Renal Cell Carcinoma: Diagnosis, Staging, and Surveillance

Chaan S. Ng[1]
Christopher G. Wood[2]
Paul M. Silverman[1]
Nizar M. Tannir[3]
Pheroze Tamboli[4]
Carl M. Sandler[1]

OBJECTIVE. This educational review focuses on the staging and radiologic evaluation of renal cell carcinoma. It includes discussion of the epidemiology, pathology, and therapeutic options of renal cell carcinoma and the implications for radiologic follow-up.

CONCLUSION. The incidence of renal cell carinoma has been increasing. Imaging plays a central role in its detection, staging, and treatment evaluation and follow-up.

Keywords: imaging, renal cell carcinoma, staging

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C. G. Wood is a consultant for Pfizer, Inc.; Antigenics, Inc.; Bristol-Myers Squibb; Ethicon, Inc.; and Bayer Healthcare.

[1]Department of Radiology, Box 368, The University of Texas M. D. Anderson Cancer Center, 1515 Holcombe Blvd., Houston, TX 77030-4009. Address correspondence to C. S. Ng (cng@mdanderson.org).

[2]Department of Urology, The University of Texas M. D. Anderson Cancer Center, Houston, TX.

[3]Department of Medical Oncology, The University of Texas M. D. Anderson Cancer Center, Houston, TX.

[4]Department of Pathology, The University of Texas M. D. Anderson Cancer Center, Houston, TX.

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Renal cell carcinoma (RCC), the eighth most common malignancy affecting adults, accounts for between 3% and 4% of new cancer cases in the United States. It is the seventh most common cancer in men and the ninth most common in women [1]. We now know that RCC actually represents a family of related disorders with distinct cytogenetic and immunohistochemical properties that have differing prognoses, imaging characteristics, and potential morbidities.

The classic clinical presentation of flank pain, hematuria, and a palpable flank mass is comparatively uncommon (5–10% of cases). However, clinical symptomatology may be quite nonspecific—for example, anorexia, tiredness, weight loss, or fever of unknown origin [2]. Other presentations include varicocele formation (from tumor thrombus in the left renal vein or the inferior vena cava [IVC]) and disseminated malignancy. RCC may also present with a variety of paraneoplastic syndromes, such as polycythemia secondary to excessive secretion of erythropoietin, hypercalcemia secondary to factors regulating calcium, and hepatic dysfunction (Stauffer syndrome). Incidentally detected tumors in asymptomatic individuals have been steadily increasing with the dissemination of imaging techniques, including CT, MR, and sonography, accounting for approximately 60% of renal tumors in the 1990s, compared with approximately 10% in the early 1970s [3, 4].

Besides identifying these incidental lesions, diagnostic imaging plays an increasing role in this disease, particularly in the context of newer surgical approaches such as laparoscopic and nephron-sparing approaches. MDCT has been a major advance, providing angiographic and 3D imaging essential for presurgical planning.

This article focuses on the epidemiology, pathology, staging, radiologic evaluation, and therapeutic options of RCC and the implications for radiologic follow-up.

Epidemiology

There were an estimated 51,190 new cases of, and 12,890 deaths from, renal cancer in 2007 in the United States, accounting for 2.3% of all cancer deaths in the United States [1]. The incidence has steadily increased during the past 50 years in the United States and has occurred in 9.1/100,000 population in 1997, with a mortality rate of 3.5/100,000 [5–7]. Reported worldwide incidence rates range from 0.6/100,000 to 14.7/100,000 [8]. Most tumors present in the fifth to seventh decade of life, with a median age at diagnosis of 66 years and median age at death of 70 years. The incidence is two to three times higher in men and is slightly more common in blacks than in whites [5]. The incidence of renal tumors at autopsy is approximately 2% [9]. The tumors are usually solitary but may be multifocal (6–25%), with bilateral RCC occurring sometime in the course of life in 4% of patients [10].

Certain genetic conditions are associated with an increased incidence of RCC, including von Hippel-Lindau disease, hereditary papillary renal cancer, and, possibly, tuberous sclerosis [11]. RCC occurs in von Hippel-Lindau disease in 35–40% of patients, occurs at a younger age, and is frequently bilateral (75%) or multifocal

(87%) [12]. RCC is also more common in acquired cystic renal disease. Long-term dialysis carries a three- to sixfold increased risk compared with the normal population. Hereditary papillary RCC is an autosomal dominant form of the disease that is associated with multifocal papillary renal tumors. The disease has a 5:1 male predominance. Other suggested risk factors include cigarette smoking; obesity; diuretic use; exposure to petroleum products, chlorinated solvents, cadmium, lead, asbestos, and ionizing radiation; high-protein diets; hypertension; kidney transplantation; and HIV infection [5, 10, 13–15].

Survival Statistics

Despite the increasing incidence of the disease in recent decades, survival has steadily improved, with a current overall 5-year survival of approximately 62% [7]. Prognosis is influenced by the extent of disease at diagnosis, with a 5-year survival rate in the absence of metastases exceeding 50%; in the presence of distant metastases, the 5-year survival rate decreases to 10% (with a 10-year survival rate of < 5%).

The possible factors that have contributed to improved survival include advances in renal imaging and surgical techniques, stage migration to smaller and lower-stage disease as a result of earlier diagnosis in asymptomatic individuals, and the introduction of immunotherapy for advanced disease. Tumor size has been found to be an independent predictor of outcome, with larger tumors having a poorer survival; for example, 5- and 10-year disease-free survivals after surgery for T1, T2, T3a, T3b, and T3c tumors are approximately 95% and 91%, 80% and 70%, 66% and 53%, 52% and 43%, and 43% and 42%, respectively [16].

Regarding the potential contribution from incidentally detected tumors, the overall 5-year survival rate is approximately 85% for such cases, compared with 53% in symptomatic cases. Although data are not available, this may very well increase in the new era in which tumors are being detected incidentally at an earlier stage and smaller size. Evidence suggests, although not conclusively, that asymptomatic tumors are smaller and of lower grade and earlier stage [3, 7].

Pathology

RCC (hypernephroma or Grawitz's tumor) is the most common tumor to affect the adult kidney, accounting for 80–90% of primary malignant renal neoplasms in adults.

On gross pathology, tumors most often appear encapsulated. Tumors may be solid, cystic, or mixed, including or engulfing fat and calcification [17]. As many as 10% of tumors have some cystic component [18], and such tumors may be more aggressive [19].

Histologic subtypes according to the Heidelberg classification [20] include clear cell ("conventional") adenocarcinoma (80%), papillary (15%), chromophobe (5%), collecting duct (1%), and unclassified (4%) [21, 22]. Each of these subtypes has differing cytogenetic and immunohistochemical profiles as well as differing prognoses. Histopathologic grading of the nuclei of the tumor is made by dividing them into the four-tier Fuhrman nuclear classification [23], with grade I being the best-differentiated and grade IV the most anaplastic.

Clear cell carcinoma displays large uniform cells with abundant clear cytoplasm rich in glycogen and lipid (Fig. 1A). Clear cell carcinoma is typically highly vascular. Papillary tumors are subdivided into type I tumors (Fig. 1B), which occur sporadically and metastasize somewhat later, and type II (Fig. 1C), which are more likely inherited, may be multiple, and often present with a higher Fuhrman grade and poorer prognosis. Collecting duct tumors, which arise from the medullary collecting duct, often occur in younger patients and are associated with a poor overall prognosis. Renal medullary carcinoma is a rare subtype, closely related to collecting duct carcinoma and having a poor prognosis, which occurs in young patients with sickle cell anemia or sickle trait. Chromophobe tumors and oncocytomas, both of which arise from collecting duct epithelium, may be confused on histologic examination but have differing immunohistochemical profiles (Fig. 1D). Chromophobe tumors have the best overall prognosis, and oncocytomas are benign.

The tumor can extend directly into the perinephric fat, ipsilateral adrenal gland, or adjacent musculature, and, less frequently, the liver, spleen, pancreas, and colon. Rarely,

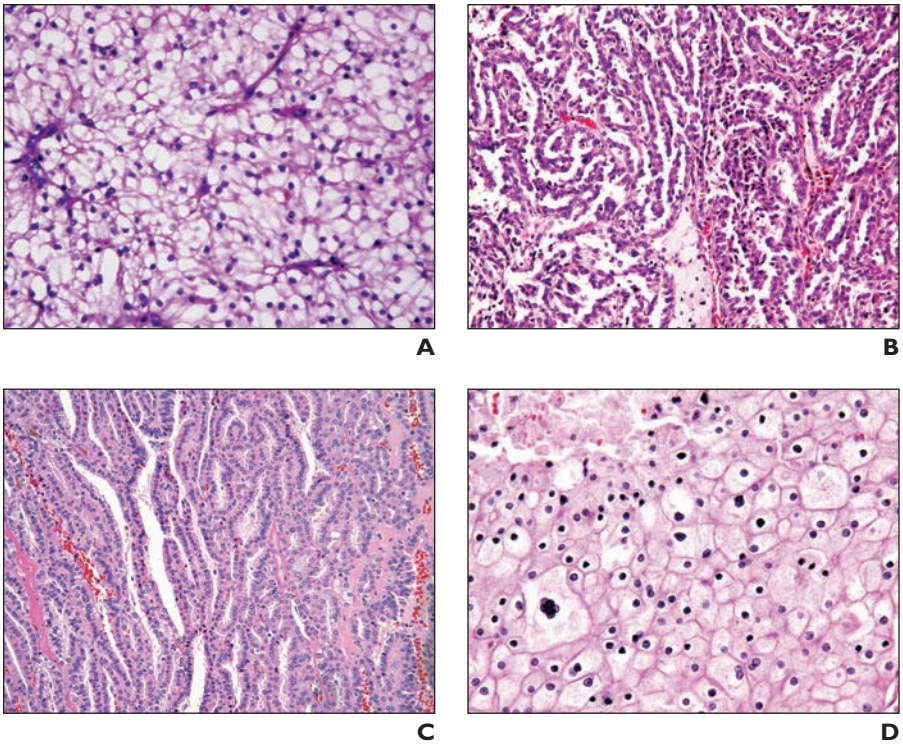


Fig. 1—Histopathologic slides of renal cell carcinoma (RCC). (H and E)
A, Conventional clear cell RCC. Tumor shows large uniform cells with abundant cytoplasm that is rich in glycogen.
B, Papillary RCC type I. Tumor papillae are lined by short cuboidal cells with basophilic cytoplasm. Nuclei are small with few inconspicuous nucleoli. Collection of foamy histiocytes is present in middle of lower half of image.
C, Papillary RCC type II. Tumor shows papillae lined by columnar to pseudostratified cells that have striking eosinophilic cytoplasm.
D, Chromophobe RCC. Note sheet of tumor cells with focal necrosis (upper left corner). Tumor cells have abundant pale flocculent cytoplasm, prominent cell membranes, perinuclear halos, and wrinkled nuclei.

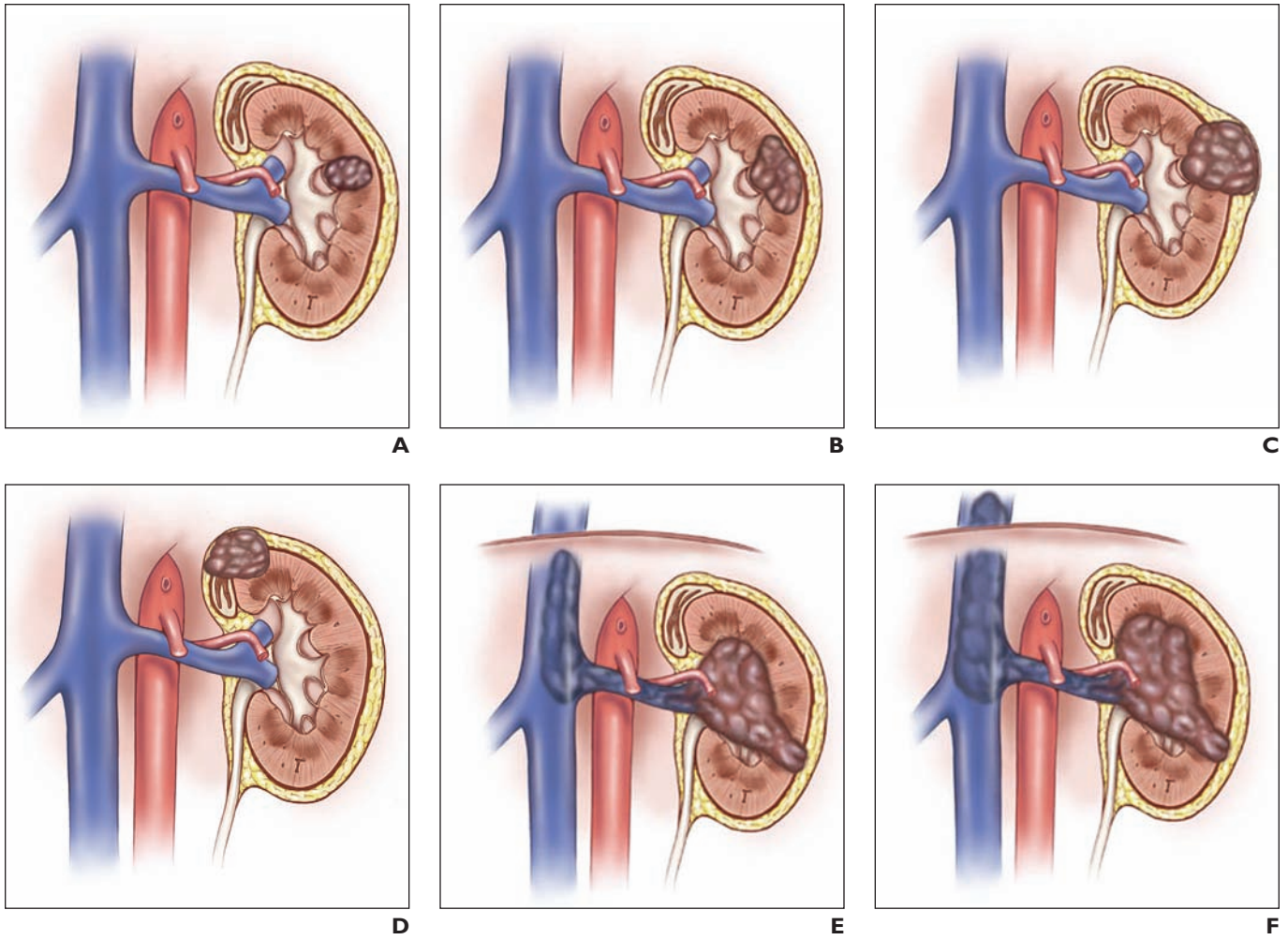


Fig. 2—Schematic diagrams of TNM staging of renal cell carcinoma. (© 2008 The University of Texas M. D. Anderson Cancer Center)
A, Stage T1 tumor < 7 cm.
B, Stage T2 tumor > 7 cm.
C and **D,** Stage T3a tumors involving perinephric fat (**C**) and adjacent adrenal gland (**D**).
E, Stage T3b tumor involving renal vein or inferior vena cava (IVC) inferior to diaphragm.
F, Stage T3c tumor involves IVC superior to diaphragm.

the tumor may invade the renal collecting system. RCC has a propensity for extending, as tumor thrombus, into the tributaries of the renal veins and subsequently to the main renal vein, the IVC, the hepatic veins, and potentially the right atrium. Hematogenous metastases are more common and occur earlier than lymphatic dissemination, the former most commonly to the lungs and bone, but essentially to any organ, including the subcutaneous tissues and skeletal muscle.

Staging

Staging systems are designed to reflect the modes of spread (Fig. 2) and are used to stratify treatment options and to assess prognoses and survival characteristics. The current version of the 2002 TNM staging of the American Joint Committee on Cancer (AJCC) and the International Union Against Cancer (UICC) is presented in Tables 1 and 2 [24].

In light of the increasing trend for the discovery of very small tumors as incidental findings on imaging studies performed for other purposes, revisions to this 1997 version have been proposed, including subclassification of T1 into T1a < 2.5 cm; T1b, 2.5–4.0 cm; and T1c, 5.0–7.0 cm tumors. The Robson classification [25] is an alternative staging system no longer used but still referred to in some of the older literature.

Prognosis is generally reflected in staging severity, with lower-stage disease being associated with longer survival rates. Five-year survival rates by TNM stage are shown in Table 3. The prognosis is noticeably adversely affected by spread of the tumor beyond the renal fascia and into the retroperitoneum (TNM T3a and higher). The natural history of the disease, however, is often unpredictable, and there are wide ranges in survival. There are reports, albeit rare (< 1:600), of stabilization or even spontaneous remissions in the face of metastatic disease [10, 26].

Crotty et al. [27] reported that 86% of chromophobe tumors in their series were Robson stage I at presentation. Beck et al. [28] reported that chromophobe and papillary histology were associated with an improved disease-free survival at 5 years compared with patients with

TABLE 1: TNM Staging of Renal Cell Carcinoma

Stage	Description
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
T1	Tumor < 7 cm in greatest dimension, limited to kidney
T1a	Tumor < 4 cm in greatest dimension, limited to kidney
T1b	Tumor > 4 cm but < 7 cm in greatest dimension, limited to kidney
T2	Tumor ≥ 7 cm in greatest dimension, limited to kidney
T3	Tumor extends into major veins or invades adrenal gland or perinephric tissues, but not beyond Gerota's fascia
T3a	Tumor invades adrenal gland or perinephric tissues but not beyond Gerota's fascia
T3b	Tumor grossly extends into renal vein(s) or vena cava below diaphragm
T3c	Tumor grossly extends into vena cava above diaphragm
T4	Tumor invades beyond Gerota's fascia
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis in a single regional lymph node
N2	Metastasis in more than one regional lymph node
MX	Distant metastasis cannot be assessed
M0	No distant metastasis
M1	Distant metastasis

Note—Adapted from current version of American Joint Committee on Cancer (2002) [24].

clear cell RCC. When controlled for size and stage of tumor, however, chromophobe, but not papillary, carcinoma offered a significantly improved survival. The times from nephrectomy to metastasis and from metastasis to death were twice those for patients with chromophobe histology when compared with those with clear cell or papillary subtypes.

It has been suggested that there are other potentially important determinants of survival that should be included in staging, including recognition of RCC tumor variants, sarcomatoid histology, histopathologic grade, molecular proliferation markers (silver-staining nucleolar organizer regions, proliferating cell nuclear antigen, and Ki-67 antigen), performance status, weight loss, hypercalcemia, and erythrocyte sedimentation rate [7, 10, 29, 30]. However, current staging does not incorporate these factors.

Twenty-five to 33% of patients have overt metastases at presentation [2, 13, 31]. The more common sites of metastases as reported in stage IV disease (TNM T4 or N1+ M1 disease) are the lung (69%), bone (43%), liver (34%), lymph nodes (22%), adrenal gland (19%), brain (7%), and thyroid, skin, and bladder (< 1% each) [32]. Rarer sites include skeletal muscle, bowel, gallbladder, pancreas, and orbits [10, 13, 33]. Large tumors tend to be associated with more advanced dissemination.

Radiologic Evaluation

The goals of radiologic imaging are to detect and stage the primary tumor. In most institutions, CT is the main imaging technique for the evaluation of the intra-abdominal component of renal tumors. In some specific instances, such as allergy to iodinated contrast medium, MRI and sonography can provide complementary information. The risks of nephrogenic systemic fibrosis (NSF) in patients with significantly impaired renal function, which is considered to be associated with some gadolinium-based MRI contrast agents, should be considered carefully when staging with MRI is deemed advisable [34].

It is generally considered that a risk-adapted approach is used for workup of other possible sites of metastases. Chest CT should be performed if the primary tumor is large or locally aggressive because metastases are more common in these patients [35]. Chest radiography without CT should be reserved for patients with a low risk of metastatic disease or for those in long-term follow-up [36, 37]. Brain MRI and nuclear medicine bone scanning are generally justified only if there

TABLE 2: TNM Stage Groupings

Stage Grouping	T Stage	N Stage	M Stage
I	T1	N0	M0
II	T2	N0	M0
III	T1	N1	M0
	T2	N1	M0
	T3	N0	M0
	T3	N1	M0
IV	T4	N0	M0
	T4	N1	M0
	Any T	N2	M0
	Any T	Any N	M1

Note—Adapted from current version of American Joint Committee on Cancer (2002) [24].

TABLE 3: Survival by TNM Stage

Disease Extent	TNM Stage	5-Year Survival Rate (%)
All organ-confined	T1–T2 N0 M0	70–90
≤ 4 cm	T1a N0 M0	90–100
> 4 but < 7 cm	T1b N0 M0	80–90
≥ 7 cm	T2 N0 M0	70–80
Invasion of perinephric fat	T3a N0 M0	60–80
Adrenal involvement	T3a N0 M0	0–30
Venous involvement	T3b–T3c N0 M0	40–65
Locally advanced	T4 N0 M0	0–20
Lymphatic involvement	Any T, N+, M0	0–20
Systemic metastases	Any T, any N, M1	0–10

Note—Adapted from current version of American Joint Committee on Cancer (2002) [24].

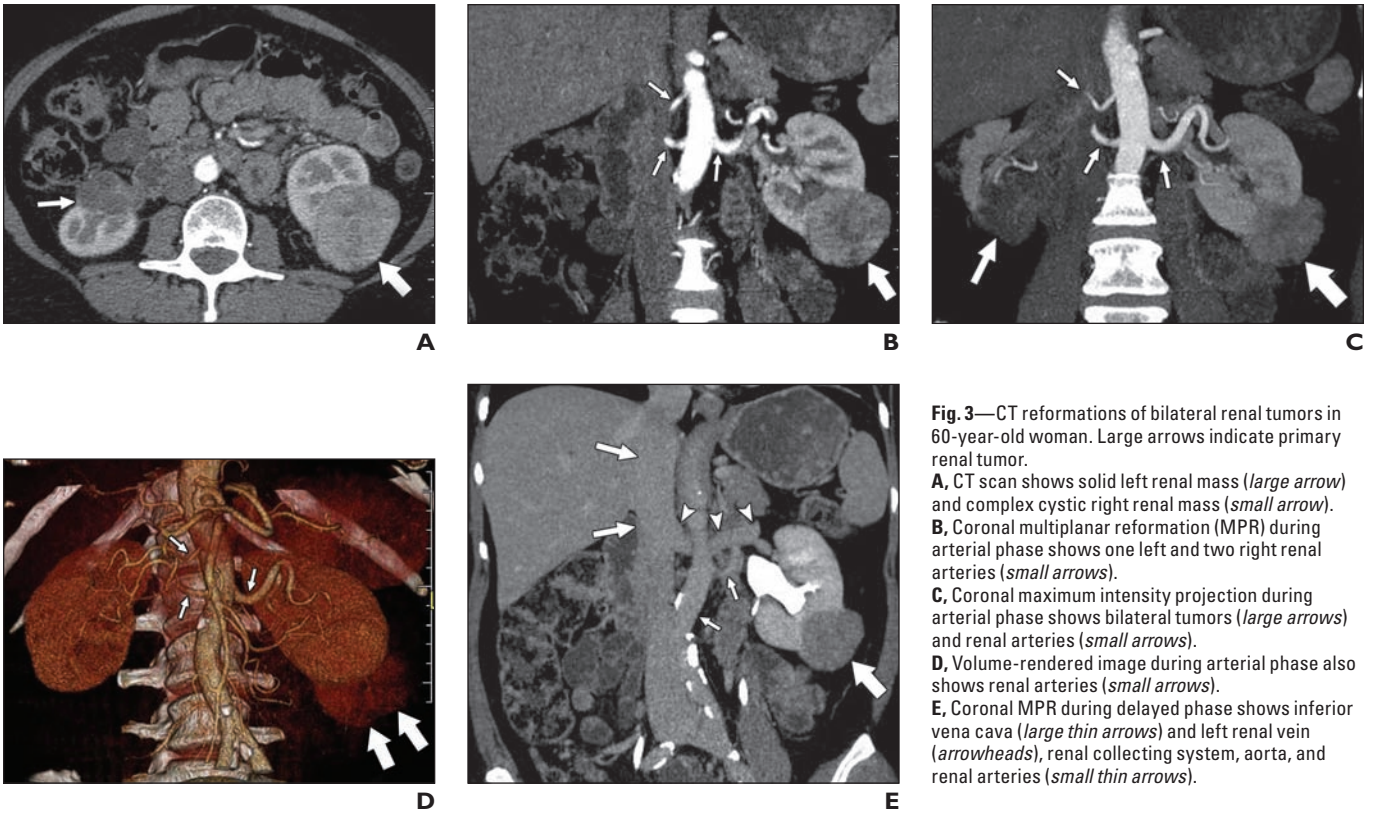


Fig. 3—CT reformations of bilateral renal tumors in 60-year-old woman. Large arrows indicate primary renal tumor.
A, CT scan shows solid left renal mass (*large arrow*) and complex cystic right renal mass (*small arrow*).
B, Coronal multiplanar reformation (MPR) during arterial phase shows one left and two right renal arteries (*small arrows*).
C, Coronal maximum intensity projection during arterial phase shows bilateral tumors (*large arrows*) and renal arteries (*small arrows*).
D, Volume-rendered image during arterial phase also shows renal arteries (*small arrows*).
E, Coronal MPR during delayed phase shows inferior vena cava (*large thin arrows*) and left renal vein (*arrowheads*), renal collecting system, aorta, and renal arteries (*small thin arrows*).

are symptoms and signs to suggest disease at these sites or if the tumor is large and locally aggressive, although even the latter is debated [31]. Technetium-99m-methylene diphosphonate (MDP) bone scanning, however, may be limited in detecting the typical osteolytic bone metastases from RCC. The value of pelvic CT in staging is also limited [38].

CT Evaluation

Suggested protocols for preoperative evaluation and follow-up using MDCT are presented in the text that follows. In addition to assessing tumor stage, preoperative evaluation focuses on delineating the tumor with particular attention to the relationship of the tumor to adjacent structures, including vascular relationships. In comparison, follow-up evaluation is directed toward surveillance for residual or recurrent disease. In general, 100–150 mL of iodinated IV contrast medium is used at a flow rate of 2–3 mL/s.

Preoperative Evaluation

For an MDCT protocol, unenhanced images of the liver and kidneys are obtained with 5-mm collimation in 5-mm increments. Unenhanced images of the kidneys allow detection of calcification or fat in the kidney, enable assessment of contrast enhancement, and assist in characterizing the lesion. IV contrast-enhanced images targeted on the kidneys are obtained in the arterial, late arterial (corticomedullary and portal venous), nephrographic, and excretory phases at 15–30, 45–60, 80–90, and 180 seconds, respectively, after commencement of the IV infusion. Imaging of the liver and the remaining abdominal structures is performed in the portal venous phase. Excretory phase images from the kidneys through the bladder are generally obtained to complete the evaluation of the entire urinary tract when requested by the referring clinician.

Multiplanar reformatted and 3D volume-rendered presentations of the renal phase images are helpful in allowing visualization of the relationships of structures, particularly for surgeons [39–41]. Such reformations are best obtained with the thinnest possible images and some degree of reconstruction interval overlap (typically, < 1.5-mm interval and 10–50% overlap) and are transferred to a workstation for creating multiplanar reformatted images, 3D volume rendering, and maximum-intensity-projection (MIP) images (Figs. 3A–3D). The late arterial phase provides a useful angiographic image of arterial and venous supply to the kidney but has limited additional usefulness for lesion detection and characterization when a nephrographic phase is used. The combination of excretory and nephrographic phases has been shown to improve lesion detection and staging [42, 43].

Several investigators have shown that clear cell RCC enhances to a greater extent and is more heterogeneous in appearance than other histologic subtypes (Figs. 4A and 4B). Kim et al. [44] showed that an increase in attenuation of 84 HU in the corticomedullary phase differentiates clear cell RCC from non–clear cell tumors with a sensitivity of 74% and a specificity of 100%. Herts et al. [45] showed that papillary tumors were more homogeneous and had a much lower tumor-to-parenchyma enhancement ratio than was present in nonpapillary subtypes, particularly with tumors smaller than 3 cm in diameter (Figs. 4C and 4D). Chromophobe tumors also are less hypervascular than clear cell tumors and tend to have a more peripheral pattern of enhancement; however, their appearance is not sufficiently characteristic to allow them to be reliably differentiated from papillary lesions (Figs. 4E and 4F). Oncocytomas cannot be reliably differentiated from RCC by imaging and thus are also considered to be surgical lesions. The

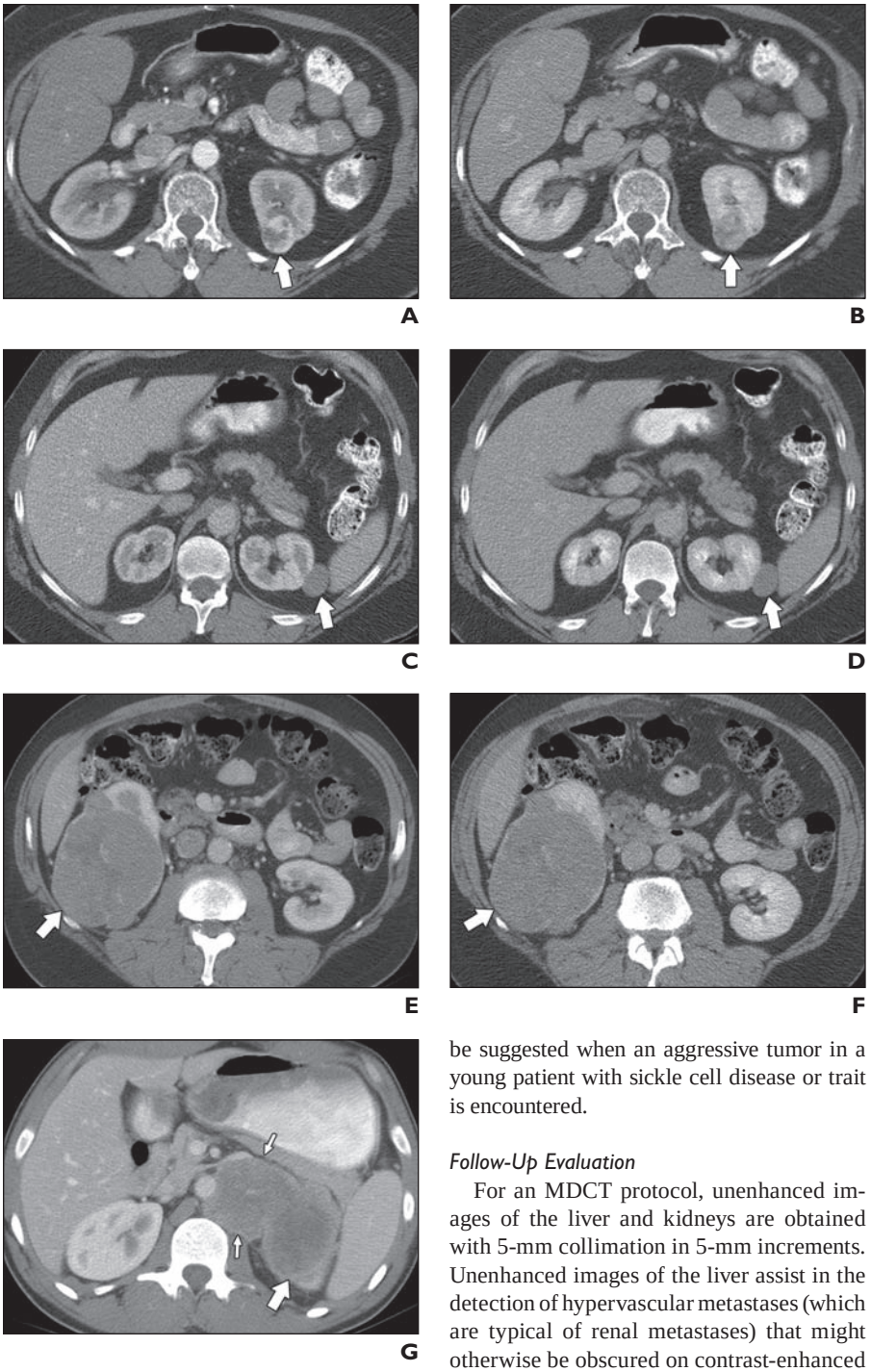


Fig. 4—CT appearances of various cell types of renal cell carcinoma (RCC).
A and **B,** Conventional clear cell RCC in 59-year-old woman. CT scans of TNM stage T1a tumor in corticomedullary and nephrogenic phases show typical hypervascularity of tumor (*arrow,* **A**) and subsequent washout (*arrow,* **B**).
C and **D,** Papillary RCC in 48-year-old man. CT scans of TNM stage T1a tumor in corticomedullary (**C**) and nephrogenic (**D**) phases show typical hypovascularity of tumor (*arrow*).
E and **F,** Chromophobe RCC in 61-year-old man. CT scans of TNM stage T2 tumor in corticomedullary (**E**) and nephrogenic (**F**) phases show hypovascularity of tumor (*arrow*).
G, Medullary RCC (*large arrow*) and adjacent paraaortic adenopathy (*small arrows*) in 36-year-old man. CT shows TNM stage T1b N1 tumor.

well-known prominent central scar that can be used to suggest the diagnosis of oncocytoma may also be present in necrotic clear cell tumors. Medullary RCC tumors are located centrally in the kidney and show variable, typically limited, contrast enhancement (Fig. 4G). They cannot be reliably distinguished from other RCCs or urothelial tumors but may be suggested when an aggressive tumor in a young patient with sickle cell disease or trait is encountered.

Follow-Up Evaluation

For an MDCT protocol, unenhanced images of the liver and kidneys are obtained with 5-mm collimation in 5-mm increments. Unenhanced images of the liver assist in the detection of hypervascular metastases (which are typical of renal metastases) that might otherwise be obscured on contrast-enhanced images. IV contrast-enhanced images of the abdomen and pelvis are obtained 70–80 seconds after the beginning of the IV infusion, acquired at 5-mm slice thickness, and reconstructed at 2.5-mm intervals. Late arterial phase images can assist in identifying hypervascular liver metastases. Delayed excretory phase images are obtained at approximately 180 seconds.

MRI Evaluation

MRI is generally only used when optimal CT cannot be performed, as in the case of a severe allergy to iodinated contrast medium or pregnancy. MRI has similar reported overall staging accuracies to those of CT [46]. Its multiplanar capability, however, is particularly useful for delineating the superior extent of tumor in the IVC [2, 14, 17].

We use coronal and axial conventional T1-weighted (TR/TE, 600/60) and axial dual-echo fast spin-echo T2-weighted (6,000/first-echo TE, 136; second-echo TE, 68) fat-suppressed images of the abdomen. Images are supplemented by dynamic contrast-enhanced 3D fast spoiled gradient-recalled echo sequences (FSPGR) to further delineate the primary tumor and liver lesions and to evaluate any vascular thrombus identified. In particular, tumor, rather than bland, thrombus is indicated by the presence of enhancing vessels in the thrombus. Multiple dynamic acquisitions can be used to obtain arterial, nephrogenic, and pyelographic-like images [47–50]. MDCT with 3D reformations and MRI have similar overall staging accuracies for RCC [51].

Sonographic Evaluation

Sonography can be useful for assessing the presence and extent of venous thrombus. It can also be helpful in distinguishing cysts from hypovascular solid tumors seen on CT (e.g., papillary RCC). Sonography can reveal the septations better because of complex interfaces to the ultrasound beam. Sonography has reported accuracies for T staging of 77–85% [52, 53] and for detection of venous thrombus of 87% [54]. However, it has limitations in visualizing the retroperitoneum and perinephric tissues [54, 55], although some proponents argue otherwise [53]. Intraoperative sonography has been effectively

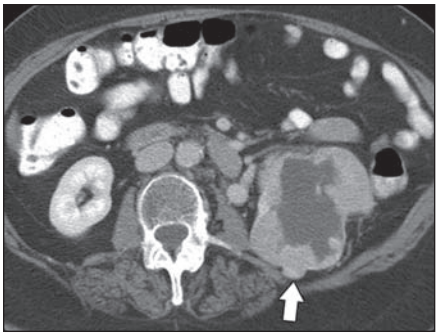


Fig. 5—Tumor involvement of perinephric fat in 72-year-old woman. CT scan shows tumor with associated perinephric nodularity (*arrow*). TNM stage T3a disease was confirmed on resection specimen.

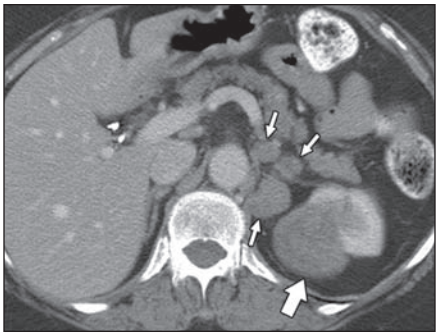


Fig. 6—Metastases to regional lymph node (TNM stage N2) in 81-year-old woman. CT scan shows enlarged left paraaortic node (*small arrows*) and adjacent stage T1b papillary renal cell carcinoma (*large arrow*).

used in patients undergoing nephron-sparing surgery to identify multifocal lesions and intrarenal tumor anatomy [56, 57].

Percutaneous Biopsy

Preoperative percutaneous biopsy of the renal lesion is generally not undertaken because the results usually do not affect what therapy will be recommended except in patients with multiple tumors or occasionally in patients with an underlying predisposing condition. Percutaneous biopsies may be considered in selected cases—for example, when an abscess or metastatic disease from a known primary tumor is suspected, especially from lymphoma or melanoma [10, 17]. Percutaneous biopsy is also generally performed in patients who will undergo ablative or thermal therapy to determine the underlying histologic subtype of the tumor.

Angiography

Approximately 20% of patients have multiple renal arteries, and many surgeons find preoperative CT or MR angiograms to be valuable, particularly when partial nephrectomy or laparoscopic approaches are planned. Three-dimensional and multiplanar reformatted images, as well as angiographic displays, aid appreciation of the relationships of the tumor to the collecting system, adjacent normal parenchyma, and vascular supply [10, 37, 38, 57].

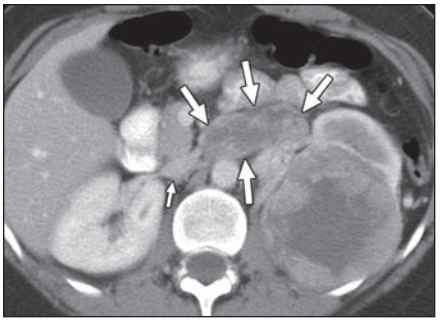
PET

The efficacy of PET in renal malignancy remains under investigation. It shows some potential in staging, the detection of unsuspected metastases, follow-up, and the evaluation of indeterminate renal masses [7, 58–61].

Recommendations for Preoperative Imaging

Patients must be adequately staged in order to plan appropriate management options. Abdominal CT and MRI are the mainstay of staging the primary tumor and of evaluating the possibility of locoregional nodal or abdominal visceral metastases, such as to the adrenal glands, liver, pancreas, and contralateral kidney. Delineation of vascular anatomy and evaluation of venous thrombosis, best provided by a multiphasic evaluation as discussed previously, are helpful when surgery is being contemplated. CT or MRI can be used, depending on local preferences and patient factors.

Controversies exist as to whether, and how best, to evaluate for the possibility of intrathoracic metastases. A stage-directed strategy is probably reasonable: For small primary tumors (T1), in which the risk of metastatic disease is small, simple chest radiography is probably satisfactory. For stage T2 or higher primary tumors, chest CT should probably be performed. Screening for bone or brain metastases is probably required only when there are suggestive symptoms.



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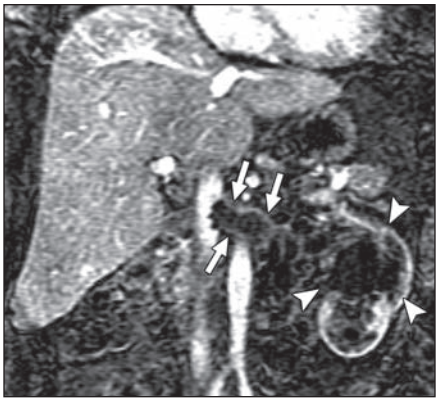

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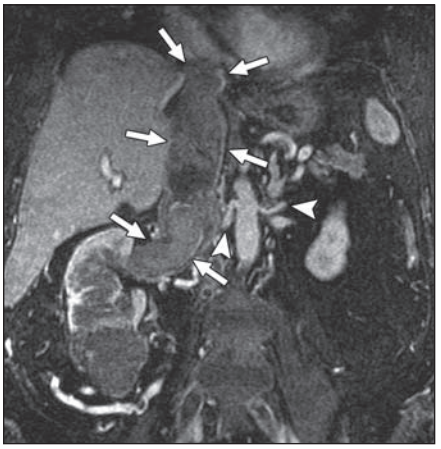

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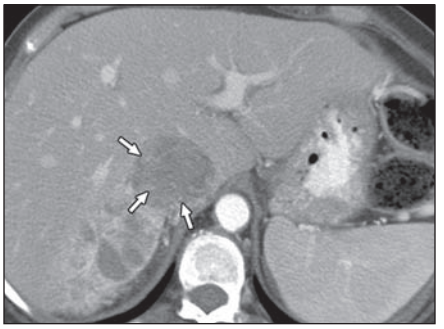


D

Fig. 7—Venous involvement of renal vein and inferior vena cava (IVC).
A, CT scan in 45-year-old woman shows enhancing tumor thrombus in expanded left renal vein (*large arrows*) (TNM stage T3b) and IVC (*small arrow*).
B, Thrombus in left renal vein extends to origin of renal vein at IVC on coronal contrast-enhanced MR image (*arrows*) (TNM stage T3b) in 68-year-old woman. Arrowheads indicate left renal tumor.
C, Thrombus in expanded right renal vein extends to supradiaphragmatic IVC on coronal contrast-enhanced MR image (*arrows*) (TNM stage T3c) in 82-year-old woman. Note aorta and renal artery origins are also visible (*arrowheads*).
D, "Salt-and-pepper" appearance of vascularized tumor thrombus (*arrows*) in expanded IVC on CT scan in 61-year-old woman.

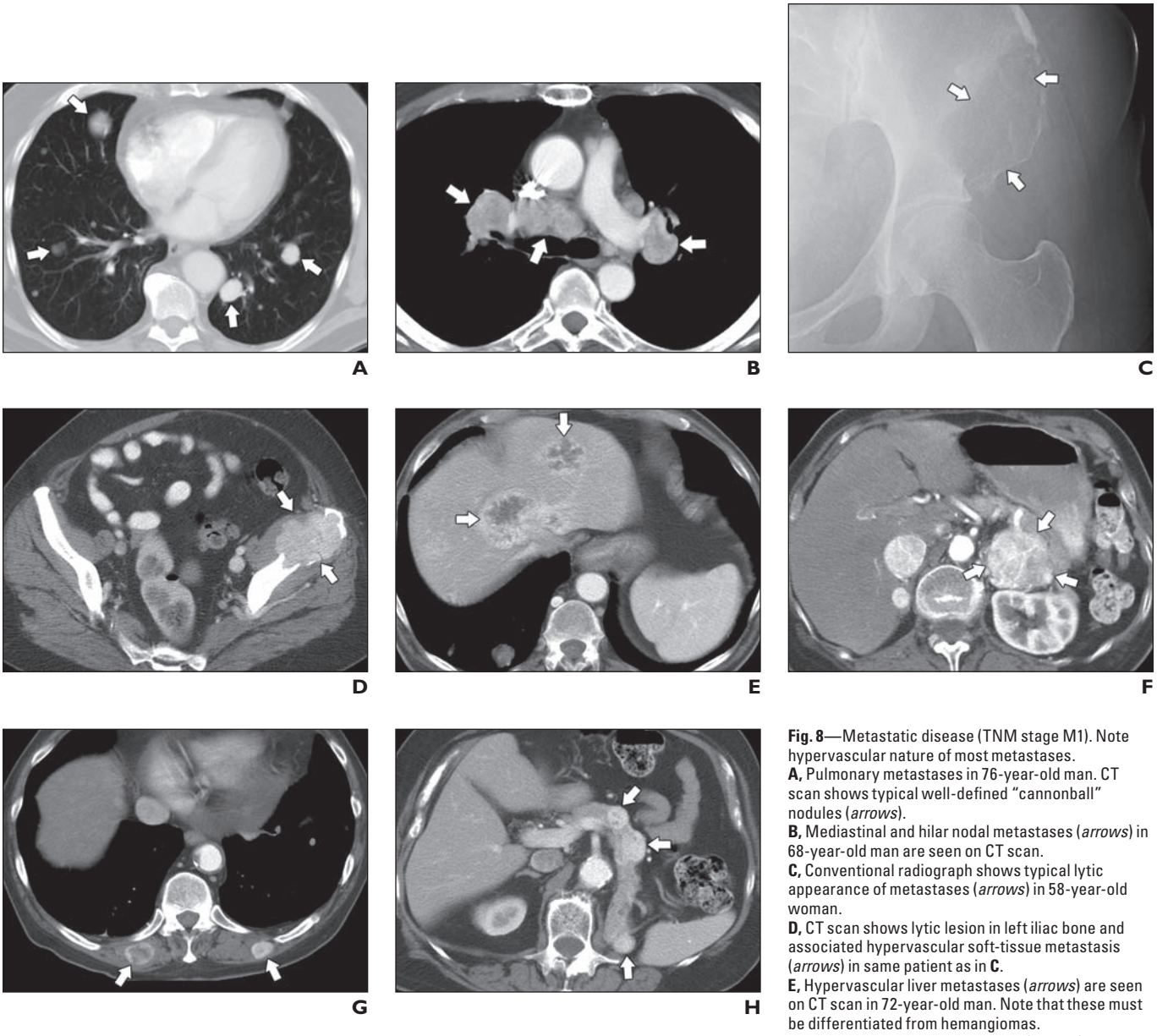


Fig. 8—Metastatic disease (TNM stage M1). Note hypervascular nature of most metastases.
A, Pulmonary metastases in 76-year-old man. CT scan shows typical well-defined "cannonball" nodules (*arrows*).
B, Mediastinal and hilar nodal metastases (*arrows*) in 68-year-old man are seen on CT scan.
C, Conventional radiograph shows typical lytic appearance of metastases (*arrows*) in 58-year-old woman.
D, CT scan shows lytic lesion in left iliac bone and associated hypervascular soft-tissue metastasis (*arrows*) in same patient as in **C**.
E, Hypervascular liver metastases (*arrows*) are seen on CT scan in 72-year-old man. Note that these must be differentiated from hemangiomas.
F, Metastases to left adrenal gland (*arrows*) in 76-year-old woman.
G, Metastases to skeletal muscle (*arrows*) in 64-year-old man.
H, Metastases to pancreas (*arrows*) in 76-year-old man.

Therapeutic Options and Implications for Radiologic Follow-Up

Surgical resection is the only effective means of cure for clinically localized renal tumors [10, 62]. Classically, this involves total nephrectomy, but more recently, partial or "nephron-sparing" nephrectomy has been shown to be equally effective in selected groups. The indications for partial nephrectomy include a tumor < 4 cm, peripheral location, absence of the contralateral kidney, bilateral renal tumors, and renal insufficiency. Another consideration is whether there is a risk of future impairment of renal function from another condition or a risk of bilateral renal tumors (e.g., patients with von Hippel-Lindau disease in whom future surgeries may be required).

Radical Nephrectomy

Total nephrectomies are typically undertaken via a retroperitoneal posterolateral approach [10]. It is "radical" when it classically includes excision of the perirenal fat, including the ipsilateral adrenal gland, and a lymph node dissection. The dissection involves the region from the diaphragmatic crus to the aortic bifurcation of the ipsilateral—and possibly the contralateral—aspects of the IVC or the aorta [7]. The sensitivity, specificity, and accuracy for the detection of perinephric extension of disease by high-resolution CT have been reported to be 96%, 93%, and 95%, respectively [63] (Fig. 5). Surgical management is not directly affected by the presence of perinephric extension of disease because a radical nephrectomy includes en bloc removal of all the contents of Gerota's fascia.

Ipsilateral adrenalectomy is included in the classic radical nephrectomy. However, ipsilateral adrenal metastases occur in only 1–10% of patients. It occurs especially in large left-sided upper pole tumors, usually

by direct extension (i.e., T3a tumors) [64]. One of the roles of imaging is to assist in allowing adrenal-sparing nephrectomies in order to reduce the risk of future adrenal insufficiency [7].

Surgery, although substantially more challenging, is not necessarily excluded in the presence of contiguous organ invasion, which typically involves the liver, diaphragm, psoas muscles, pancreas, and bowel (Robson stage IVA, or TNM T4 disease). Both CT and MRI may have difficulty in distinguishing abutment of tumor from invasion of adjacent organs.

Partial (Nephron-Sparing) Nephrectomy

Partial nephrectomy is a relatively new technique. When evaluating this possibility, the relationship of the tumor to the rest of the kidney and, in particular, to the arterial supply to the tumor and the remainder of the kidney, is important. Nephron-sparing surgery has been shown to be equally as efficacious as total nephrectomy, with reported local recurrence rates of < 2% [10] and 5-year survival rates of 87–90%, which are comparable to those from radical nephrectomy [57]. However, in the case of a solitary kidney, a risk of developing proteinuria, focal segmental glomerulosclerosis, and progressive renal failure exists if more than 50% of the renal mass is removed [57].

Both total and partial nephrectomies can be undertaken laparoscopically. Some surgeons supplement the laparoscopic approach with direct "hand assistance" in the operative field. Laparoscopic approaches reduce perioperative morbidity and length of the hospital stay. However, operation times are generally longer, and morcellation of the sample leads to difficulties in pathologic staging and introduces the risk of tumor seeding [10]. Cryoablation and radiofrequency ablation, which may be undertaken laparoscopically or percutaneously, are promising techniques for treating small tumors [30, 57, 65].

Nodal Status and Dissection

The presence of nodal metastases is an adverse prognostic factor [66, 67]. Using a cutoff of 1 cm for short-axis nodal size, sensitivity and specificity have been reported to be 83% and 88% [68] and overall accuracies have been reported to be 83–89% [68, 69] (Fig. 6). However, radiologic assessment of nodal status, in common with other tumors, has its limitations. Enlarged (> 1 cm) nodes are not necessarily metastatic but may be reactive—that is, false-positive (58% in one series by Studer et al. [70]—which may be more common in necrotic tumors or tumors that involve the renal vein. Conversely, small nodes may contain micrometastases—that is, false-negative metastases (4% in the series by Studer et al.).

It is reported that 3–22.5% of patients who undergo radical nephrectomy without clinically evident metastases have regional nodal involvement at surgery [67, 71]. In pathologic series, the prevalence of metastatic nodes in cases of occult RCC diagnosed only at autopsy is reported at 14% [72].

Accurate determination of nodal staging requires tissue; some surgeons therefore advocate routine retroperitoneal nodal dissection. However, the clinical value of this is controversial, in particular as to whether it affects survival, and surgeons vary in their approach [10, 26, 57, 67, 73].

Venous Involvement

Extension of tumor into the renal veins has been reported to occur in 20–35% of patients, and into the IVC, in 4–10% [74–76], the latter being infrahepatic (50%), intrahepatic (40%), or intraatrial (10%) [77] (Figs. 7A–7C). IVC thrombus is more common from right-sided tumors because of the shorter renal vein on the right [53, 76].

Identification of thrombus in the venous system, especially the IVC, is particularly important because it affects surgical management, typically necessitating an anterior abdominal approach. Furthermore, if thrombus extends into the heart, a combined thoracic and intracardiac approach with cardiac bypass may be required.

Current CT techniques have reported sensitivities and specificities for detecting renal vein thrombus of 85% and 98%, respectively [78]. Color Doppler sonography has reported sensitivities and specificities for detecting thrombus in the renal veins of 75% and 96%, respectively, with 100% accuracy for detection of thrombus in the IVC [54]. MRI has similar reported sensitivity and specificity for detecting thrombus in the renal vein of 86–94% and 75–100%, respectively, as well as 100% accuracy for detecting IVC thrombus [79, 80]. MRI, with its multiplanar capability, is probably the best technique for identifying the superior extent of IVC involvement [49, 81].

Fortunately, prognosis is not adversely affected by tumor in the venous system or by its

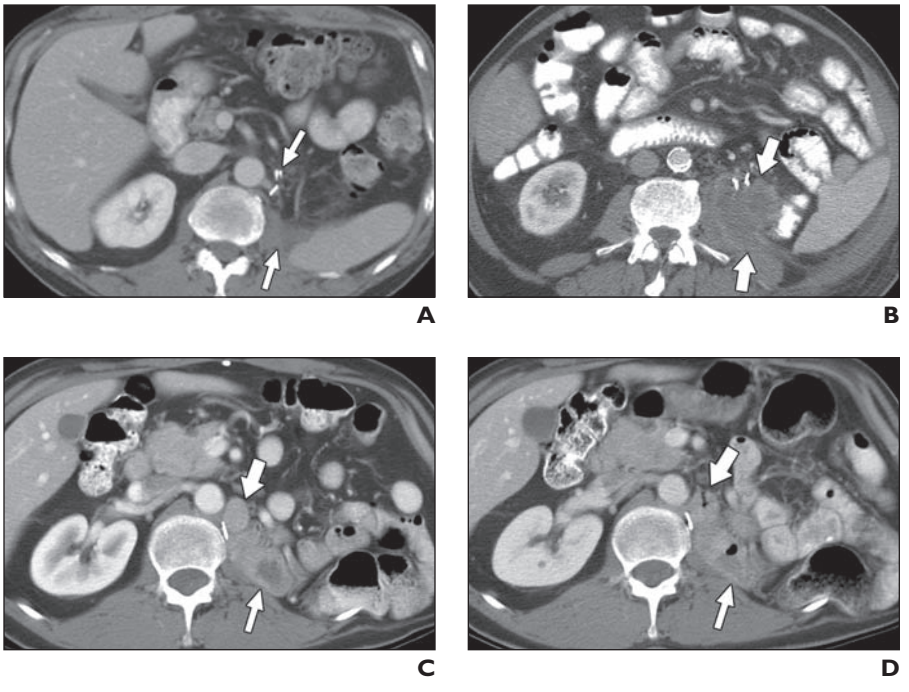


Fig. 9—Local recurrence after nephrectomy as seen on CT.
A, Postsurgical appearances in left nephrectomy bed (*lower arrow*) in 52-year-old man resolved at follow-up. Note associated surgical vascular clips (*upper arrow*).
B, Local tumor recurrence is seen in left nephrectomy bed (*arrows*) in same patient as in **A**.
C, Pitfall of unopacified small bowel is seen in left nephrectomy bed of 58-year-old man, which could be misinterpreted as adenopathy (*large arrow*) and local tumor recurrence (*small arrow*) without careful tracing of bowel.
D, Follow-up CT scan in same patient as in **C** shows gas in bowel loops (*large* and *small arrows*).

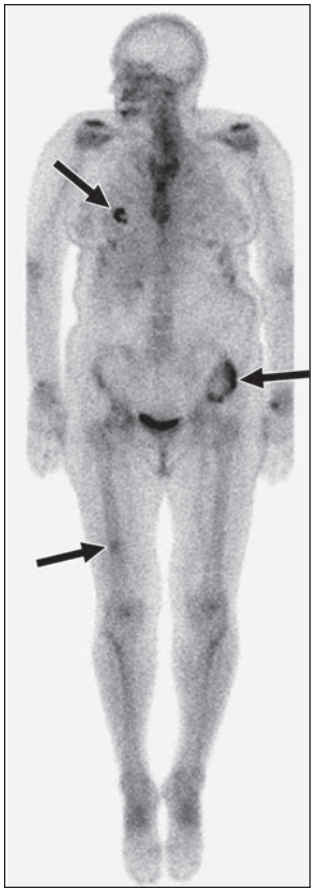


Fig. 10—Metastatic bone disease in same 58-year-old woman as in Figures 8C and 8D. Bone scintigram shows uptake in left iliac bone, right rib, and right femur (*arrows*).

level in the IVC, provided the tumor is free-floating and can be successfully removed (5-year survival rates of 50–69% in the absence of metastatic disease). However, prognosis is severely impaired if tumor invades the wall of the IVC (5-year survival rate, 25%), although this can improve if the involved IVC can be resected completely (5-year survival rate, 57%) [2, 66, 82]. Unfortunately, current imaging techniques have some limitations in distinguishing bland thrombus from tumor thrombus and in distinguishing invasive from noninvasive tumor with respect to the vessel wall [2]. Intravascular tissue that enhances after IV contrast administration or that contains neovascularization (the thread-and-streak sign) is good evidence of tumor thrombus rather than bland thrombus (Fig. 7D).

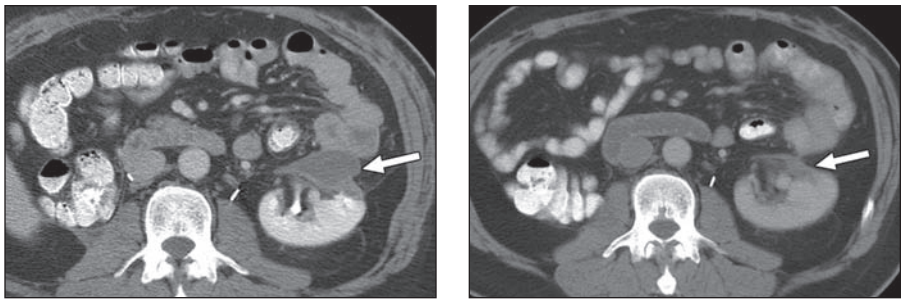
Metastatic Disease and Palliation

In the context of metastatic disease, a nephrectomy may still be indicated for symptomatic relief—for example, severe pain or hematuria; in a small number of cases (≈ 0.3%), regression of metastases has been reported after resection of the primary tumor. Cytoreductive nephrectomy has been shown to offer a survival benefit in selected patients with metastatic disease [83]. Preoperative embolization can provide symptomatic relief and reduce intraoperative bleeding in large tumors. Also, resection is sometimes performed to obtain material needed in immunotherapy. Radiation therapy is sometimes used for palliation—for example, pain from bone metastases.

TABLE 4: Stage-Specific Postoperative Imaging Surveillance After Radical Nephrectomy for Localized Renal Cell Carcinoma

Stage	Chest Radiography	Abdominal CT
T1	Yearly	
T2	Every 3 and 6 months, then every 6 months for 3 years, then annually	2 and 5 years
T3	3 and 6 months, then every 6 months for 3 years, then annually	2 and 5 years

Note—Adapted from Levy et al. [95].



A **B**

Fig. 11—CT appearances after partial nephrectomy in 55-year-old man.
A, CT scan obtained 6 weeks after left partial nephrectomy shows low-density lesion (*arrow*) at surgical site that could be confused with mass lesion.
B, Six months after partial nephrectomy, note resolution of postoperative changes (*arrow*). Also note previous right nephrectomy.

Immunotherapy and Targeted Therapies

The mainstay of systemic therapy for metastatic RCC has historically been immunotherapy (or cytokine therapy) with interleukin-2 (IL-2) and interferon-α (IFN-α). High-dose IL-2 has consistently produced a 15–20% response rate, 6–8% complete remission rate, and approximately 5% cure rate [84, 85]; however, it is a fairly toxic regimen. IFN-α has provided modest survival benefit, has a more favorable toxicity profile, and is more easily administered than IL-2. As a result, IFN-α has been adopted as the control arm in many clinical trials of novel agents.

Novel therapies for metastatic RCC have targeted the consequences of von Hippel-Lindau (*VHL*) gene inactivation and the resulting upregulation of hypoxia-inducible factor (*HIF*) target genes, notably vascular endothelial growth factor (*VEGF*) and platelet-derived growth factor (*PDGF*). Four targeted agents are presently in clinical use for metastatic RCC: sunitinib, sorafenib, temsirolimus, and bevacizumab. Sunitinib (Sutent, Pfizer), a multityrosine kinase inhibitor (MKI), has shown an objective response rate (ORR) of 31% and a median progression-free survival of 11 months for sunitinib-treated patients [86, 87]. It is considered the standard-of-care treatment for patients with advanced, good- and intermediate-risk, conventional clear cell RCC. Sorafenib (Nexavar, Bayer HealthCare), another MKI, is considered second-line therapy after cytokine failure [88]. Temsirolimus (Torisel, Wyeth), an inhibitor of mammalian target of rapamycin (mTOR), is considered the standard of care for patients with poor-risk metastatic RCC, irrespective of histology [89, 90]. Bevacizumab (Avastin, Genentech), a humanized antibody to *VEGF*, has shown promise in patients with good- and intermediate-risk metastatic RCC [91] but has not yet been approved for metastatic RCC by the U.S. Food and Drug Administration (FDA).

Postoperative Surveillance and Recurrent Disease

Local recurrence in the nephrectomy bed occurs in approximately 20–40% of patients, typically in the first 5 years after nephrectomy [17, 36]; the risks are highest when the resection margins are incomplete. Isolated recurrences

in the nephrectomy bed are uncommon (1.8%) [92], and resection is typically difficult [10] but in selected patients may improve survival.

Chae et al. [93] analyzed the patterns of recurrence in 194 patients with RCC who had undergone complete resection. Tumor recurrence was found in 21% of the patients within a mean time of 17 months. Tumor recurrence occurred within 2 years in 83% of the patients. The recurrence rate was highest for those with an original tumor greater than 5 cm and, as expected, for those with a higher Fuhrman grade and higher stage at the time of presentation.

Metastasectomies are of uncertain value [10, 94] but may be efficacious in certain subgroups—for example, those with a solitary site of disease and a prior disease-free interval of greater than 1 year [26]. Resection of solitary metastases, typically to the lung, can result in 5-year survival of 25–60% [10].

The likelihood of developing metastases is directly related to tumor stage. In one series after radical nephrectomy, metastatic disease occurred in 7.1% of patients with stage T1 disease, 26.5% with stage T2, and 39.4% with stage T3 disease, with the chance of developing recurrent metastases greatest in the first three postoperative years [95]. Sites of metastatic disease include the lung (Figs. 8A and 8B), bone (Figs. 8C and 8D), liver (Fig. 8E), adrenal gland (Fig. 8F), skeletal muscle (Fig. 8G), and pancreas (Fig. 8H).

CT is the most sensitive imaging technique for follow-up in the abdomen. A meticulous technique is required; for example, unopacified small-bowel loops, which inevitably occupy the nephrectomy bed, can mimic local recurrence (Fig. 9). Sonography has not been found to be reliable in assessing the nephrectomy bed. During the surveillance period, it is recommended that evaluation of potential intrathoracic disease be undertaken by chest radiography, with chest CT, bone scanning (Fig. 10), and brain MRI reserved for patients with suspicious clinical symptoms, signs, and abnormal blood chemistries. A suggested stage-specific postoperative imaging surveillance protocol after radical nephrectomy for localized RCC is presented in Table 4, although some argue for more intensive surveillance [71].

The follow-up strategy after nephron-sparing surgery is similar, except that particular attention should be paid to the remnant kidney, where local recurrence rates are in the region of 4–6% (Fig. 11). These occur a maximum of 6–24 months after surgery in patients with stage T3 disease, and later than 48 months in stage T2 disease. Recurrences are most likely the result of undetected microscopic multifocal RCC in the remnant kidney [57]. In pathologic series, multifocality in primary tumors < 5 cm in size is 19% [96]. A suggested stage-specific postoperative imaging surveillance protocol after partial nephrectomy for localized RCC is presented in Table 5. Careful follow-up is also required for patients who have undergone ablation therapies (Fig. 12).

More specialized follow-up may be required for patients with end-stage renal disease, acquired cystic disease of the kidney, or von Hippel-Lindau disease [10]. One of the features of RCC is that it can have an unpredictable time course, with recurrence-free intervals of up to 30 years; prolonged periods of follow-up may therefore be needed [53].

TABLE 5: Stage-Specific Postoperative Imaging Surveillance After Partial Nephrectomy For Localized Renal Cell Carcinoma

Stage	Chest Radiography	Abdominal CT
T1		
T2	Yearly	Every 2 years
T3	Every 6 months for 3 years, then yearly	Every 6 months for 3 years, then yearly

Note—Adapted from Novick [57].

References

1. Jemal A, Siegel R, Ward E, Murray T, Xu J, Thun MJ. Cancer statistics, 2007. *CA Cancer J Clin* 2007; 57:43–66
2. Choyke Pl, Newhouse JH, Bluth EI, et al. ACR appropriateness criteria: renal cell carcinoma staging, 2002. American College of Radiology Website. www.acr.org. Accessed December 9, 2002
3. Luciani LG, Cestari R, Tallarigo C. Incidental renal cell carcinoma: age and stage characterization and clinical implications—study of 1092 patients (1982–1997). *Urology* 2000; 56:58–62
4. Jayson M, Sanders H. Increased incidence of serendipitously discovered renal cell carcinoma. *Urology* 1998; 51:203–205
5. Chow WH, Devesa SS, Warren JL, Fraumeni JF Jr. Rising incidence of renal cell cancer in the United States. *JAMA* 1999; 281:1628–1631
6. Katner HP, Baynham SA. Increasing incidence of renal cell cancer. *JAMA* 1999; 282:2119–2120; discussion 2121
7. Pantuck AJ, Zisman A, Belldegrun AS. The changing natural history of renal cell carcinoma. *J Urol* 2001; 166:1611–1623
8. Parkin DM, Pisani P, Ferlay J. Estimates of the worldwide incidence of 25 major cancers in 1990. *Int J Cancer* 1999; 80:827–841
9. Choyke PL, Amis ES Jr, Bigongiari LR, et al. Renal cell carcinoma staging. American College of Radiology. ACR appropriateness criteria. *Radiology* 2000; 215[suppl]:721–725
10. Russo P. Renal cell carcinoma: presentation, staging, and surgical treatment. *Semin Oncol* 2000;

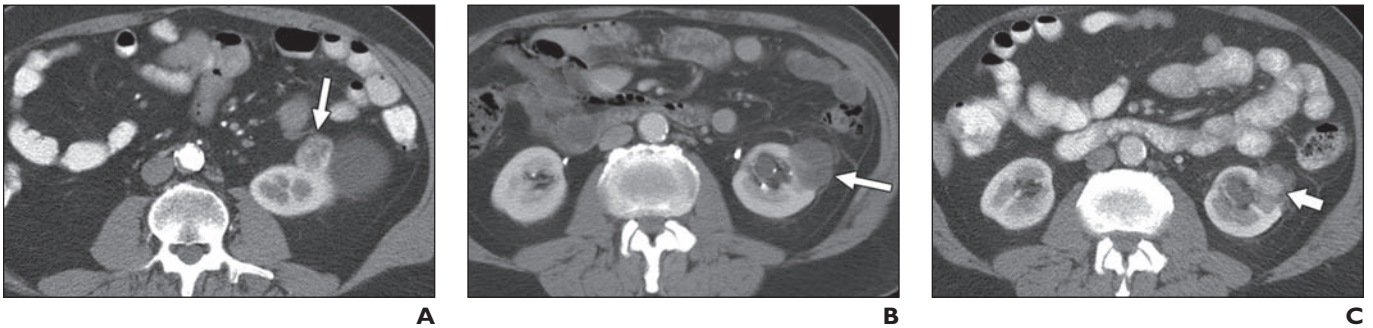


Fig. 12—Local recurrence after cryoablation as seen on CT of 61-year-old man.
A, Scan before ablation shows hypervascular tumor (*arrow*) adjacent to cyst.
B, Scan 2 months after ablation shows low-density lesion with minimal marginal enhancement, typical of postablation changes (*arrow*).
C, Local recurrence (*arrow*) is seen 18 months after ablation.

27:160–176
11. Bjornsson J, Short MP, Kwiatkowski DJ, Henske EP. Tuberous sclerosis-associated renal cell carcinoma: clinical, pathological, and genetic features. *Am J Pathol* 1996; 149:1201–1208
12. Levine E, Weigel JW, Collins DL. Diagnosis and management of asymptomatic renal cell carcinomas in von Hippel-Lindau syndrome. *Urology* 1983; 21:146–150
13. Figlin RA. Renal cell carcinoma: management of advanced disease. *J Urol* 1999; 161:381–386; discussion 386–387
14. Pretorius ES, Wickstrom ML, Siegelman ES. MR imaging of renal neoplasms. *Magn Reson Imaging Clin N Am* 2000; 8:813–836
15. Godley P, Kim SW. Renal cell carcinoma. *Curr Opin Oncol* 2002; 14:280–285
16. American Cancer Society. How is kidney cancer staged? 2007. American Cancer Society Website. www.cancer.org/docroot/CRI/content/CRI_2_4_3X_How_is_kidney_cancer_staged_22.asp?rnav=cri. Accessed October 16, 2007
17. Hilton S. Imaging of renal cell carcinoma. *Semin Oncol* 2000; 27:150–159
18. Parienty RA, Pradel J, Parienty I. Cystic renal cancers: CT characteristics. *Radiology* 1985; 157:741–744
19. Brinker DA, Amin MB, de Peralta-Venturina M, Reuter V, Chan DY, Epstein JI. Extensively necrotic cystic renal cell carcinoma: a clinicopathologic study with comparison to other cystic and necrotic renal cancers. *Am J Surg Pathol* 2000; 24:988–995
20. Kovacs G, Akhtar M, Beckwith BJ, et al. The Heidelberg classification of renal cell tumours. *J Pathol* 1997; 183:131–133
21. Shanks JH. Pathology of renal cell carcinoma: recent developments. *Clin Oncol (R Coll Radiol)* 1999; 11:263–268
22. Bostwick DG, Eble JN. Diagnosis and classification of renal cell carcinoma. *Urol Clin North Am* 1999; 26:627–635
23. Fuhrman SA, Lasky LC, Limas C. Prognostic significance of morphologic parameters in renal cell carcinoma. *Am J Surg Pathol* 1982; 6:655–663
24. American Joint Committee on Cancer. *AJCC cancer staging manual*. New York, NY: Springer-Verlag, 2002
25. Robson CJ. Staging of renal cell carcinoma. *Prog Clin Biol Res* 1982; 100:439–445
26. Rini BI, Vogelzang NJ. Prognostic factors in renal carcinoma. *Semin Oncol* 2000; 27:213–220
27. Crotty TB, Farrow GM, Lieber MM. Chromophobe cell renal carcinoma: clinicopathological features of 50 cases. *J Urol* 1995; 154:964–967
28. Beck SD, Patel MI, Snyder ME, et al. Effect of papillary and chromophobe cell type on disease-free survival after nephrectomy for renal cell carcinoma. *Ann Surg Oncol* 2004; 11:71–77
29. Delahunt B. Histopathologic prognostic indicators for renal cell carcinoma. *Semin Diagn Pathol* 1998; 15:68–76
30. Tsui KH, Shvarts O, Smith RB, Figlin RA, deKernion JB, Belldegrun A. Prognostic indicators for renal cell carcinoma: a multivariate analysis of 643 patients using the revised 1997 TNM staging criteria. *J Urol* 2000; 163:1090–1095; quiz 1295
31. Staudenherz A, Steiner B, Puig S, Kainberger F, Leitha T. Is there a diagnostic role for bone scanning of patients with a high pretest probability for metastatic renal cell carcinoma? *Cancer* 1999; 85:153–155
32. Zagoria RJ, Bechtold RE. The role of imaging in staging renal adenocarcinoma. *Semin Ultrasound CT MR* 1997; 18:91–99
33. Ng CS, Loyer EM, Iyer RB, David CL, DuBrow RA, Charnsangavej C. Metastases to the pancreas from renal cell carcinoma: findings on three-phase contrast-enhanced helical CT. *AJR* 1999; 172:1555–1559
34. Broome DR, Girguis MS, Baron PW, Cottrell AC, Kjellin I, Kirk GA. Gadodiamide-associated nephrogenic systemic fibrosis: why radiologists should be concerned. *AJR* 2007; 188:586–592
35. Choyke Pl, Amis ES, Bigongiari LR, et al. ACR appropriateness criteria: renal cell carcinoma staging, 1998. American College of Radiology Website: www.acr.org. Accessed December 9, 2002
36. Chin AI, Lam JS, Figlin RA, Belldegrun AS. Surveillance strategies for renal cell carcinoma patients following nephrectomy. *Rev Urol* 2006; 8: 1–7
37. Curry NS, Francis IR, Baumgarten DA, et al. ACR appropriateness criteria: renal cell carcinoma staging, 2007. American College of Radiology Website: www.acr.org. Accessed March 27, 2008
38. Fielding JR, Aliabadi N, Renshaw AA, Silverman SG. Staging of 119 patients with renal cell carcinoma: the yield and cost-effectiveness of pelvic CT. *AJR* 1999; 172:23–25
39. Sheth S, Scatarige JC, Horton KM, Corl FM, Fishman EK. Current concepts in the diagnosis and management of renal cell carcinoma: role of multidetector CT and three-dimensional CT. *RadioGraphics* 2001; 21[spec no]:S237–S254
40. Urban BA, Ratner LE, Fishman EK. Three-dimensional volume-rendered CT angiography of the renal arteries and veins: normal anatomy, variants, and clinical applications. *RadioGraphics* 2001; 21:373–386; questionnaire 549–555
41. Wunderlich H, Reichelt O, Schubert R, Zermann DH, Schubert J. Preoperative simulation of partial nephrectomy with three-dimensional computed tomography. *BJU Int* 2000; 86:777–781
42. Kopka L, Fischer U, Zoeller G, Schmidt C, Ringert RH, Grabbe E. Dual-phase helical CT of the kidney: value of the corticomedullary and nephrographic phase for evaluation of renal lesions and preoperative staging of renal cell carcinoma. *AJR* 1997; 169:1573–1578
43. Yuh BI, Cohan RH. Different phases of renal enhancement: role in detecting and characterizing renal masses during helical CT. *AJR* 1999; 173: 747–755
44. Kim JK, Kim TK, Ahn HJ, Kim CS, Kim KR, Cho KS. Differentiation of subtypes of renal cell carcinoma on helical CT scans. *AJR* 2002; 178: 1499–1506
45. Herts BR, Coll DM, Novick AC, et al. Enhancement characteristics of papillary renal neoplasms revealed on triphasic helical CT of the kidneys. *AJR* 2002; 178:367–372
46. Beer AJ, Dobritz M, Zantl N, Weirich G, Stollfuss J, Rummeny EJ. Comparison of 16-MDCT and MRI for characterization of kidney lesions. *AJR* 2006; 186:1639–1650
47. Choyke PL. Detection and staging of renal cancer. *Magn Reson Imaging Clin N Am* 1997; 5:29–47
48. Zhang J, Israel GM, Krinsky GA, Lee VS. Masses and pseudomasses of the kidney: imaging spectrum on MR. *J Comput Assist Tomogr* 2004; 28:588–595
49. Hallscheidt PJ, Fink C, Haferkamp A, et al. Preoperative staging of renal cell carcinoma with inferior vena cava thrombus using multidetector CT and MRI: prospective study with histopathological correlation. *J Comput Assist Tomogr* 2005; 29:64–68
50. Tuite DJ, Geoghegan T, McCauley G, Govender P, Browne RJ, Torreggiani WC. Three-dimensional gadolinium-enhanced magnetic resonance breath-hold FLASH imaging in the diagnosis and staging of renal cell carcinoma. *Clin Radiol* 2006; 61: 23–30
51. Hallscheidt PJ, Bock M, Riedasch G, et al. Diagnostic accuracy of staging renal cell carcinomas using multidetector-row computed tomography and magnetic resonance imaging: a prospective study with histopathologic correlation. *J Comput Assist Tomogr* 2004; 28:333–339
52. Frohmuller HG, Grups JW, Heller V. Comparative value of ultrasonography, computerized tomography, angiography and excretory urography in the staging of renal cell carcinoma. *J Urol* 1987; 138:482–484
53. Bos SD, Mensink HJ. Can duplex Doppler ultrasound replace computerized tomography in staging patients with renal cell carcinoma? *Scand J Urol Nephrol* 1998; 32:87–91
54. Habboub HK, Abu-Yousef MM, Williams RD, See WA, Schweiger GD. Accuracy of color Doppler sonography in assessing venous thrombus extension in renal cell carcinoma. *AJR* 1997; 168: 267–271
55. Fritzsche PJ, Millar C. Multimodality approach to staging renal cell carcinoma. *Urol Radiol* 1992; 14:3–7
56. Campbell SC, Fichtner J, Novick AC, et al. Intraoperative evaluation of renal cell carcinoma: a prospective study of the role of ultrasonography and histopathological frozen sections. *J Urol* 1996; 155:1191–1195
57. Novick AC. Advances in the management of local-

ized renal cell cancer. *Can J Urol* 2000; 7: 960–966
58. Montravers F, Grahek D, Kerrou K, et al. Evaluation of FDG uptake by renal malignancies (primary tumor or metastases) using a coincidence detection gamma camera. *J Nucl Med* 2000; 41:78–84
59. Ramdave S, Thomas GW, Berlangieri SU, et al. Clinical role of F-18 fluorodeoxyglucose positron emission tomography for detection and management of renal cell carcinoma. *J Urol* 2001; 166:825–830
60. Shvarts O, Han KR, Seltzer M, Pantuck AJ, Belldegrun AS. Positron emission tomography in urologic oncology. *Cancer Control* 2002; 9:335–342
61. Majhail NS, Urbain JL, Albani JM, et al. F-18 fluorodeoxyglucose positron emission tomography in the evaluation of distant metastases from renal cell carcinoma. *J Clin Oncol* 2003; 21:3995– 4000
62. Marshall FF, Stewart AK, Menck HR. The National Cancer Data Base: report on kidney cancers. The American College of Surgeons Commission on Cancer and the American Cancer Society. *Cancer* 1997; 80:2167–2174
63. Catalano C, Fraioli F, Laghi A, et al. High-resolution multidetector CT in the preoperative evaluation of patients with renal cell carcinoma. *AJR* 2003; 180:1271–1277
64. Sandock DS, Seftel AD, Resnick MI. Adrenal metastases from renal cell carcinoma: role of ipsilateral adrenalectomy and definition of stage. *Urology* 1997; 49:28–31
65. Hafron J, Kaouk JH. Ablative techniques for the management of kidney cancer. *Nat Clin Pract Urol* 2007; 4:261–269
66. Giberti C, Oneto F, Martorana G, Rovida S, Carmignani G. Radical nephrectomy for renal cell carcinoma: long-term results and prognostic factors on a series of 328 cases. *Eur Urol* 1997; 31: 40–48
67. Blom JH, van Poppel H, Marechal JM, et al.; EORTC Genitourinary Group. Radical nephrectomy with and without lymph node dissection: preliminary results of the EORTC randomized phase III protocol 30881. *Eur Urol* 1999; 36:570–575
68. Johnson CD, Dunnick NR, Cohan RH, Illescas FF. Renal adenocarcinoma: CT staging of 100 tumors. *AJR* 1987; 148:59–63
69. Fein AB, Lee JK, Balfe DM, et al. Diagnosis and staging of renal cell carcinoma: a comparison of MR imaging and CT. *AJR* 1987; 148:749–753
70. Studer UE, Scherz S, Scheidegger J, et al. Enlargement of regional lymph nodes in renal cell carcinoma is often not due to metastases. *J Urol* 1990; 144:243–245
71. Saidi JA, Newhouse JH, Sawczuk IS. Radiologic follow-up of patients with T1-3a,b,c or T4N+M0 renal cell carcinoma after radical nephrectomy. *Urology* 1998; 52:1000–1003
72. Johnsen JA, Hellsten S. Lymphatogenous spread of renal cell carcinoma: an autopsy study. *J Urol* 1997; 157:450–453
73. Schafhauser W, Ebert A, Brod J, Petsch S, Schrott KM. Lymph node involvement in renal cell carcinoma and survival chance by systematic lymphadenectomy. *Anticancer Res* 1999; 19:1573–1578
74. Kearney GP, Waters WB, Klein LA, Richie JP, Gittes RF. Results of inferior vena cava resection for renal cell carcinoma. *J Urol* 1981; 125:769– 773
75. Davits RJ, Blom JH, Schroder FH. Surgical management of renal carcinoma with extensive involvement of the vena cava and right atrium. *Br J Urol* 1992; 70:591–593
76. Kallman DA, King BF, Hattery RR, et al. Renal vein and inferior vena cava tumor thrombus in renal cell carcinoma: CT, US, MRI and venacavography. *J Comput Assist Tomogr* 1992; 16:240–247
77. Oto A, Herts BR, Remer EM, Novick AC. Inferior vena cava tumor thrombus in renal cell carcinoma: staging by MR imaging and impact on surgical treatment. *AJR* 1998; 171:1619–1624
78. Welch TJ, LeRoy AJ. Helical and electron beam CT scanning in the evaluation of renal vein involvement in patients with renal cell carcinoma. *J Comput Assist Tomogr* 1997; 21:467–471
79. Hricak H, Thoeni RF, Carroll PR, Demas BE, Marotti M, Tanagho EA. Detection and staging of renal neoplasms: a reassessment of MR imaging. *Radiology* 1988; 166:643–649
80. Roubidoux MA, Dunnick NR, Sostman HD, Leder RA. Renal carcinoma: detection of venous extension with gradient-echo MR imaging. *Radiology* 1992; 182:269–272
81. Goldfarb DA, Novick AC, Lorig R, et al. Magnetic resonance imaging for assessment of vena caval tumor thrombi: a comparative study with venacavography and computerized tomography scanning. *J Urol* 1990; 144:1100–1103; discussion 1103–1104
82. Hatcher PA, Anderson EE, Paulson DF, Carson CC, Robertson JE. Surgical management and prognosis of renal cell carcinoma invading the vena cava. *J Urol* 1991;145:20–23; discussion 23–24
83. Kassouf W, Sanchez-Ortiz R, Tamboli P, et al. Cytoreductive nephrectomy for T4NxM1 renal cell carcinoma: the M. D. Anderson Cancer Center experience. *Urology* 2007; 69:835–838
84. Yang JC, Sherry RM, Steinberg SM, et al. Randomized study of high-dose and low-dose interleukin-2 in patients with metastatic renal cancer. *J Clin Oncol* 2003; 21:3127–3132
85. McDermott DF, Regan MM, Clark JI, et al. Randomized phase III trial of high-dose interleukin-2 versus subcutaneous interleukin-2 and interferon in patients with metastatic renal cell carcinoma. *J Clin Oncol* 2005; 23:133–141
86. Motzer RJ, Hutson TE, Tomczak P, et al. Sunitinib versus interferon-alfa in metastatic renal-cell carcinoma. *N Engl J Med* 2007; 356:115–124
87. Motzer RJ, Figlin RA, Hutson TE, et al. Sunitinib versus interferon-alfa (IFN-α) as first-line treatment of metastatic renal cell carcinoma (mRCC): updated results and analysis of prognostic factors. *J Clin Oncol* 2007; 25[meeting abstracts suppl]:5024
88. Escudier B, Eisen T, Stadler WM, et al. Sorafenib in advanced clear-cell renal-cell carcinoma. *N Engl J Med* 2007; 356:125–134
89. Hudes G, Carducci M, Tomczak P, et al. Temsirolimus, interferon-alfa, or both for advanced renal-cell carcinoma. *N Engl J Med* 2007; 356:2271– 2281
90. Dutcher JP, Szczylik C, Tannir N, et al. Correlation of survival with tumor histology, age, and prognostic risk group for previously untreated patients with advanced renal cell carcinoma (adv RCC) receiving temsirolimus (TEMSR) or interferon-alpha (IFN). *J Clin Oncol* 2007; 25[meeting abstracts suppl]:5033
91. Escudier B, Koralewski P, Pluzanska A, et al. A randomized, controlled, double-blind phase III study (AVOREN) of bevacizumab/interferon-{alpha}2a vs placebo/interferon-{alpha}2a as first-line therapy in metastatic renal cell carcinoma. *J Clin Oncol* 2007; 25[meeting abstracts suppl]:3
92. Itano NB, Blute ML, Spotts B, Zincke H. Outcome of isolated renal cell carcinoma fossa recurrence after nephrectomy. *J Urol* 2000; 164:322– 325
93. Chae EJ, Kim JK, Kim SH, Bae SJ, Cho KS. Renal cell carcinoma: analysis of postoperative recurrence patterns. *Radiology* 2005; 234:189–196
94. Sella A, Swanson DA, Ro JY, et al. Surgery following response to interferon-alpha-based therapy for residual renal cell carcinoma. *J Urol* 1993; 149:19–21; discussion 21–22
95. Levy DA, Slaton JW, Swanson DA, Dinney CP. Stage-specific guidelines for surveillance after radical nephrectomy for local renal cell carcinoma. *J Urol* 1998; 159:1163–1167
96. Baltaci S, Orhan D, Soyupek S, Beduk Y, Tulunay O, Gogus O. Influence of tumor stage, size, grade, vascular involvement, histological cell type and histological pattern on multifocality of renal cell carcinoma. *J Urol* 2000; 164:36–39

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