



## **DIAGNOSIS AND STAGING OF RENAL CELL CARCINOMA: RADIODIAGNOSIS**

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### **ABSTRACT**

The single most common renal malignancy in adults is renal cell carcinoma. Renal malignancy is less frequent in childhood and is most often Wilms' tumour . Radiodiagnosis play important role in diagnosing Renal cell carcinoma and its staging and classification.

**Keywords:** Renal cell carcinoma,abdominal x-ray(IVU), Ultrasonography,Computed tomography,Magnetic Resonance Imaging

## INTRODUCTION

Renal cell carcinoma (RCC) is the most common malignancy of the kidney and accounts for approximately 3% of adult cancers (1). RCC is more common in men than in women (ratio 2:1), and the median age at diagnosis is approximately 60 years. Although primarily a cancer of the proximal tubular epithelium (85%), RCC also includes nonepithelial kidney tumors, Wilms' tumor, and tumors of the renal pelvis (1, 2)

Annual estimates of the incidence for RCC indicate steady increases, with over a third of newly diagnosed patients presenting with advanced or metastatic disease (5-8). Surgical resection (including cytoreduction nephrectomy and/or metastasectomy) remains the most viable treatment option in patients regardless of the stage of disease at presentation (9-11). Despite recent advances in cancer therapy, the prognosis for patients with metastatic RCC remains dismal, with <5% overall 5-year survival. The role of systemic therapy in this setting has been studied; however, it has a limited effect on outcome and overall survival.

Based on morphologic, cytogenetic, and molecular criteria, there are five distinguishable types of RCC: clear cell (60%- 80%), papillary (7%-14%), chromophobe (4%-10%), oncocytic (2%-5%), and collecting duct carcinomas (1%-2%) (12, 13). A small percentage of patients have tumors of undefined cellular morphology. Several genetic mutations are associated with hereditary RCC (e.g., von Hippel-Lindau gene and *c-met* protooncogene). The sporadic forms of clear cell carcinoma likewise have a high frequency of *VHL* mutations or hypermethylation (6). The various tumor types have widely different disease courses; for example, genetic variants of papillary and collecting duct tumors are particularly aggressive cancers associated with short survival times (14), and eosinophilic variants of chromophobe tumors often have an indolent clinical course (15). Recent evidence suggests increased mortality (median survival of 9.4 months) in patients with non-clear-cell tumors, which tend to be resistant to chemotherapy and immunotherapy (2). Sarcomatoid tumors are high-grade transformants within each tumor type that carry a particularly poor prognosis for survival (16).

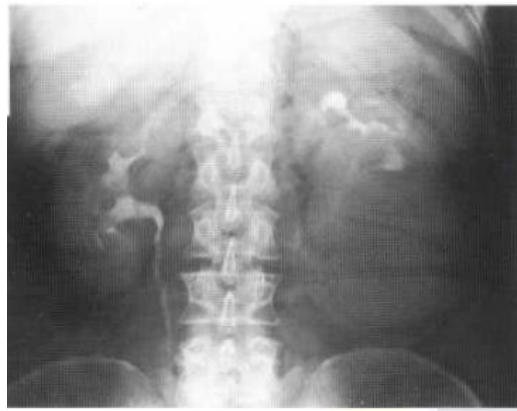
RCC is classified first according to disease stage and then according to disease grade. Stage of disease, defined using the TNM classification, differentiates size of primary tumor (T0-T4), lymph node involvement (N0-N2), and extent of metastasis into the vena cava and other tissues (M0-M1) (17). Tumor (nuclear) grade (G1-G4) reflects the differentiation of tumor cells as defined microscopically by increased nuclear size, irregularity, and nucleolar prominence (18). Nuclear grade is highly predictive of the development of metastatic disease.

**Renal cell carcinoma** Renal cell carcinoma accounts for approximately 85% of adult renal malignancies, with a male to female predominance of approximately 2.5:1. It represents 3% of new cancer diagnoses and has an

incidence of 11/100 000, which appears to be rising. Median age of onset is 55 years but occasional cases may be encountered in young adults and children. Renal cell carcinoma usually originates from the proximal convoluted tubule within the cortex, although less common histological variants, such as the papillary cystadenocarcinoma, originate from further distally within the nephron. There is an increased incidence of renal cell carcinoma in Von Hippel-Lindau disease and long-term renal dialysis. Advanced renal cell carcinoma has a wide variety of symptoms, usually related to metastases and/or tumour bulk (loin mass, malaise, anorexia, pyrexia of unknown origin). More commonly they present as haematuria or as an incidental mass on CT or ultrasound of the abdomen for some other condition. Renal cell carcinoma may metastasise to bone, brain, lung, liver and soft tissues. It is not rare to see an apparently solitary metastasis from a renal cell carcinoma, especially to bone or soft tissue, and they are characteristically expansile, vascular and (in the case of bone) osteolytic. Sometimes the metastatic disease is the presenting symptom. There have been improvements in chemotherapy of disseminated renal cell carcinoma, particularly with the use of interferon, and a simple examination to assess the kidneys (usually ultrasound) is justified in patients with metastatic disease of unknown origin. Occasionally tumours produce an erythropoietin-like substance and present as polycythaemia or one of its complications. On rare occasions they present as spontaneous perinephric haemorrhage.

### **Radiological Investigation:**

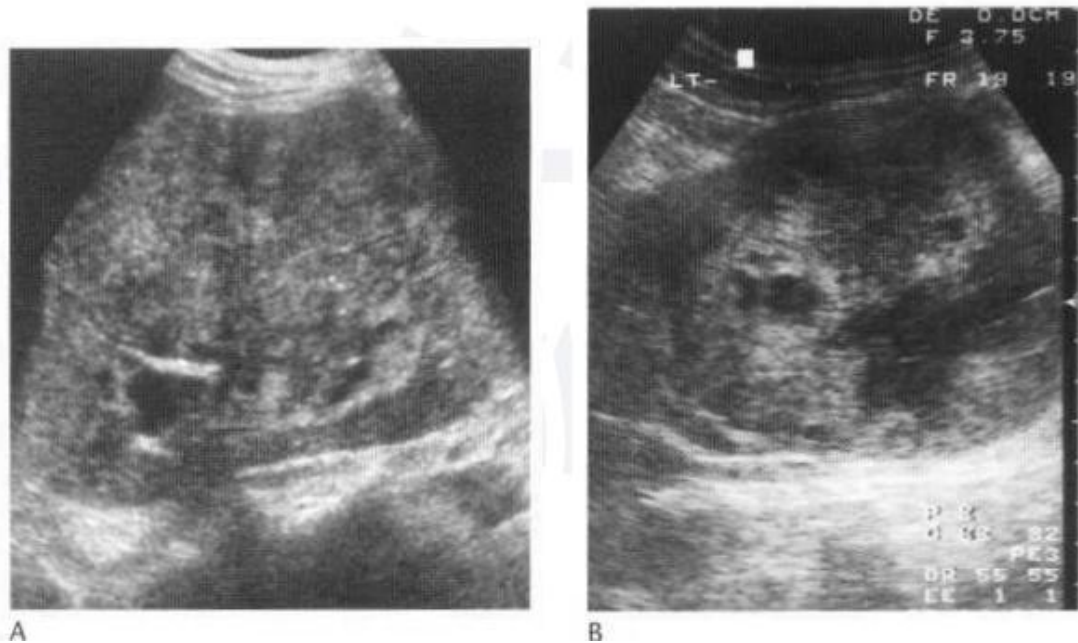
The IVU is the traditional modality used to investigate haematuria. Large tumours may be visible as a soft-tissue mass on the preliminary plain films. Up to 10% of renal cell carcinoma show some calcification on plain films. Similarly, if calcification is seen in association with a renal mass then it is most likely to represent a renal cell carcinoma, especially if the calcification is dense, central and amorphous. Following contrast injection renal cell carcinoma is usually detected as a mass which displaces the adjacent calyces and distorts the renal outline (Fig. 1).



**Figure 1:** Renal cell carcinoma on IVU. The tumour appears as a large, left lower pole mass distorting the adjacent pelvicalyceal system.

Occasionally the appearances are of a mass with loss of renal function if the tumour has occluded the renal vein. Renal cell carcinoma usually shows similar enhancement to normal renal tissue on the nephrogram but a minority of tumours are poorly vascular and therefore have an appearance similar to simple cysts and require further investigation, usually with ultrasound to confirm their nature. One-third of tumours less than 3 cm diameter are not seen in IVU and therefore, even if this investigation is normal, further investigation with ultrasound should be considered, especially if haematuria persists.

Noma usually appears as a solitary mass bulging from the outline. It is usually iso- or hypocochoic compared to normal kidney but around 10% may be hyperechoic, especially if small. Some show some heterogeneity, although small lesions may not. Areas of hyperechogenicity with acoustic shadowing may be seen if macroscopic calcific foci are present (Fig. 2).



**Figure 2:** Renal cell carcinoma on ultrasound. Two examples, one appearing as a solid mass of intermediate echogenicity replacing the normal renal architecture (A) and the other similar apart from substantial central necrosis (B)

On CT and MRI the features are of a soft-tissue mass that is at least partly solid, often lobulated and associated with loss of the normal renal architecture in the area affected. Generally, smaller tumours appear more homogeneous and well defined, becoming more heterogeneous, containing more substantial areas of necrosis and becoming less well defined as they enlarge. On CT they are usually isodense or hypodense compared to normal renal tissue, occasionally hyperdense. They enhance variably with intravenous

contrast but almost always less than normal renal tissue (Fig. 3).



**Figure 3:** Renal cell carcinoma on CT appearing as a heterogeneously enhancing mass associated with destruction of the normal renal architecture

Around a third have detectable areas of calcification. On MRI they appear of intermediate signal on the T1-weighted sequence, high signal on STIR and variable but often intermediate to high on T2-weighted sequences. In 10-15% of cases the tumour is predominantly cystic but evidence of malignant tissue is still usually apparent in the form of enhancing soft-tissue areas within the walls of the lesion. Occasionally renal cell carcinoma is predominantly infiltrating,

Showing obliteration of normal renal architecture on ultrasound, MRI and CT with little mass effect. The important differential diagnosis in these cases is infiltrative transitional cell carcinoma involving renal parenchyma, which is treated with nephroureterectomy. Radiological clues to this condition are obliteration of renal sinus fat and tumour within the pelvicalyceal system. Once the diagnosis has been made the tumour should be staged. Two formal systems are available. The Robson classification (Box 30.1) and the TNM classification of the International Union

**Box 30.1 Staging of renal cell carcinoma-Robson classification**

Stage I	Limited by the renal capsule
Stage II	Tumour has breached the renal capsule (perirenal involvement) but is limited by Gerota's fascia
Stage IIIa	Tumour invasion into renal vein or inferior vena cava
IIIb	Tumour involvement of regional lymph nodes
IIIc	Venous and lymph node invasion
Stage IV	Invasion of adjacent viscera or distant metastases

*Primary tumour (T)*

TX	Primary tumour cannot be assessed
T0	No evidence of primary tumour
T1	Tumour limited to the kidney; 7.0 cm or less in maximum diameter
T2	Tumour limited to the kidney; above 7.0 cm in maximum diameter
T3a	Tumour extends into perinephric tissue (including the adrenal gland) but remains confined by Gerota's fascia
Tab	Tumour extends into the renal vein or inferior vena cava below the diaphragm
T3c	Tumour extends into the inferior vena cava above the diaphragm
T4	Tumour invades beyond Gerota's fascia

*Nodal status (N)*

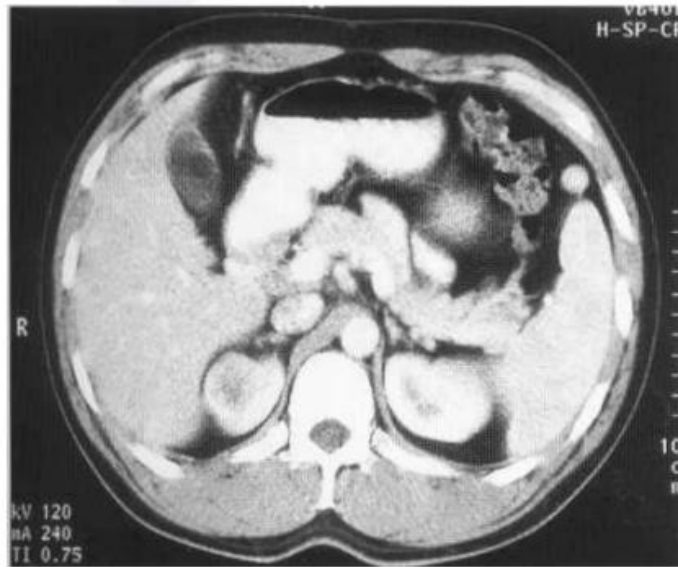
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis in a single regional lymph node
N2	Metastasis in more than one regional lymph node

*Distant metastasis (M)*

MX	Distant metastases cannot be assessed
M0	No distant metastases
m1	Distant metastases

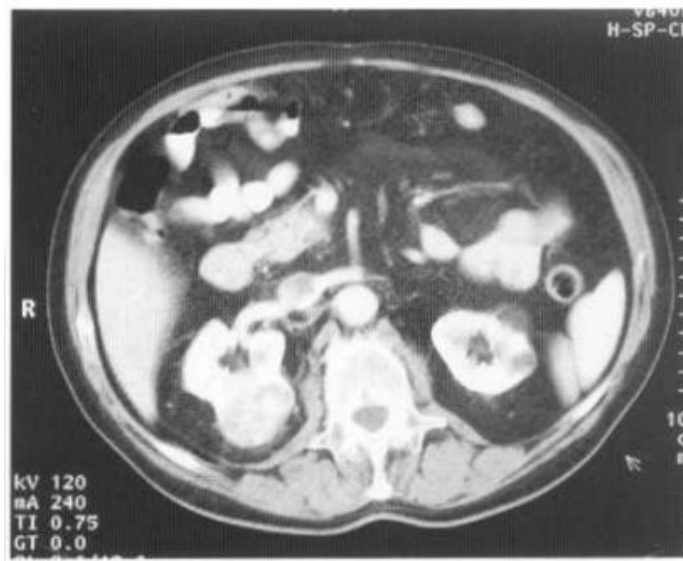
Against Cancer (Box 30.2). The TNM classification is detailed and incorporates the general principles of tumour staging found throughout the TNM system. The Robson classification is the one most commonly used routinely. Its advantages are its simplicity and good correlation with prognosis as well as indicating specific problems the surgeon may encounter. Ultrasound is very often performed as part of the diagnostic process for renal cell carcinoma, and initial staging is undertaken. However, the accuracy of ultrasound staging is inferior to that of CT and MRI, which are usually indicated for definitive preoperative staging. Both CT and MRI are over 90% accurate for most aspects of staging except the differentiation between stage I and stage II.

The error rate for this is of the order of 50%. Tumours that are confined by the renal capsule (stage 1) should show a normal peri nephric space (Fig. 4).



**Figure 4:** Stage I renal cell carcinoma on postcontrast CT. The tumour is small and confined to the kidney.

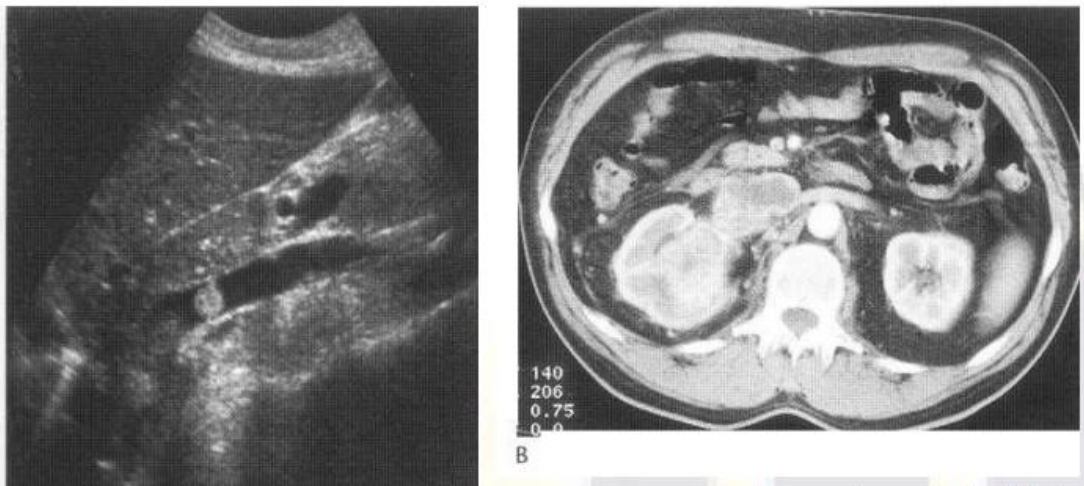
Tumour extension through the renal capsule (stage II) may show bulk tumour in the perinephric (Fig. 5).



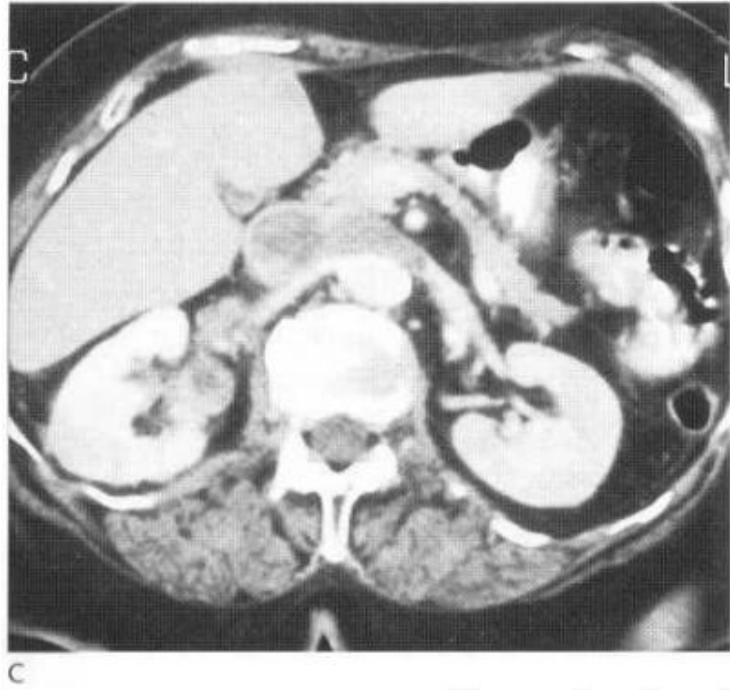
**Figure 5:** Stage II renal cell carcinoma on postcontrast CT. The tumour MO extends to the margin of the kidney and shows some local nodular m1 extension through the renal capsule.

This differentiation may be difficult. Tumours may breach the capsule without showing bulk tumour outside it, Secondary signs to be sought under these circumstances include tumour extending to the margin of the kidney and having an ill defined peripheral outline, thickening of the perinephric fascia and soft-tissue strands within the perinephric space. These features, however, may also occur in some stage I tumours due to adjacent reactive inflammatory or oedematous change. Renal cell carcinoma also acquires a collateral or parasitic blood supply which is often visible in the perinephric space and may be mistaken for tumour extension through the capsule. Conventionally stages I and II are treated with radical nephrectomy and show little prognostic difference. Currently, however, nephron-sparing surgery (partial nephrectomy) is increasingly being offered under certain circumstances. These include situations where there is only one functioning kidney and/or where the tumour is small (less than 4 cm diameter) and- localised, especially if there is a possibility of a more benign pathology such as an oncocytoma. In these patients it becomes space much more important to attempt accurate differentiation between stage I and II. It is also important to perform a careful study of the healthy renal tissue on the affected side and in the contralateral kidney, as tumours may be multifocal within the same kidney or bilateral in up to 2%. Partial nephrectomy also depends on being able to preserve a separate blood supply to the remaining healthy renal tissue and therefore generally requires preoperative assessment of the renal vasculature, usually performed with MR or CT angiography.

Stage III tumours are treated with radical nephrectomy and thrombectomy and/or lymphadenectomy. MR and CT are both highly accurate in the demonstration of venous invasion. Renal cell carcinoma has a predilection to invade the renal vein at the hilum and extend along it into the inferior vena cava (Fig. 6).







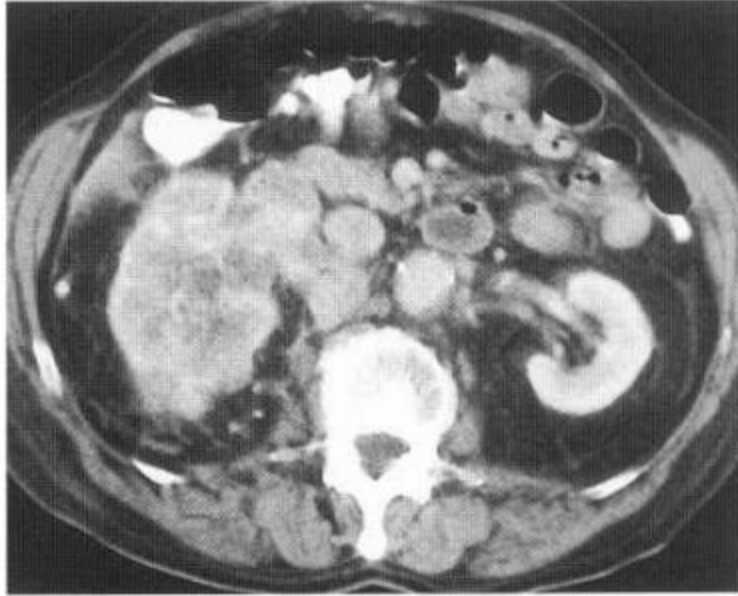
**Figure 6:** Renal cell carcinoma with vascular involvement. (A) Ultrasound shows tumour as a soft-tissue nodule of intermediate echogenicity within the inferior vena cava. Postcontrast CT (B, different case) shows a right renal cell carcinoma extending along the renal vein into the inferior vena cava and (C) into the contralateral renal vein.

Further extension is usually superiorly with the flow of blood, occasionally as far as the right atrium. Sometimes tumour extends into the contralateral renal vein. Interestingly it is almost always intraluminal tumour, the inferior vena cava wall itself being rarely invaded. The disturbance of blood flow in the inferior vena cava may lead to thrombus formation and pulmonary emboli. On CT, if there is adequate opacification of the venous system the demonstration of a filling defect within the renal vein and/or inferior vena cava is highly reliable, good-quality spiral CT having an accuracy of the order of 96%. Care must be taken to evaluate all sections to avoid misdiagnosing a central stent, in of unopacified blood returning from the lower limbs as tumour. On MRI, tumour within the blood vessels is well demonstrated on good-quality conventional sequences as a soft-tissue mass compared to the signal void of flowing blood (Fig. 7).



**Figure 7:** Heterogeneous mass of renal carcinoma in the right kidney on MRI (T 2 - weighted sequence) extending along the right renal vein into the inferior vena cava.

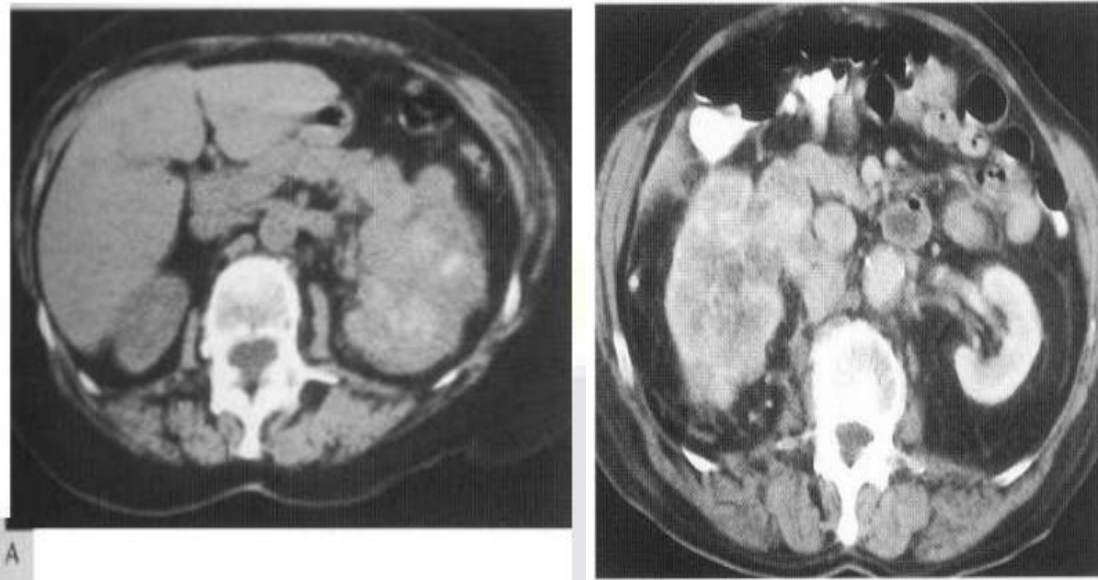
The appearances can be complex because tumour in the inferior vena cava may cause upstream blood in the vena cava below the renal veins to slow down sufficiently to appear as a high-signal column that may be mistaken for retrograde extension of tumour. It is important to assess extension into the contralateral renal vein and the superior limit of inferior vena cava involvement. Extension to the level of the hepatic veins or right atrium requires the involvement of a hepatic or cardiac surgeon. Usually the lymphatic drainage from the kidney follows the renal veins to the lateral aortic nodes close to the origins of the renal arteries. These are usually the first nodes to be involved with metastatic carcinoma. Drainage from this site is via the lumbar trunks to the cisterna chyli. Occasionally lymphatic channels bypass the first-order nodes and drain directly to the mediastinum. The overall accuracy for staging lymph node involvement with CT is around 83-89% and depends on the detection of lymph node enlargement above 1 cm diameter (Fig. 8).

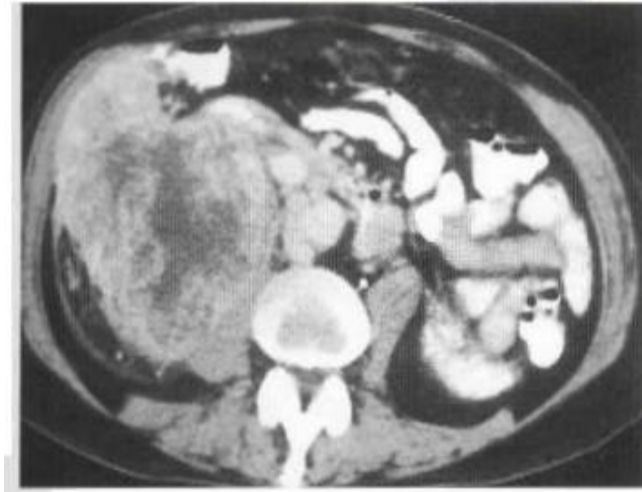


**Figure 8:** Large right renal cell carcinoma with lymph node metastases including a large node that is displacing the inferior vena cava anteriorly.

Unfortunately this leads to a substantial number of false positives due to reactive inflammatory hyperplasia (up to 43% in some studies). Enlargement above 2 cm diameter is almost always due to metastases. Microscopic metastasis without enlargement is uncommon. MRI staging depends on the same criteria and therefore has a similar accuracy.

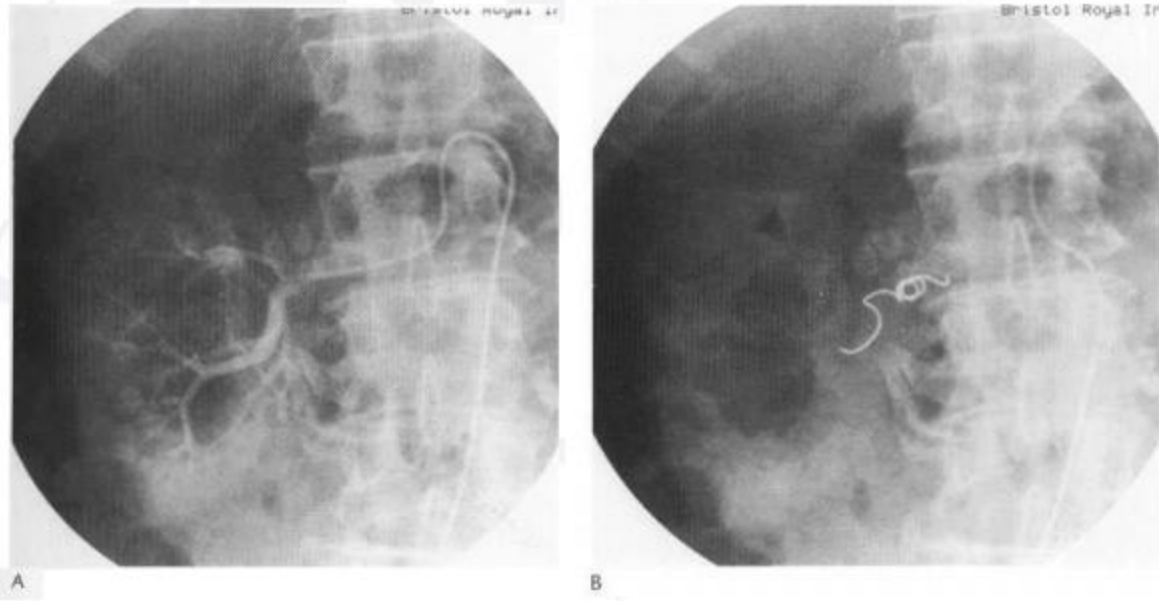
Stage IV tumours (Fig. 30.63) show invasion into adjacent organ





**Figure 9:** Stage IV tumours. Left renal cell carcinoma with areas of calcification seen on the unenhanced CT (A). The tumour has invaded into the tail of the pancreas (B). Right renal cell carcinoma invading the psoas muscle, anterior abdominal wall and adjacent bowel (C).

The organs involved are predictable from the relationships of the kidneys and include posterior extension into the psoas muscle and quadratus lumborum, superiorly into the adrenal glands, laterally into the abdominal wall, posterosuperiorly into the diaphragm, and anteriorly into colon, liver and duodenum (on the right) and pancreas, jejunum, stomach and spleen (on the left). Loss of the fat line between the tumour and adjacent structures on CT or MRI is common and in itself does not necessarily indicate invasion, the diagnosis requiring the demonstration of density/signal change and/or enlargement. Common sites for distant metastases include lung, liver, bone, brain and soft tissue throughout the body. They are classically extremely vascular and may be expansile, especially in bone or soft tissue. Although they are usually multiple, a solitary metastasis is sometimes encountered and may be the presenting complaint. Stage IV tumours have a poor prognosis and are treated palliatively, which may include surgery, chemotherapy and radiotherapy. Severe haematuria may be palliated with renal arterial embolisation (Fig. 10) or radiotherapy.



**Figure 10:** Right renal angiogram (A) demonstrating the malignant circulation of a renal cell carcinoma. Embolisation with an intra-arterial coil (B) has been performed.

The diagnosis of renal cell carcinoma is radiological and preoperative biopsy is not routinely indicated. In metastatic disease that is being managed nonsurgically, however, biopsy is often required as it is the only means of obtaining histology.

## CONCLUSION

Thus radiological investigation important for diagnosing and staging the RCC.

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