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ARTICLE

Detection, staging and surveillance in renal cell carcinoma

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Abstract

This article discusses the computed tomography (CT) and magnetic resonance (MR) scanning techniques used for the detection and staging of renal cell carcinoma and their pitfalls. Comparison between the Robson and recent modifications to the TNM classifications is also addressed. The accuracy of CT and MR in the staging of renal cell carcinoma and the role of positron emission tomography (PET) scanning is outlined and finally the surveillance of patients who have had curative treatment of renal cell carcinoma is briefly addressed.

Keywords: *Kidney: CT techniques; kidney: MR techniques; kidney neoplasms: CT; kidney neoplasms: MR; kidney neoplasms: staging; positron emission tomography (PET).*

Introduction

Renal cell carcinoma is the most common primary tumor of the renal parenchyma accounting for 85–90% of solid renal tumors in adults, with approximately 31 200 new cases diagnosed annually in the United States in 2000[1–3]. With the widespread use of cross sectional imaging techniques, the detection of asymptomatic renal cell carcinomas has risen sharply. These incidental tumors are usually smaller in size, with lower tumor stage, and nuclear grade, with improved survival rates, compared to symptomatic tumors. In addition, 5-year survival rates improved from 45% in the 1970s to around 61% in the 1990s. Lead time and length time biases due to earlier detection account in part for this improved survival[4–6].

Scanning techniques

Computed tomography (CT)

The CT scanning technique that is most widely used for renal mass evaluation consists of unenhanced images, followed by images after iodinated intravenous contrast administration. The nephrographic phase of contrast administration, is the most sensitive phase for tumor detection[7,8]. Some centers include arterial and corticomedullary phases of imaging as well, as they are useful for assessing tumor vascularity and for performing 3D image reconstructions[9,10]. Scanning the kidneys in the early phases (arterial and corticomedullary) only has been shown in several studies to result in both false positive and false negative interpretations (Figs 1(A) and (B))[7,8].

Magnetic resonance (MR)

A combination of unenhanced breath-held T1 and T2-weighted images, with chemical shift and fat suppression followed by 3D breath-hold fat-suppressed gadolinium-enhanced T1-weighted sequences at multiple time points during and after contrast administration are essential for the diagnosis and staging of renal cell carcinoma[11–13].

Types of renal cell carcinoma

There are five main types of renal cell carcinoma, the most common being the clear cell type[14]. Papillary

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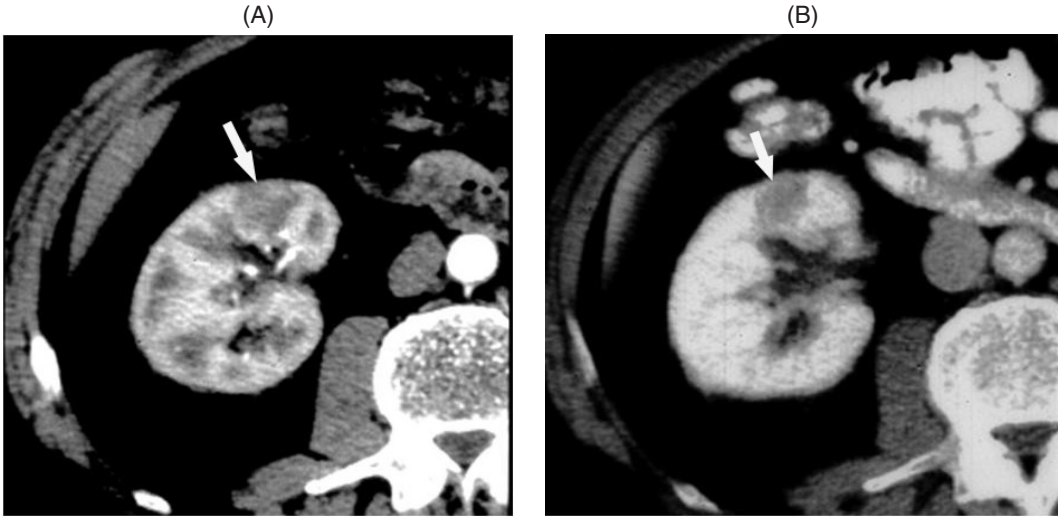

Figure 1 **Corticomedullary phase image (A) demonstrates differential areas of enhancing cortex and medulla making detection of mass lesions difficult, with suggestion of a mass (arrow). However in the nephrographic phase (B) a solid mass (arrow) in the anterior aspect of the interpolar region of the right kidney is well delineated, which was subsequently proven to be a renal cell carcinoma.**

cancers are the next most common: chromophobe cancers have the best prognosis; collecting duct tumors (Bellini's) and medullary cancers are rare.

Hereditary renal cancers

There are various renal cancers that are hereditary[15]. Families with von Hippel–Lindau disease and tuberous sclerosis tend to get clear cell cancers, whereas in the Birt–Hogg Dube syndrome, the tumors tend to be of the chromophobe type. Medullary carcinomas and papillary cancers can also be hereditary. In patients with hereditary leiomyomas, renal papillary cancers can occur.

Staging

The two most common staging systems that have been used for renal cell cancer staging are the Robson and TNM classification. Tumor staging for renal cell carcinoma has been incorporated into the TNM system of the UICC in 1997, which has been modified in 2002 (Table 1). The tumor stage is the most important factor affecting the prognosis and survival rate. Tumor type also affects survival, with aggressive anaplastic renal cell carcinomas having a worse prognosis compared to clear cell carcinoma[16–19].

In patients with organ-confined disease, the 5-year survival rate is between 60% and 90% but falls to between 5% and 10% in those with distant metastases.

The role of preoperative imaging is to define the tumor, detect and delineate the extent of venous involvement if any, as well detect the presence of local and distant metastases.

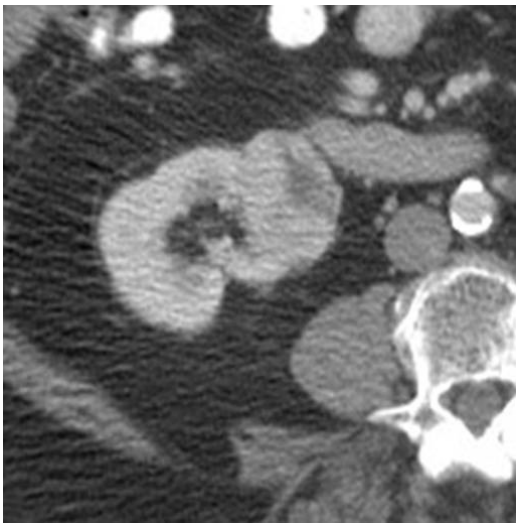

Figure 2 **Renal cell carcinoma in medial aspect of lower pole of right kidney shows no evidence of perinephric extension (T1), which was confirmed at surgery.**

Tumors confined to the renal parenchyma

Tumors confined to the renal parenchyma can be either T1 or T2 based on size (T1 $\leq$ 7 cm and T2 $\geq$ 7 cm). T1 tumors were recently sub-classified into T1a for tumors <4 cm and T1b for tumors between 4 and 7 cm. Previous studies have shown that CT tends to understage renal cancers as subtle perinephric extension goes undetected. However in a study by Catalano *et al.*[20] who studied 40 patients with renal cancer using multidetector CT

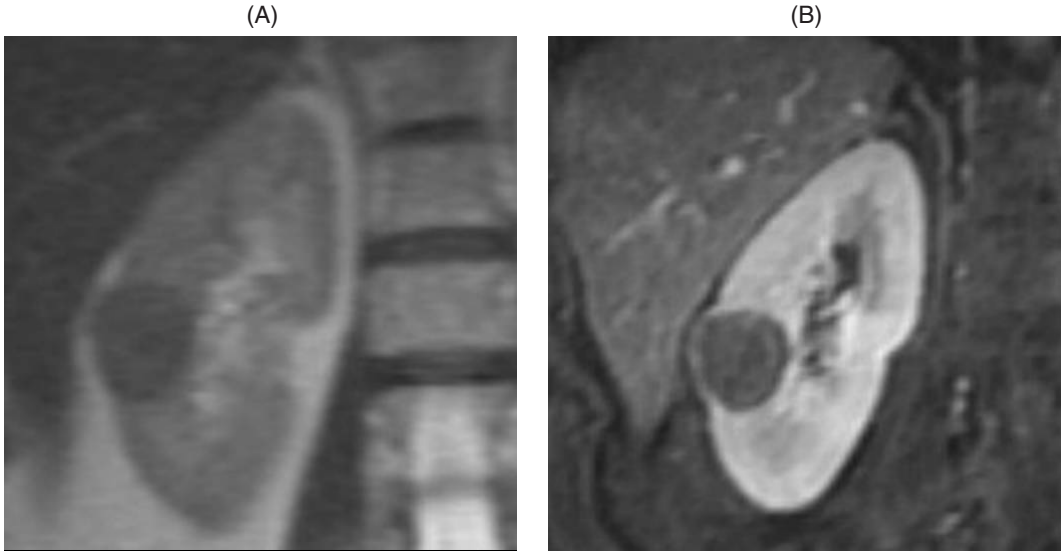

Figure 3 **Coronal T1 and coronal contrast-enhanced gradient echo image after gadolinium enhancement shows well defined renal mass arising from the lower pole of the right kidney. No perinephric extension (T1) lesion was diagnosed at imaging and confirmed at surgery and pathology.**

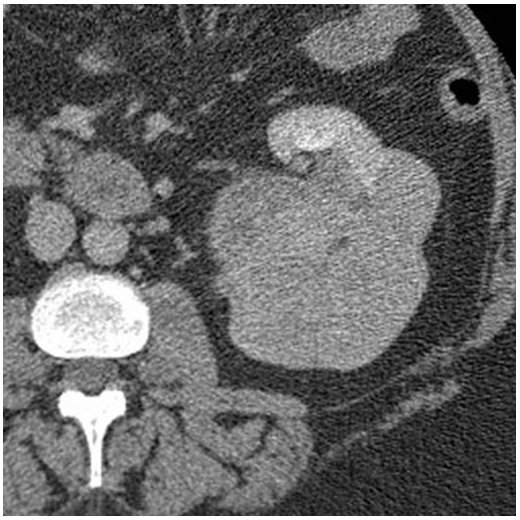

Figure 4 **There is no perinephric stranding seen extending from this large mass in the lower pole of the left kidney, placing it as a T2 tumor, but at pathology perinephric extension was confirmed, upstaging this tumor to T3.**

(MDCT), all patients with Stage I disease were correctly diagnosed, with only one patient with subtle perinephric extension being understaged (Figs 2 and 3(A) and (B)).

Perinephric extension

In prior studies, it has been shown that imaging using CT and MR had low accuracy rates for the detection of perinephric tumor extension, as stranding in the perinephric fat is non-specific and can be due to many non-neoplastic causes.

Table 1 TNM classification and staging system of renal cell carcinoma (UICC, 2002)

T-classification			
T1	Confined to kidney, T1a < 4 cm, T1b < 7 cm		
T2	Confined to kidney, >7 cm		
T3	Confined to Gerota's fascia		
T3a	Extending to ipsilateral adrenal or perirenal fat		
T3b	Extending to renal vein or IVC below diaphragm		
T3c	Extending to IVC above diaphragm		
T4	Extending beyond Gerota's fascia		
N-classification			
N0	No regional lymph node metastasis		
N1	Metastasis in one regional lymph node		
N2	Metastasis in more than one regional lymph node		
Nx	Regional lymph nodes cannot be evaluated		
M-classification			
M0	No distant metastasis		
M1	Distant metastasis		
Mx	Distant metastasis cannot be evaluated		
Stage I	T1	N0	M0
Stage II	T2	N0	M0
Stage III	T3	N0	M0
	T1, T2, T3	N1	M0
Stage IV	T4	N0, N1	M0

More recently Catalano *et al.*[20] showed that MDCT had 95% accuracy for perinephric tumor infiltration with a sensitivity of 96% and specificity of 93% (Figs 4 and 5(A) and (B)).

Venous involvement

Approximately 23% of renal cell carcinomas invade the renal veins and 7% invade the inferior vena cava. The presence and superior extent of tumor thrombus are

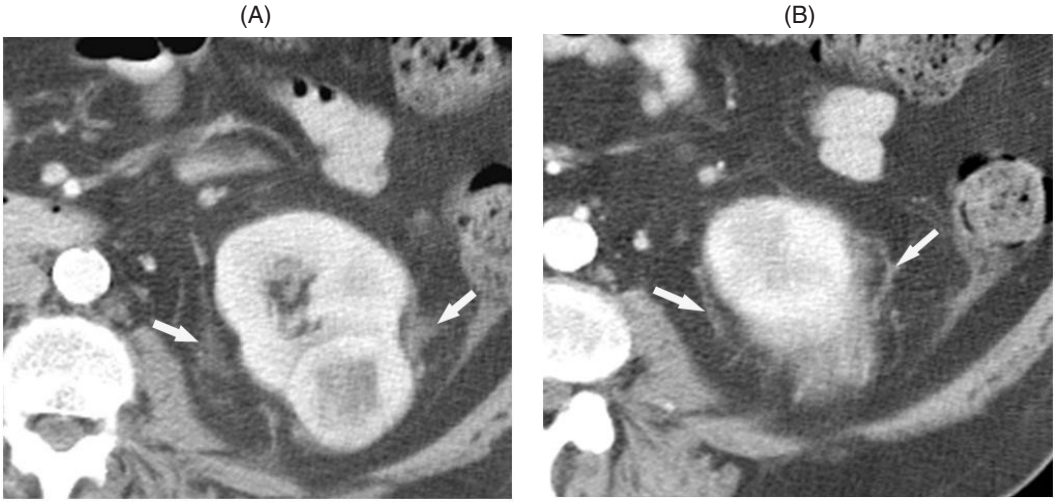

Figure 5 **Perinephric stranding (arrows) seen extending from this solid left lower pole renal cell carcinoma, leading to a false positive CT staging of a T3 tumor: at pathology there was no perinephric extension, thereby downstaging this to a T1.**

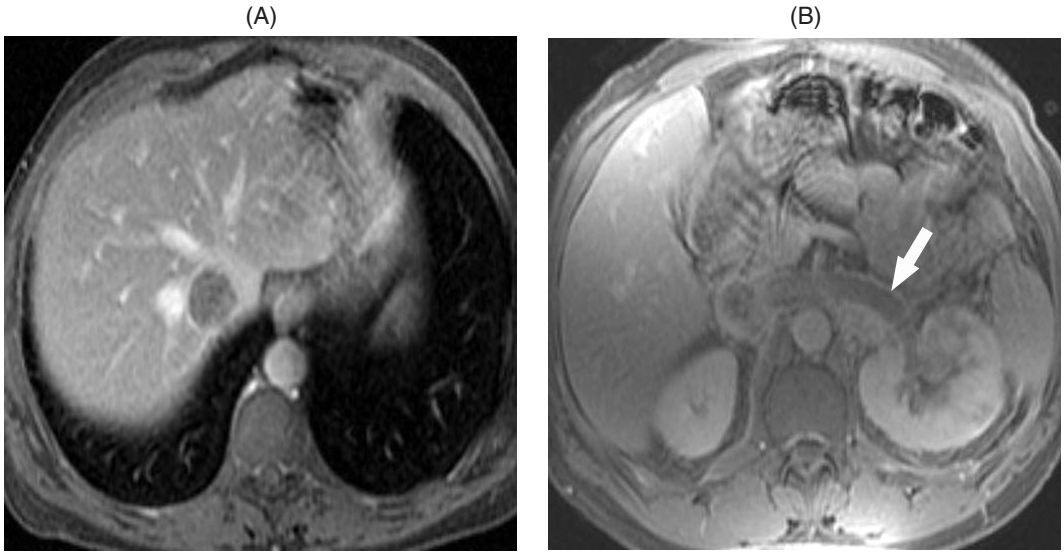

Figure 6 **Gadolinium-enhanced axial gradient echo images demonstrate intrahepatic and LRV (arrow) thrombus extending from a left renal cell carcinoma.**

essential to plan the surgical approach, as the detection of supradiaphragmatic extension will require a thoraco-abdominal surgical approach[21].

In a recent study of 23 patients with suspected IVC thrombus, the accuracy of MDCT and MR in detecting the extent of thrombus, were compared by Hallscheidt *et al.*[22]. In this study both modalities were equally accurate (72–88%).

MRI is the most common modality used to define the presence and extent of tumor thrombus, as it is not only reliable in defining extent, but can also differentiate between bland and malignant thrombus (Fig. 6(A) and (B)).

In a study of a small number of patients by Sohaib *et al.*[23] MRI had a specificity of 89% and accuracy of 94% for detecting transmural invasion by tumor. The most reliable sign for IVC wall invasion in this study was the presence of tumor on either side of the IVC wall (transmural extension).

Nodal metastases

Lymph node metastases occur in about 15% of patients in the absence of other metastases[24,25]. Lymph node positivity rate increases in the more advanced T tumors: being about 13% in T1–T3 tumors but increasing to 37% in T4 tumors. The overall 5-year survival rates for tumors that do not have nodal or venous involvement is 43–100%, in contrast to 8–35% for tumors with nodal involvement.

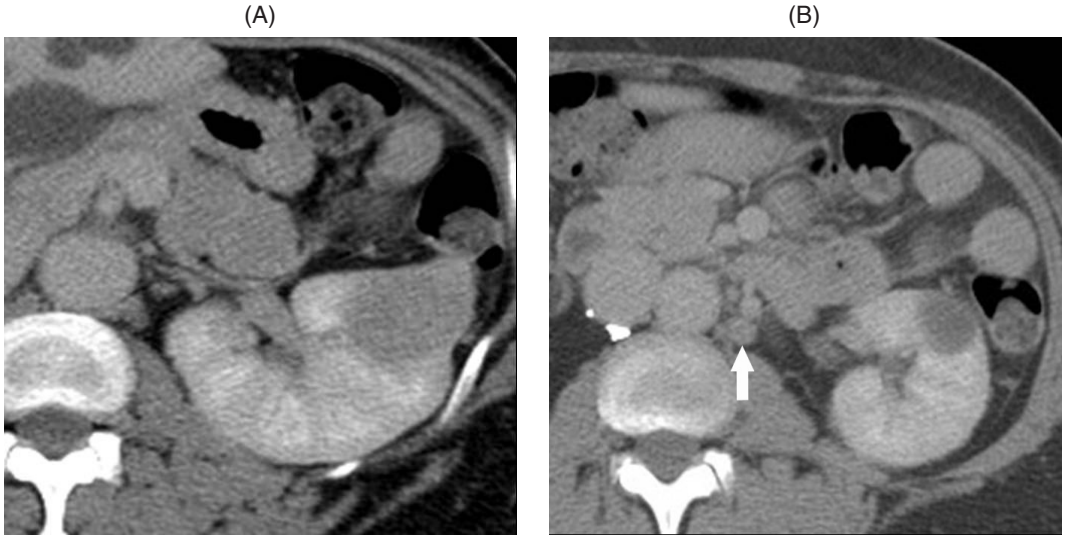

Figure 7 **Left para-aortic nodes slightly larger than 10 mm (arrow) in a patient with left upper pole renal cell carcinoma, led to a false positive diagnosis of node positivity. At pathology these enlarged nodes were due to reactive hyperplasia and not metastasis.**

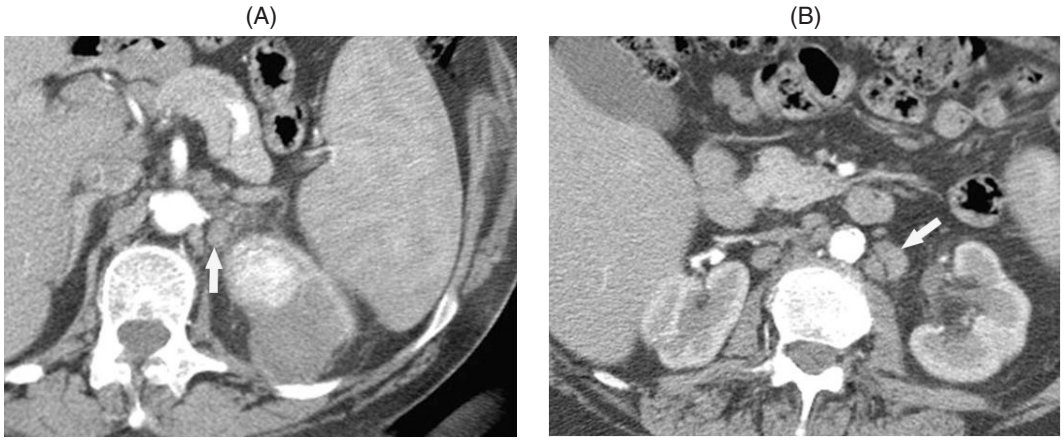

Figure 8 **Left upper pole renal carcinoma with slightly enlarged nodes (arrows) proved to represent metastatic disease.**

CT and MR have in the past been insensitive to detect nodal metastases in normal-sized nodes. False negative rates of about 10% have been reported using a cut-off in node size of 10 mm (Figs 7 and 8(A) and (B)).

More importantly false positive rates of up to 58% due to reactive hyperplasia have been reported. In a recent study by Catalano *et al.*[20], using MDCT, the authors had very high accuracy with 13/14 true positive cases for nodal metastases.

MR lymphography using ultrasmall iron oxide particles has been shown recently to have very high specificity for nodal metastases in small sub-centimeter nodes[26]. In a study of 80 patients with prostate cancer, Harisinghani *et al.*[27] have shown that using this technique, sensitivity improved from 35.4% to 90.5% and specificity from 90.4% to 97.8% for pelvic nodal metastases detection. Forty-five of 63 nodes did not meet size criteria for malignancy, but were accurately characterized by lymph node MRI.

Ipsilateral adrenal gland involvement

Overall incidence of adrenal metastases is between 1.2% and 8.5%, being about 1% in T1–T2 tumors. CT with normal appearing ardenal glands has a high negative predictive value for adrenal involvement with metastases, but a positive CT is not always due to malignancy, as adrenal adenomas are more commonly seen even in patients with underlying extra-adrenal malignancy[28–30].

Overall staging accuracy of MR vs. CT

In a study of 82 renal cell carcinomas, by Hallscheidt *et al.*[31] MDCT and MR were equivalent in the overall

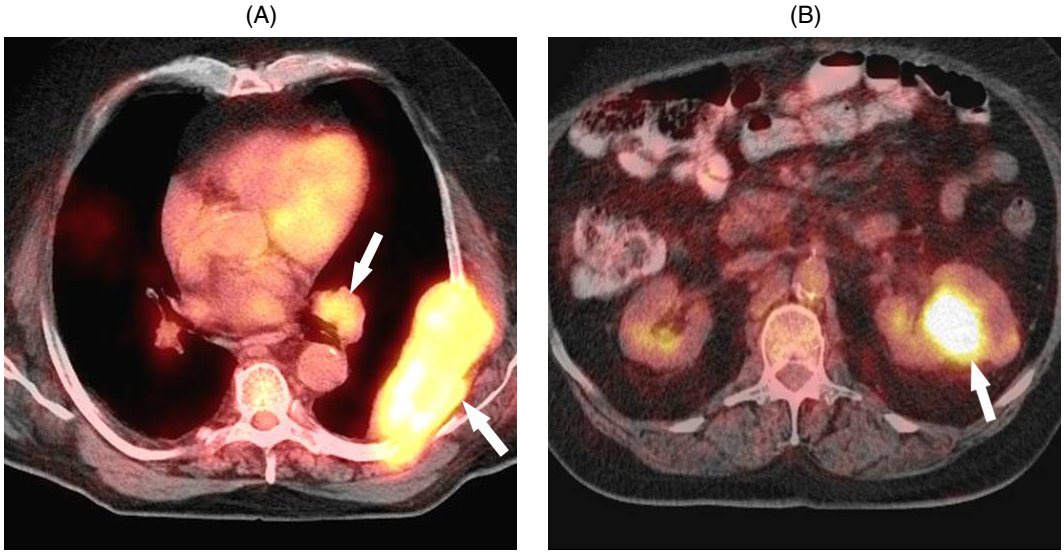

Figure 9 **Fused PET-CT image (A) demonstrates metastatic disease to the left hilar lymph node and chest wall (arrows) as well as the primary tumor (B) in the left kidney (arrow).**

staging of renal cell carcinoma. In this study, overall accuracy for two readers was 83% and 80% for CT compared to 87% and 78% for MRI. Overall accuracy for both modalities and both readers was 80% for all tumors and 85% for T1 tumors.

Role of fluorodeoxyglucose (FDG)-positron emission tomography (PET)

PET is not very accurate in distinguishing a renal cell carcinoma from other solid renal neoplasms and is therefore not used in the initial workup of a solid renal mass. But it appears moderately useful in the detection of metastatic disease (Fig. 9(A) and (B)) and local recurrence[32,33].

Surveillance following nephrectomy

In a recent study of 194 patients, Chae *et al.*[34] reported an incidence of recurrence or metastases in 21%, with common sites being lung, bone, the nephrectomy bed and the liver. Tumor recurrence was seen within 2 years in over 80% of patients, the mean time to recurrence being 17 months. More advanced stage tumors with higher nuclear Fuhrman grade were more likely to recur or metastasize[35].

In most centers in the United States no systematic follow up regimen is universally accepted. In one center, for T1 and T2 tumors, annual chest X-rays are performed; with 6 monthly chest X-rays for 3 years; CT of the abdomen is performed at 6, 12, 24 and 36 months for T3 and T4 tumors[36,37]. The European Association of Urology has adopted a guideline which uses CT as an optional exam for all T1 and T2 tumors and T3 and T4 tumors only after year 3[38].

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