiovascular events, and deaths in a graded response to a decrease in estimated glomerular filtration rate [6]. In evaluations of this finding among patients undergoing surgery for RCC, radical nephrectomy was associated with increased risk of overall mortality and cardiac events compared with partial nephrectomy [6, 7]. Because of improvement in long-term outcome due to use of nephron-sparing surgery and mounting evidence showing equivalent oncologic outcomes of partial nephrectomy and radical nephrectomy, urologists are becoming more aggressive in their attempts at nephron-sparing surgery [8]. Initially, partial nephrectomy was reserved for tumors smaller than 4 cm in greatest dimension (T1a). In light of the data on renal preservation, several groups have found equivalent oncologic outcomes among properly selected patients with tumors as large as 7 cm in diameter (T1b) [9]. The current American Urological Association guidelines for management of a T1 renal mass call for partial nephrectomy when technically feasible [10]. Partial nephrectomy for tumors larger than 7 cm (T2) also appears to be safe and effective but for a highly selective group of patients, including those with a solitary kidney, preexisting renal insufficiency, and an appropriate tumor location [11]. Although partial nephrectomy preserves renal function, the risk of complications after nephron-sparing surgery is higher than after radical nephrectomy. In a prospective randomized European Organization for Research and Treatment of Cancer study that included 541 patients undergoing partial as opposed to radical nephrectomy, the investigators found greater risk of severe hemorrhage, urinary fistula, and reoperation for complications in the partial nephrectomy group [12].

As a result of the expanding indications for partial nephrectomy and the need for standardized reporting of outcome, several groups [13–15] have attempted to generate methods of preoperative scoring to quantify renal tumor size, location, and depth based on preoperative imaging findings. The standard technique of partial nephrectomy includes clamping of the renal artery with or without the renal vein and sharp excision of the renal mass. The time a vessel is clamped is the warm ischemia time. The accepted safe warm ischemia time is debatable, but the cutoff likely falls between 20 and 30 minutes [16, 17]. Identifying predictive characteristics of renal tumors that can be used to identify risk of prolonged warm ischemia time or surgical complications is the objective of these scoring systems.

Three anatomic classification and scoring systems are used: RENAL nephrometry score (radius, exophytic or endophytic, nearness to collecting system or sinus, and anterior or posterior location relative to polar lines); Padua score (preoperative aspects and dimensions used for anatomic assessment, developed by researchers at Padua University); and C (centrality) index [13–15]. In the Padua and RENAL nephrometry scoring systems, a renal lesion is assigned a value based on several anatomic properties (Table 2). The Padua score was internally validated with 164 patients, and in multivariate analysis, the score was the only significant predictor of the risk of complications [15]. These findings later were externally validated in a cohort of 240 patients with similar findings [18].

The C index is calculated with measurements obtained from a 2D CT scan to determine the lengths of two sides of a right triangle. The Pythagorean theorem is used to calculate the hypotenuse of the triangle. The hypotenuse is indicative of the proximity of the center of the lesion to the center of the kidney (Fig. 1). This number is divided by the radius of the tumor to obtain the C index. In a multivariate analysis that included 133 patients [13], C index and tumor size were the only significant predictors of warm ischemia time.

Although evidence supports the three anatomic classification systems in predicting surgical outcome, it is difficult to state that one of these methods is superior to the others on the basis of currently available evidence. For the purposes of this review, these scoring systems illustrate the anatomic considerations made by the urologist when reviewing renal images and may assist in evaluation of feasibility, safety, and postoperative risk in performance of partial nephrectomy. Additional anatomic considerations in planning partial nephrectomy are proximity to the ureter or ureters, number of renal arteries and veins present,

TABLE 2: Complexity Scoring Systems for Renal Lesions

Padua[a]	RENAL[a]	C Index[b]
Polar location (superior, inferior, medial)	Radius of tumor	Distance between kidney center and tumor center
Exophytic or endophytic nature	Exophytic, endophytic nature	Radius of tumor
Renal rim (lateral or medial)	Nearness to collecting system or sinus	
Renal sinus involvement	Anterior or posterior location	
Collecting system involvement	Location relative to polar lines	
Tumor size (radius)		
Anterior or posterior location		

[a]Points or score assigned.
[b]Measurements used to calculate a value.

and for more advanced lesions, identification of collateral feeding vessels. Finally, as in any surgical procedure, the patient's medical condition and presence of comorbid conditions must be taken into account in determining the risk of surgical intervention.

Locally Advanced Disease (T3–4N1)

Fat Invasion (T3a)

Limitations in the clinical staging of RCC with imaging focus largely on inability to correctly identify T3a disease by invasion into both the renal sinus and perinephric fat. Several groups have presented contrasting reports on the importance of renal sinus fat invasion and its effect on survival [19, 20]. Although there is debate regarding the prognostic significance of renal sinus fat invasion versus perinephric fat invasion, both are currently grouped together as category T3a [5]. Perinephric fat invasion has been found to be a significant predictor of recurrence and cancer-specific survival from tumors larger than 7 cm (T2) [21]. Outcome after partial nephrectomy for advanced-stage disease has been evaluated. At the Mayo Clinic, the cases of patients with T2 or greater RCC undergoing partial nephrectomy were evaluated, and the findings were compared with those for a matched cohort who underwent radical nephrectomy. Of interest was that the risk of recurrence was greater among patients undergoing partial nephrectomy (6% vs 3% for radical nephrectomy), and two of the four recurrences after partial nephrectomy were in patients with T3a disease [22]. On the basis of the scant data available, it is unclear whether preoperative knowledge of fat invasion should influence surgical strategy.

Tumor Thrombus (T3b–c)

Renal cell carcinoma has a propensity for invasion into the lumen of the renal vein and inferior vena cava (IVC) in 4–23% of cases [23, 24]. MRI has been the study of choice for determining the presence and extent of venous tumor thrombus and bland thrombus [25]. With the advent of MDCT, the routine use of MRI for preoperative evaluation in locally advanced RCC has been questioned. Hallscheidt et al. [26] compared MDCT and MRI for utility in estimating the extent of tumor thrombus and found that the rate of diagnosis of tumor thrombus with MRI was not significantly greater than that with MDCT. With MDCT, tumor thrombus level was predicted with 96% accuracy, showing that MDCT is an effective imaging modality for preoperative evaluation and surgical planning [27].

Vascular involvement in RCC is a predictor of perioperative morbidity and mortality. In addition to characterizing a venous tumor thrombi as T3b or T3c, extent of involvement has been defined with several criteria, including thrombus level (level 0, renal vein; I, < 2 cm above renal vein; II, > 2 cm above renal vein but below hepatic veins; III, at the hepatic veins but below the diaphragm; IV, above the diaphragm [Fig. 2]). In a review of outcome among patients undergoing nephrectomy with tumor thrombectomy at the Mayo Clinic, perioperative complication rates increased with tumor thrombus level (level 0, 12%; I, 18%; II, 20%; III, 26%; IV, 47%) [28]. In the revision of the American Joint Committee on Cancer TNM classification, renal vein invasion was reassigned to T3a, and T3b was considered IVC involvement with tumor thrombus below the diaphragm. Category T3c remains IVC involvement above the diaphragm. These changes were made as a result of several studies showing improved survival among patients with metastatic and those with

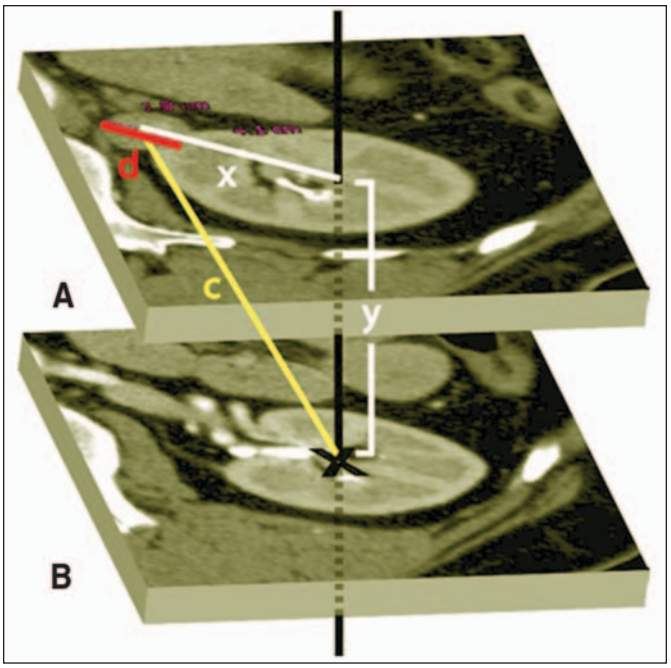

Fig. 1—Schematic shows C index scoring method. Middle plane is identified by averaging image section numbers showing most upper and lower kidney borders. At this middle section, kidney center (X) is placed in center of ellipse drawn around kidney periphery. Distance *y* is number of sections scrolled up and down to reach section with maximum tumor diameter divided by thickness of each section. Distance *x* is measured from central 90° axial reference point to tumor center. Tumor diameter is measured parallel to line drawn to measure *x*. Distance *c* is calculated and divided by tumor radius to determine C index. Reprinted with permission from [13].

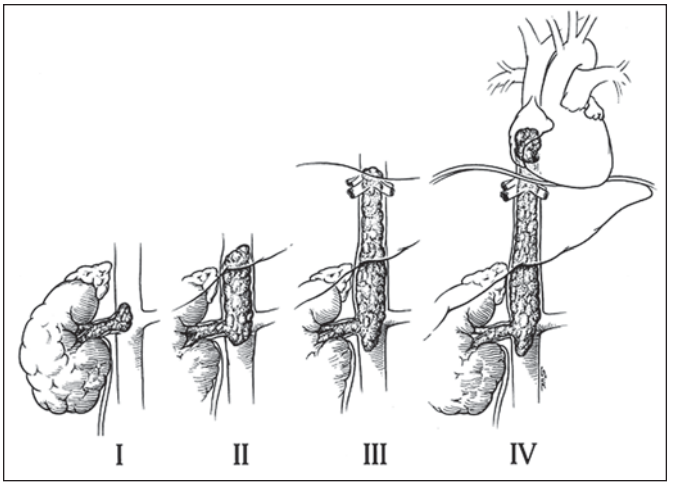

Fig. 2—Drawing shows inferior vena cava tumor thrombus defined by surgical level. (Reprinted with permission from [60])

nonmetastatic disease who had only renal vein involvement compared with patients with thrombus extension into the IVC [29–31]. Preoperative identification of a tumor thrombus and its level are helpful in counseling patients regarding prognosis, treatment options, surgical approach, and risk of complications.

Another finding shown to be a significant prognostic factor is invasion of the IVC wall (rather than luminal infiltration) by RCC tumor thrombus. Zini et al. [32] found the risk of death among patients with RCC invading the renal vein ostium wall was six times as great as that among patients without such invasion. Preoperative MRI had 90% sensitivity in estimation of wall invasion, as did IVC anteroposterior diameter of 18 mm and mean largest renal vein ostium diameter of 14 mm. Another evaluation [33] showed MRI had 100% sensitivity, 89% specificity, and 92% accuracy in prediction of IVC wall invasion. This finding may provide prognostic information but, more important, may aid in preoperative planning. Although much more rare than venous luminal infiltration (tumor thrombus), preoperative identification of venous wall invasion may assist in determining the extent of IVC resection and reconstruction, use of neoadjuvant therapy, and identification of patients who can be treated without surgery.

In addition to being prognostic factors, venous tumor thrombus and wall invasion are extremely important in preoperative surgical planning. Level III and IV thrombi are most often approached through a midline or chevron incision, which allows excellent exposure of the IVC and renal pedicles and access to the right atrium through extension of the incision via sternotomy if necessary. Vascular bypass (cardiopulmonary or venovenous) is used for successful removal of selected level III and most level IV tumor thrombi. Although urologists must be resourceful in the face of unexpected findings at surgery, preoperative identification and assessment of thrombus level with appropriate preoperative imaging are critical. Determining the appropriate incision and minimizing unexpected findings likely results in more successful outcome and may help to lower operative morbidity and mortality.

Nodal Involvement (TX–3aN1)

Clinical node staging is inaccurate. The positive predictive value of the finding of nodes larger than 1 cm on preoperative images is only 42% [34]. However, most urologists probably would agree that the presence of clinical nodes raises concern about the presence of regionally advanced disease, which warrants a more aggressive preoperative evaluation for evidence of distant metastasis or the addition of lymphadenectomy to surgery. The role of lymphadenectomy in the surgical treatment of RCC is controversial. Attempts to answer the question of therapeutic benefit and how to select patients with the greatest potential of benefiting have been largely unrevealing. What is clear, on the basis of the results of a European Organization for Research and Treatment of Cancer randomized study, is that for patients with clinical N0M0 disease with low-risk primary tumors, lymphadenectomy is unnecessary and would result in understaging in 1% of cases [35]. Those advocating lymphadenectomy in patients at higher risk believe that excision of pathologically node-positive disease in the absence of metastasis not only may improve staging but also may have therapeutic benefit [36].

Identification of cases of clinical node-positive disease or other high-risk findings may lead to selection of patients with pathologically positive lymph nodes, who may receive benefit from lymphadenectomy. In an attempt to identify which patients are at high risk, Blute et al. [37] retrospectively reviewed the cases of all patients undergoing nephrectomy with lymphadenectomy for RCC at the Mayo Clinic. With the data they were able to determine five high-risk features: tumor size larger than 10 cm, grade 3 or 4, category pT3 or pT4, histologic tumor necrosis, and presence of a sarcomatoid component. Patients with two or more of those features were more likely to have positive lymph nodes.

Crispen et al. [38] identified the cases of 169 patients with two or more of the five high-risk features, 64 (38%) of whom had lymph node–positive disease after lymphadenectomy. To gain insight into the regional landing zones for RCC nodal metastasis, the investigators located the positive lymph nodes in the retroperitoneum and recommended a standard template for dissection. The template includes the nodes from the ipsilateral great vessel and the interaortocaval region from the crus of the diaphragm to the bifurcation of the aorta. These findings nicely illustrate the appropriate templates for dissection if lymph node dissection is planned. Reporting the location of occult nodal disease calls to attention the need for adequate radiologic assessment of the retroperitoneum with particular attention to the nodes within the template for dissection. We perform lymphadenectomy on all patients with clinical node positive disease and select patients considered at high risk because of tumor size and stage. We found that 22% of patients with pathologically node-positive disease without metastasis had durable disease-free survival for a median follow-up period of 43 months (Delacroix SE Jr, et al., presented at the 2009 annual meeting of the American Urological Association). Surgery with curative intent for locally advanced RCC requires aggressive resection. Preoperative identification of clinically node-positive disease alters the planned surgical procedure and is critical to the urologist.

Adrenal Glands and Adjacent Structures (T4)

The historic definition of radical nephrectomy as described by Robson et al. in 1969 [39] included surgical excision of the kidney and Gerota fascia and ipsilateral adrenalectomy with lymphadenectomy from the crus of the diaphragm to the bifurcation of

the aorta. The necessity of adrenalectomy has been questioned because of the reported low incidence of adrenal invasion by RCC and the morbidity of adrenal insufficiency. In two of the largest series of ipsilateral adrenal involvement at the time of radical nephrectomy, the incidence was 5.5% and 5.7% [40, 41]. The authors evaluated the potential predictors of adrenal gland involvement and found that 89% of adrenal involvement occurred when the renal tumor was in the upper pole or was multifocal. In addition, when renal vein involvement was present, there was a greater likelihood of spread to the ipsilateral adrenal gland [41]. In a 2008 multivariate analysis, Ito et al. [42] identified the following predictors of ipsilateral adrenal involvement: tumor size larger than 5.5 cm, clinical category T3 or greater, and the presence of lymph node or distant metastasis. These predictors are often useful to urologists in determining the surgical plan for the adrenal gland, but the use of imaging has been found highly effective for detecting adrenal involvement, and the imaging findings often determine the need for surgical removal.

Evaluating the use of MDCT for staging of RCC, Catalano et al. [43] reviewed the CT findings on 40 patients and were able to identify all nine of nine patients with ipsilateral adrenal involvement. This result is consistent with the work of Gill et al. [44], who found a 100% negative predictive value of CT in the detection of adrenal gland involvement. In a recent review of the necessity of adrenalectomy, O'Malley et al. [45] proposed a management strategy for the appropriate use of ipsilateral adrenalectomy during radical nephrectomy. If preoperative CT or MRI findings are abnormal and venous tumor extension, upper pole tumors, or tumors larger than 7 cm are present, the authors recommend adrenalectomy. Although the accepted clinical parameters set forth in the proposed strategy may vary slightly among urologists, what is uniformly agreed is that any abnormal CT or MRI findings warrant surgical excision.

The designation of disease involving adjacent organs or structures (T4) confers a poor prognosis [46, 47]. Although this is a rare occurrence (1–1.5% of nephrectomy cases), preoperative findings suggestive of local invasion can often incorrectly label a patient as having unresectable or incurable disease. The disease of patients with T4 lesions often is downstaged after surgical resection, which is why we offer surgical resection to all patients with suspected T4 disease who are physically able to tolerate surgery and have lesions considered resectable. Concern about adjacent organ invasion does require the coordination of additional surgical teams to assist with resection if necessary. Involved structures are most commonly the colon, pancreas, diaphragm, liver, spleen, and bowel mesentery. The difficulty in evaluating patients eligible for surgical resection lies in preoperatively determining the extent of RCC involvement outside of the Gerota fascia. At our institution, Margulis et al. [46] identified the cases of 30 patients with suspected T4 disease at preoperative evaluation. In 18 of the 30 cases (60%), disease was downstaged after complete surgical resection showed the poor predictive value of adjacent organ involvement on preoperative images. Better preoperative assessment of adjacent organ invasion would be of great benefit because patients with pathologically confirmed T4 disease had a median survival period of only 2.3 months, raising the question whether surgical resection provided any benefit to these patients. The integration of systemic therapy and surgery may change the sequence of intervention in the care of patients with suspected adjacent organ involvement.

Treatment of Metastatic Disease (TX–3aNX–1M1)

Response to Systemic Therapy

In addition to the initial identification of metastatic disease to guide the use of systemic therapy, subsequent imaging is used to quantify the response to treatment. Surgical resection in the management of distant metastasis, termed cytoreductive nephrectomy, is the standard of care of patients who are eligible for surgery. This standard is based largely on the results of prospective randomized trials by Flanigan et al. [48] and Mickisch et al. [49], which showed improved survival among patients undergoing nephrectomy followed by interferon α therapy compared with interferon α therapy alone. Since approval of the first systemic targeted therapies in December 2005, there has been a shift from immunotherapy (interferon and high-dose interleukin 2) to the newer therapies because of their ease of administration (many oral regimens) and data showing improved overall survival with their use [1]. Although the usefulness of cytoreductive nephrectomy in conjunction with these contemporary systemic therapies has not been proved, the standard of care of patients with metastatic clear cell RCC who are surgical candidates continues to include cytoreduction followed by systemic therapy. This standard is based on the assumption that the therapeutic benefit of cytoreduction in the era of immune therapy will persist in the era of targeted therapies. Clinical trials are being performed to answer this question [50].

To establish an objective standardized method of evaluating response to systemic therapies, the Response Evaluation Criteria in Solid Tumors (RECIST) were published in 2000 and revised in 2008. RECIST has become the standard by which we report response or progression of disease in patients undergoing systemic therapy. These criteria define the minimum size of measurable lesions, the number of lesions that should be followed, and the use of a one-dimensional measure of disease burden. Response is classified into complete (disappearance of all target lesions), partial (≥ 30% decrease in size of lesions), stable disease (< 30% response to < 20% progression), and progressive disease (≥ 20% increase in disease burden). In the more recent version of RECIST, CT is the imaging modality of choice because newer modalities, including PET/CT, have not been validated [51].

Criticism of RECIST for measuring tumor responses in RCC is based on the evidence that metastatic sites do not have to shrink 30% to have a meaningful response to targeted therapy [52]. These criteria were originally developed for measuring response to cytotoxic chemotherapy and may not be as useful for targeted therapy. Because of the increased vascularity of RCC and the regression of this vasculature with targeted therapy, there is often a decrease in the attenuation of these lesions in response to therapy. As a result of these concerns, several attempts have been made to identify more accurate imaging criteria for objective grading of responses to targeted molecular therapy.

Choi et al. [53] evaluated the use of CT findings 8 weeks after initiation of treatment with a targeted agent (imatinib) to determine the responses of gastrointestinal stromal tumors. These finding were then correlated with the ^{18}F-FDG PET findings. The authors were able to characterize patients on the basis of a change in attenuation in addition to size. A 10% decrease in tumor size and 15% decrease in tumor attenuation had a sensitivity of 97% and specificity of 100% in predicting good response on the basis of FDG PET criteria. Additional imaging criteria in the management of RCC have been stud-

TABLE 3: Comparison of Imaging-Based Evaluation Criteria: Response to Systemic Therapy

Response	RECIST	Choi et al. [53]	Response	Size and Attenuation on Contrast-Enhanced CT	Morphology, Attenuation, Size, and Structure
Complete response	Disappearance of all lesions	Disappearance of all new lesions	NA	NA	NA
	Lymph nodes < 10 mm	No new lesions			
Partial response	≥ 30% decrease in size of the target lesions	≥ 10% decrease in size or ≥ 15% decrease in tumor attenuation at CT	Favorable	No new lesion *and*	No new lesion *and*
		No new lesions		≥ 20% decrease in tumor size	≥ 20% decrease in tumor size
		No obvious progression of nonmeasurable disease		≥ 10% decrease in tumor size and ≥ 50% nonlung target lesions have ≥ 20 HU decrease in mean attenuation	One or more predominantly solid enhancing lesions with marked central necrosis or marked decreased attenuation (≥ 40 HU)
				One or more nonlung target lesions have ≥ 40 HU decrease in mean attenuation	
Stable disease	Does not meet criteria for partial response or progressive disease	Does not meet criteria for complete response, partial response, or progressive disease	Indeterminate	Does not fit criteria for favorable or unfavorable	Does not fit criteria for favorable or unfavorable
Progressive disease	≥ 20% increase in size of the target lesions (minimum 5-mm increase)	≥ 10% increase in tumor size	Unfavorable	Any ≥ 20% increase in tumor size	Any ≥ 20% increase in tumor size in absence of marked central necrosis or markedly decreased attenuation
		Does not meet criteria for partial response based on tumor attenuation at CT		Any new metastasis	Any new metastasis
		New lesions		Any marked central fill-in of a target lesion	Any marked central fill-in
		New intratumoral nodules or increase in size of existing intratumoral nodules		Any new enhancement in a homogeneously hypoattenuating nonenhancing mass	Any new enhancement in a homogeneously hypoattenuating nonenhancing mass

Note—RECIST = Response Evaluation Criteria in Solid Tumors, NA = not applicable.

ied. Smith et al. [54] proposed size and attenuation on contrast-enhanced CT criteria, which were followed by morphology, attenuation, size, and structure criteria [55]. Similar to the criteria described by Choi et al., those described by Smith et al. account for tumor size and attenuation, and morphology, attenuation, size, and structure criteria add identification of tumor central necrosis. The four sets of response criteria are summarized in Table 3. Reports of changes in target lesion size and attenuation and identification of central lesion necrosis can assist the treating physician, even in the absence of an established method of grading responses. This information gives treating physicians a measure of response and therefore may help to guide surgical and medical therapy.

Presurgical Targeted Molecular Therapy

Although targeted molecular therapies have been associated with improved survival among patients with metastatic RCC, a large number of patients with metastatic disease continue to have minimal responses or experience disease progression soon after initiation of therapy. In an attempt to select for responders who may derive greater benefit from aggressive surgical therapy, these targeted therapies are being evaluated for presurgical use in the care of both patients with metastatic disease and those with regionally advanced disease [56]. There are inconsistent reports of tumor thrombus progression and regression in patients treated with these agents with a tumor thrombus in situ [57, 58]. In a clinical trial, presurgical therapy may be useful for identification of patients more likely to respond to therapy and therefore more likely to benefit from cytoreductive nephrectomy. In a recent evaluation of patients with metastatic disease undergoing systemic therapy with the prima-

TABLE 4: Imaging Characteristics Evaluated in Management of Renal Cell Carcinoma

Initial Evaluation	Response to Systemic Therapy
Size	Size (absolute and percentage change)
Enhancement, attenuation (HU)	Enhancement, attenuation (presence or absence, percentage change)
T category (AJCC 2010)	Time interval at which comparison is made
Size	Presence of necrosis
Fat invasion	Intratumoral nodules
Venous involvement and extent	Change in lymph node status (size)
Adjacent organ involvement (i.e., adrenal)	Presence of new lesions
Polar location	
Anterior or posterior location	
Percentage exophytic or endophytic	
Involvement of collecting system and renal sinus involvement	
Number of vessels	
Number of ureters	
Collateral neovascularity	
Nodal involvement (> 1 cm, number, locations)	
Metastasis (location, size, and number of lesions)	
Any anatomic variant	

Note—AJCC = American Joint Committee on Cancer.

ry tumor in place [59], patients with a 10% or greater response in the primary tumor within 60 days of the initiation of therapy had a significantly better median overall response (24.5% vs 7.2%). These findings may support the use of presurgical therapy as a litmus test for better selection of patients who may benefit from cytoreductive nephrectomy. Until data clearly support their presurgical use, these targeted therapies should be reserved for clinical trials. Imaging characteristics useful to urologists and oncologists evaluating patients with RCC are listed in Table 4.

Conclusion

Surgical excision of RCC is the mainstay of therapy for both local and metastatic disease. Summarizing the information needed in evaluation of RCC is a challenging pursuit because advances in treatment of this disease are rapidly evolving. Adequate preoperative radiologic assessment provides the urologist with the information critical for determining the suitability of partial nephrectomy, the appropriate surgical approach, and the need to assemble an appropriate surgical team to minimize unexpected findings at the time of the operation. In the evaluation of systemic therapies for metastatic disease, the radiologic assessment is crucial for defining response and progression and guiding treatment.

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