CT/MRI in staging renal cell carcinoma

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Abstract

Renal cell carcinoma (RCC) is the eighth most common malignancy. It accounts for approximately 3% of newly diagnosed cancers and has been reported to occur in 11 out of 100,000 individuals. The incidence of RCC has increased by 40% in the USA from 1974 to 1990. There appears to be a true increase in the incidence of RCC over and above that attributable to the increased number detected by abdominal cross-sectional imaging. This increase has been accompanied by improved 5-year survival as the tumors detected by imaging are diagnosed at an earlier stage when they are still resectable. The male to female ratio is approximately 2:1; the majority present in the fifth to seventh decade of life and the racial distribution is equal. The majority of cases occur sporadically, but predisposing factors can sometimes be identified. RCC occurs in about 36% of patients with von Hippel–Lindau disease and invasive RCC is three to six times more common among long-term dialysis patients than in the general population.

Staging classifications

Two systems of clinical staging are in common use: the Robson classification (Table 1) and the TNM classification of the International Union Against Cancer (UICC) (Table 2). There is an approximate correlation between these two systems as shown in Table 3.

Most urological surgeons continue to refer to Robson’s classification, which is essentially a surgical staging approach. This system includes the important staging variables that have survived scrutiny over the years. Confinement within the renal capsule, penetration into the perirenal fat, invasion into the renal vein and lymph node metastases are all important in determining the prognosis (Table 3).

The TNM system uses the general principles employed for the staging of all tumors and its proponents argue that it is more specific and more detailed, but acknowledge that it is more complicated than the Robson system.

| Stage | Characteristics |
|-------|-----------------|
| I     | Tumor confined within capsule |
| II    | Extracapsular spread to perinephric fat but confined to Gerota’s fascia |
| III   | Tumor involvement of renal vein, IVC or regional lymph nodes |
| IV    | Invasion of adjacent organs or distant metastases |

Staging and prognosis

A clear relationship exists between survival and the macroscopic extent of tumor spread. Opinions differ regarding the value of tumor size for predicting survival. The overwhelming evidence is that tumor size alone is ineffective as an indicator of prognosis in the absence of involved nodes or metastatic disease and without local invasion of perirenal fat or other structures.
However, a clear relationship exists between tumor size and the development of metastases and because of this, the suggestion of a poorer prognosis for larger tumors is corroborated by several studies. Spread to the retroperitoneal nodes or beyond the renal fascia markedly reduces patients’ survival. The importance of venous invasion is more controversial. Some patients with venous invasion, but without lymph node involvement, may survive as long as patients with tumors confined to the kidney, but more recently it has been shown unequivocally that venous invasion reduces survival time.

### Table 2 Staging RCC: Robson’s classification vs. TNM system

| Robson | Disease extent | TNM   |
|--------|----------------|-------|
| I      | Tumor confined to kidney (small, intrarenal) | T1    |
|        | Tumor confined to kidney (large) | T2    |
| II     | Tumor spread to perinephric fat but within Gerota’s fascia | T3a   |
| IIIA   | Tumor spread to renal vein or cava | T3b   |
| IIIB   | Tumor spread to local lymph nodes | N1-N2 |
| IIIC   | Tumor spread to local vessels and lymph nodes | T3b, N1-N2 |
| IVA    | Tumor spread to adjacent organs (excluding ipsilateral adrenal) | T4    |
| IVB    | Distant metastasis | M1    |

### Table 3 Survival and anatomical extent of renal cell cancer

| Anatomical extent of tumors | Survival (%) | 5-year | 10-year |
|-----------------------------|--------------|--------|---------|
| Within renal capsule        |              | 65     | 56      |
| Renal vein (RV) alone       |              | 55     | 49      |
| RV + perinephric fat        |              | 50     | 33      |
| RV + regional nodes         |              | 0      | 0       |
| Perinephric fat alone       |              | 47     | 20      |
| Regional nodes alone        |              | 33     | 17      |
| Invading nearby structures  |              | 0      | 0       |

There appears to be a difference between mobile, non-obstructive vena caval tumor thrombus and intracaval tumor thrombus with direct wall invasion. Patients with mobile tumors have a median survival of 9.9 years, whereas in those with unresectable venous wall involvement, the median survival is only 1.2 years.

Metastases are a strong indicator of poor patient survival. Common sites of metastases include the lungs, the bones, central nervous system (CNS) and adrenal glands. In general, patients with distant metastases have 5-year survival rates of 5–10% and 10-year survival rates of less than 5%.

### Staging and surgery

Early work by Robson et al. showed that survival rates are significantly improved by radical nephrectomy compared with simple or partial nephrectomy and since then ‘radical’ nephrectomy has been the preferred method of treatment for RCC. Since the perinephric fat and Gerota’s fascia are routinely resected during radical nephrectomy, accurate differentiation between Stage I and Stage II (T1 vs. T3a) has not been essential. More recently, however, less aggressive surgery has been advocated for some patients with low-grade, non-invasive tumors, especially in the presence of a solitary kidney or if the tumors are multiple. Current data indicate that for low-grade, low-stage RCC, 4 cm or smaller, conservative nephron-sparing surgery (either partial nephrectomy or tumor enucleation) gives an outcome comparable to that of radical nephrectomy. For these patients the distinction between Stage I and Stage II is important. Furthermore, the diagnosis of Stage II disease (T3a) carries some prognostic significance. Stage II disease includes spread, either direct or hematogenous, to the ipsilateral adrenal, so identification of disease within the adrenal gland is extremely important when partial nephrectomy is being considered. About 6% of patients with RCC have ipsilateral adrenal involvement, the risk being higher for tumors replacing the entire kidney and for upper pole left-sided tumors.

Resection of ipsilateral and aortocaval lymph nodes is recommended by some surgeons, but there is little evidence that it improves survival, and it is not universally performed. Nevertheless, it is important to detect lymph node involvement preoperatively, since it usually occurs at the same time as blood-borne spread and carries a poor prognosis. Local lymph node involvement may be an ineffective barrier to tumor spread, as the incidence of distant metastases is 50% higher in patients with infiltrated lymph nodes.

Venous extension has been reported to occur in 20% of patients with RCC at presentation and involvement of the inferior vena cava (IVC) in 5–10%. These figures are probably too high for the large number of small tumors currently incidentally detected by imaging. In one series of over 400 patients there was no renal vein involvement in tumors less than 2.5 cm in diameter. Nonetheless, accurate assessment of the venous extension of RCC is essential for planning the proper surgical approach. Tumor extension into the renal vein only can be dealt with by routine ligation of the renal vein to prevent embolization. Extension into the IVC necessitates a midline abdominal incision for adequate access to the IVC so that it can be cleared. Delineating the upper margin of the tumor extent is very important. Forty percent of tumor thrombi are intrahepatic and whether or not the tumor extends above the hepatic veins is vital information, since this necessitates a thoracic surgical approach. For the 5–10% of tumors with caval involvement which extend into the right
atrium, cardiopulmonary bypass is necessary to remove the whole tumor thrombus.

Detection of all metastatic sites is important because the role of radical nephrectomy in patients with metastatic RCC is limited. Nephrectomy improves survival if metastases are to one organ only, particularly bone. The incidence of regression of multiple metastases following nephrectomy is extremely low (0.3%) and the mortality significantly greater. Thus, in patients with multiple metastases, treatment is usually palliative. Patients with solitary metastases which can be completely excised may have a reasonable 5-year survival of 25–35%. The majority of these patients have pulmonary metastases only.

**Imaging in staging**

Interpretation of any imaging used to stage RCC must include evaluation of:

- Tumor size.
- Tumor interface with the renal parenchyma.
- Perinephric tumor extension.
- Local and regional lymph node enlargement.
- The presence and extent of venous invasion.
- Spread into contiguous organs.
- Involvement of the adrenal glands.
- Local or distant metastatic spread.

Over the past decade, computed tomography (CT) has become the most widely used imaging technique for the diagnosis and staging of RCC. Increasingly, magnetic resonance imaging (MRI) is proving to be a valuable method for staging and seems to be at least as accurate as CT. Ultrasonography is also used to stage RCC but in a relatively high proportion of cases, overlying bowel gas precludes adequate visualization of the renal vessels, the infrahepatic IVC and the retroperitoneum.

**CT**

The overall accuracy of spiral CT in staging RCC ranges between 72 and 90%.

**Technique**

With helical and multidetector CT, the choice of the optimal protocol to maximize the sensitivity of detection, characterization and staging of RCC is important. Scans at 25–70 s after contrast medium show cortical but not medullary enhancement (corticomedullary phase) and scans at 100–120 s show homogeneous renal parenchymal enhancement (nephrogram phase). Scans at 3–5 min after contrast medium show pelvicalyceal filling (excretory phase). Both corticomedullary and nephrogram phase images should be obtained for optimal detection of renal parenchymal masses. For mass characterization also, the nephrogram phase is more sensitive than the corticomedullary phase, but characterization is optimal when both are used. A few renal cell cancers enhance very early, but some do not enhance fully until the nephrogram phase. Data on the best enhanced phase for staging RCC are more limited. In the one published series of 90 tumors, staging accuracy was 91% using unenhanced, corticomedullary and nephrogram phases, but was less when plain plus corticomedullary phase or plain plus nephrogram phases were used (81 and 86%, respectively). Using biphasic scans through the liver after contrast medium increases the detection of liver metastases from RCC. Advances in multidetector CT also permit sophisticated 3D techniques to be used and these are discussed in the section on nephron-sparing surgery.

Our own technique for detection, characterization and staging of renal masses is to obtain an unenhanced scan using 5 mm collimation, and then to give 100–150 ml of non-ionic contrast medium (300 mg I/ml) at 2–3 ml/s. Scans at 5 mm collimation are obtained from below upwards through the kidneys at 40–50 s (when filling of the renal veins is optimal). A further series of scans at 5 mm intervals is then obtained through the liver and kidneys scanning from above downwards at 90–100 s.

**Perinephric spread (Stage I vs. Stage II)**

On CT, Robson’s Stage I (T1-T2) tumors are defined as being entirely within the kidney with an intact renal capsule. The adjacent perinephric fat and renal fascia appear normal. Stage II tumors (T3a) are diagnosed when there is extension of tumor into the perinephric space. The most specific sign of spread is the presence of a discrete mass measuring at least 1 cm in diameter within the perinephric space. Although the specificity of this finding is 98% for Stage II (T3a) tumor spread, its sensitivity is only 46% because this finding is absent in the majority of patients with perinephric extension. Renal capsular invasion is difficult to diagnose unless the tumor obviously extends into the perinephric space. Recognized signs on CT include:

- An indistinct tumor margin.
- Blurring of the renal outline.
- Thickening of the perirenal fascia.
- Strands of soft tissue spreading into the perinephric fat resulting in ‘webs’ or ‘wispy’ densities.

False-positive diagnoses occur and in up to 50% of patients with Stage I (T1-T2) disease, there is perirenal stranding and fascial thickening without perinephric tumor spread caused by:

- Perinephric edema.
- Fat necrosis.
- Fibrosis from previous inflammation, stone disease, etc.
Renal cancers are responsible for about 60% of all cases of spontaneous renal and perirenal hemorrhage, and blood in the perirenal space may mask or simulate extracapsular extension. Unenhanced vascular collaterals may also simulate perinephric soft tissue nodules. Focal thickening of Gerota’s fascia contiguous with the tumor tends to be a more reliable indicator of invasion than generalized uniform thickening.

Until recently the sensitivity of CT for identifying Stage II (T3a) tumors has only been between 44 and 50% with a specificity of 90% when all the signs are present. Using multidetector CT and 1 mm collimation higher sensitivity (96%) for diagnosis of perinephric fat invasion has been reported.

**Venous invasion (Stage III)**

Evaluation of the venous system is the single most important function of imaging in staging RCC. It is critical both for the detection of venous invasion and for showing its extent. Spiral CT has a reported sensitivity of 85%, specificity of 98% and accuracy of 96% for detecting venous involvement by RCC.

On CT, the most important sign of venous tumor invasion is a persistent filling defect within the renal vein or IVC following intravenous contrast medium administration. No false-positive results for the diagnosis of tumor thrombus have been reported for this sign. Ipsilateral renal vein enlargement on CT without identifiable tumor thrombus is not a reliable sign of venous tumor extension. This sign is associated with a 65% false-positive rate and 90% false-negative rate for diagnosing tumor, partly because 78% of RCCs are hypervascular, causing increased flow with enlargement of the renal vein. Conversely, tumor thrombus does not necessarily cause enlargement of the veins.

Errors in the diagnosis of venous tumor extension on CT are relatively infrequent. On the right side, where the renal vein is short and straight, the diagnosis may be more difficult than on the left, where the vein is longer. Large, right-sided tumors can be associated with marked distension of the ipsilateral renal vein and vena cava making clear delineation of the IVC difficult. False-positive diagnoses can result from apparent filling defects caused by streaming of contrast medium, layering of flow, or rapid opacification of the renal veins while the lower extremity venous return remains unopacified. Spiral or multidetector CT with ‘biphasic’ imaging has greatly diminished these potential mistakes. Also, improved longitudinal reconstructions from axially acquired spiral CT images have largely overcome the previously encountered difficulty in visualizing the upper extent of tumor in the IVC. The cephalad extent of tumor related to the level of the hepatic veins is crucial for the planning of surgery and can now be shown with greater certainty.

The distinction between direct venous extension of malignancy and bland blood clot on CT is usually extremely difficult, and does not alter the patient’s management. The only reliable sign is neovascularity or enhancing tumor vessels within the thrombus, but this may be difficult to recognize. A less reliable distinction between the two can be made when bland thrombus is seen within the IVC, separate from a patent entry of the renal vein, and malignant thrombus is inferred because of direct continuity of the filling defect. Diagnosis of direct invasion of the wall of the IVC by malignant thrombus is also unreliable using CT.

**Lymph nodes**

The lymphatic drainage of the kidney is highly variable. Usually, there are collecting lymphatic vessels from an intrarenal plexus, with four or five trunks, which follow the renal veins and end in the ipsilateral para-aortic lymph nodes. Efferents from the lateral aortic nodes pass to the contralateral side to form the lumbar trunk, which terminates in the cisterna chyli. However, direct connections to the thoracic duct and mediastinum do exist, accounting for the uncommon finding of mediastinal and hilar lymph node involvement, particularly on the right side, at presentation.

Demonstration of lymph node involvement identifies disease as Robson Stage III or N1-N2 in the TNM system. As with all cross-sectional imaging techniques, detection of lymph node involvement on CT relies on detecting an increase in the size of the infiltrated nodes and the limitation of using size criteria for identifying lymphatic metastases in RCC is well recognized. False-positive rates as high as 43% have been reported caused by reactive hyperplasia and other benign conditions when 1 cm was used as the upper limit of normal. Primary tumor necrosis or thrombus within the IVC is associated with a higher rate of reactive lymphadenopathy with a resultant increase in false-positive results. However, lymph nodes larger than 2 cm are almost always involved by metastatic tumor. False-negative results caused by microscopic invasion of lymph nodes occur in only 4–5% of patients. The overall accuracy of lymph node staging by CT in RCC is reported to be between 83 and 89%.

When considered overall, and taking into account detection of lymph node infiltration and venous invasion, the sensitivity of CT in distinguishing between Robson’s Stage I and III is 88–95%, and the specificity is 99–100%.

**Stage IV disease (T4); M1**

The diagnosis of Stage IV disease can be achieved accurately with CT. Direct tumor invasion of adjacent muscles, including the diaphragm, psoas, quadratus lumborum, or erector spinae muscles, is well shown. Disease in the contralateral kidney or adrenal is well delineated, as well as invasion of the liver, colon, pancreas or spleen. Loss of fat planes between the tumor
sequences have several advantages. They can replace T1-weighted spin-echo sequences for imaging the liver and the in- and out-of-phase images detect any intracellular lipid within renal or adrenal masses.

Axial fat-suppressed respiratory-triggered FSE T2-weighted images are then acquired through the same area. The fat suppression increases the conspicuity of the kidneys by reducing both the chemical shift artifact and the dynamic range of abdominal signal intensities.

Gadolinium-enhanced sequences are performed as a 2-dimensional (2D) or 3-dimensional (3D) study. Irrespective of whether 2D or 3D imaging is chosen, we prefer the study to be performed in a coronal plane. For imaging renal neoplasms this has the advantage of allowing assessment of both kidneys, the renal arteries, the entire IVC, and the spine in a relatively small number of slices. For 2D imaging, breathhold fat-saturated T1 GRE images are acquired before and during an intravenous injection of 20 ml gadolinium. Postcontrast axial sequences are then acquired to evaluate the renal parenchyma in the corticomедullary and nephrographic phases (30 and 90 s). Later sequences are also acquired to visualize the IVC optimally. We now perform the postcontrast examination using a 3D study which is of particular value for evaluating the IVC and if required also provides reliable, accurate images of the renal parenchyma. As with the 2D examination, a breathhold precontrast set of images is acquired with the arms elevated to reduce phase-wrap. A low flip angle (30°) is applied using an enhanced fast gradient-recalled echo 3D (EFGRE 3D) sequence. The low flip angle improves soft tissue contrast. Twenty-eight sections are obtained in the coronal plane before the administration of contrast medium. The image volume includes the renal kidney and the IVC. The total breathhold required is usually 22–30 s and the sequences are repeated three times with a 5 s delay between repetitions.

**Extension into the perirenal space**

MRI has the same limitations as CT in identifying early extension into the perinephric space. Although MRI appears slightly more sensitive than CT, it is equally non-specific for distinguishing between Robson’s Stage I and II disease (T1-T2 vs. T3a). Thus, tumor extension into the perinephric space is suggested by strands of low signal intensity on T1-weighted images and intermediate signal intensity on T2-weighted images. Detection of perinephric invasion, or its absence, can be improved by using fat-suppressed contrast-enhanced images, with enhancement of previously low signal intensity areas in the perinephric tissue indicating extrarenal tumor extension. In small tumors, as with CT, the negative predictive value for invasion of the perinephric fat has been reported to be high, but inability to detect microscopic extension into the perinephric space reduces the sensitivity to 60–70%. As with CT, the specificity of MR is substantially higher at 94%.

**CT/MRI in staging renal cell carcinoma**

CT is an ideal method for detecting distant metastases (M1). Adrenal metastases may be the only evidence of Stage IV disease. CT has a very high sensitivity for the detection of ipsilateral adrenal involvement by RCC but lower specificity (100 and 76%, respectively). Occasionally confusion may arise between adrenal metastases and benign incidental adrenal cortical adenomas. RCC may also be associated with pheochromocytomas as part of the von Hippel–Lindau syndrome. A synchronous tumor occurs in the contralateral kidney in about 2% of cases, but multifocal lesions in the same kidney occur more frequently. CT is also a sensitive technique for the detection of hemogenous spread to the liver and lung. Liver metastases tend to be vascular and enhance after intravenous injection of contrast medium.

Invasion of the IVC may result in the appearance of the Budd-Chiari syndrome, which causes confusion when checking for metastases. The lung is the most common site of metastases from RCC with metastases to the lungs demonstrated in 50–60% of cases at autopsy. The incidence of lung metastases is substantially higher in patients with extensive abdominal disease, especially with IVC involvement, than in those with limited renal disease. Accurate staging of lung disease is of great importance, as complete resection of a solitary pulmonary metastasis can increase the 5-year survival rate from 32 to 56%. Spiral CT is the most sensitive technique for the detection of focal lung lesions, including lung metastases, and is indicated for full staging of all patients in whom surgery is planned.

The sensitivity and specificity for CT in the overall staging of Stage IV RCC are 98 and 99%, respectively.

**MRI**

MR protocols for evaluation of patients with renal cell cancer vary widely and have evolved in recent years with the development of surface coils, gradients and new pulse sequences. At our institution, all renal examinations are performed with a phased-array surface coil centered over the kidneys to increase the signal-to-noise ratio.

A coronal T2-weighted single shot fast-spin-echo (FSE) sequence is acquired initially as a localizer. From this a field of view is chosen and the remainder of the examination can be tailored from this.

T1-weighted gradient echo (GRE) sequences have now largely replaced T1-weighted spin-echo sequences. These are performed from the upper aspect of the liver to the lower margin of the kidneys at a slice thickness of 6 mm with 1 mm intervals between slices. The TE is altered when acquiring these T1-weighted GRE sequences to allow chemical shift in- and out-of-phase imaging. GRE sequences have several advantages. They can replace T1-weighted spin-echo sequences for imaging the liver and the in- and out-of-phase images detect any intracellular lipid within renal or adrenal masses.
A major advantage of MRI in staging RCC includes direct imaging in the sagittal and coronal planes, which is particularly helpful for showing the full extent of IVC tumor thrombus. The most important role of MRI is in assessing venous involvement.

Tumor thrombus in the renal vein and IVC can be suspected on T1-weighted spin-echo pulse sequences if the signal void of flowing blood is replaced by a relatively high signal produced by tumor thrombus. Tumor thrombi emit signals of intensity similar to that of the primary neoplasm on different pulse sequences. Occasionally, slow flow within a vessel causes confusion by emitting a signal that is misinterpreted as tumor thrombus. On time-of-flight GRE images, flowing blood has markedly increased signal intensity and appears white, whereas tumor thrombus has medium signal intensity and appears as a filling defect. Imaging in the sagittal and coronal planes is particularly helpful for assessing the superior extent of caval tumor thrombus in relation to the diaphragm, hepatic veins and right atrium. A coronal 2D or 3D contrast medium-enhanced GRE sequence centered on the renal vessels and IVC confirms the presence of thrombus. Administration of contrast medium may also allow the distinction between direct tumor extension and bland thrombus.

Conventional spin-echo sequences have a very high accuracy for detecting venous invasion. However, limited flip-angle GRE techniques facilitate the imaging of vascular structures and their use in RCC has allowed accuracies of 100% in assessing venal caval invasion, 88% for renal vein tumor thrombus and 80% for atrial invasion. Intravenous administration of gadopentate dimeguline may improve the accuracy further, particularly when combined with 3D magnetic resonance venography (MRV).

Whatever the technique used, MRI appears to be the best method for detecting venous involvement and defining its upper limit. The accuracy is extremely high, and negative predictive values for vascular invasion can be as high as 98 or 99%. MRI has been shown to be superior to CT for delineating the upper extent of the tumor thrombus in the IVC. However, most of these studies did not use multidetector or spiral CT and may underestimate the current performance of state-of-the-art CT. Detection of invasion of the IVC wall necessitates resection of the affected segment and subsequent vascular reconstruction. To date wall invasion has not been reliably detected by imaging but MRI does appear able to make this diagnosis. Breach of the wall allows definite diagnosis of invasion, and invasion may be suspected if there is thickening, altered signal and/or enhancement of the vessel wall. The most reliable signs of vessel wall invasion are a tumor signal on each side of the vessel wall and vessel wall enhancement.
where the contralateral kidney is threatened by other conditions affecting its function (such as stone disease, reflux nephropathy, renal artery disease, diabetes mellitus or glomerulonephritis) or in conditions where there is a hereditary increased risk of multiple RCC (e.g. von Hippel–Lindau disease, hereditary papillary RCC). Elective indications include small localized RCCs which are often detected incidentally or indeterminate cystic lesions considered to have malignant potential.

Imaging plays a major role in the selection and preoperative evaluation of patients for nephron-sparing surgery. The surgeon needs to know the position of the kidney, and of the tumor within the kidney, as well as information about the depth of renal parenchymal invasion, the relationship of the tumor to the pelvicalyceal system, and the detailed anatomy of the renal arteries and veins. All of this information can be satisfactorily provided by 3D volume-rendered CT. The largest published prospective series evaluated 97 masses in 60 patients. Precontrast images were obtained at 5 mm intervals with vascular phase images at 3 mm intervals and homogeneous parenchymal phase images at 5 mm intervals. The number and position of tumors were satisfactorily shown in all cases and 96% of surgically identified renal arteries and 93% of surgically identified renal veins were demonstrated. A smaller retrospective study of 41 lesions in 38 patients using contrast-enhanced MR indicated that this technique can also identify lesions suitable for partial nephrectomy.

Recurrent RCC

Twenty to 30% of patients with RCC that appear to be localized at the time of surgery relapse following radical nephrectomy. However, less than 5% have isolated local recurrence and in the majority of cases there are distant metastases. Data for recurrence following open, or laparoscopic, partial nephrectomy and partial renal ablation using radiofrequency or cryotherapy are not yet available.

The stage of the tumor at the time of presentation is the most important determinant of recurrent disease. The presence of lymph node involvement, a high Fuhrman grade on histology and the presence of a sarcomatoid (spindle cell) architecture also increase the risk of recurrence. Lymph node infiltration at surgery is a particular strong predictor of recurrent disease and, even if lymphadenectomy is performed, most tumors relapse with distant metastases. This is of great importance since up to 20% of patients who undergo radical nephrectomy for RCC without metastases detected by imaging have regional lymph node involvement at surgery.

The median time to relapse following nephrectomy is 15–18 months and 85% of relapses occur within 3 years. Tumors with involved nodes tend to recur earlier. Very late relapse, often solitary in the lung, bone, pancreas or skeletal muscle, can also occur. Lung metastases are the most frequent site of distant relapse accounting for 50–60%. These metastases may either be hemorrhagic, producing consolidation, or lymphatic. Mediastinal nodal infiltration may accompany the lung metastases. Bone metastases occur less frequently, are most commonly seen in the lumbar spine, thoracic spine and ribs, and are usually lytic. Less commonly, distant relapse occurs in the contralateral kidney, adrenal gland, or brain.

Unusually, distant relapse, either solitary or multiple, occurs in the pancreas and typically appears hypervascular on enhanced CT, unlike primary carcinoma of the pancreas, which is typically hypovascular. Pancreatic relapse may occur many years following nephrectomy.

Local recurrence produces an enhancing mass at the site of nephrectomy. Following radical nephrectomy normal structures, such as bowel, may simulate a recurrent mass. Distortion of the tail of the pancreas as it drops into the left renal fossa can be particularly confusing. Recurrences may infiltrate the adjacent quadratus lumborum and psoas muscle. The lymph nodes close to the renal vascular pedicle are the most frequently involved by recurrence. Direct invasion of the colon or small bowel can occur and when advanced can result in peritoneal carcinomatosis or mesenteric nodal disease.

The management of isolated local recurrence in the renal fossa remains controversial because of lack of evidence. In the past, locally recurrent tumors tended to be diagnosed late when patients were symptomatic and hence surgical treatment was often dangerous with significant morbidity and mortality. However, early detection by CT surveillance increases the diagnosis of small recurrences, making surgery feasible and less dangerous. Although the majority of patients eventually develop metastases, surgical treatment of isolated renal fossa recurrence seems to prolong survival.

It has been recommended that routine follow-up after radical nephrectomy for RCC should be stage-dependent, so that regular follow-up is carried out in patients operated on for locally advanced disease. Guidelines for follow-up also have to take into account the cost effectiveness of imaging. In recent years, encouraging results have been achieved using immunotherapy in patients with relapse with metastatic disease following nephrectomy, particularly with metastases located predominantly in the lung. Response rates as high as 30% have been reported. For these reasons, follow-up of patients after radical nephrectomy is advisable. Controversy surrounds the frequency of investigations and whether or not CT should be routinely used.

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