# 8 Transitional Cell Carcinoma

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CONTENTS



## 8.1 Introduction

Transitional cell carcinoma (TCC) of the urothelium is the second most common urological tumor after prostate carcinoma (Herranz-Amo et al. 1999), and usually presents with hematuria. Although these tumors are most commonly encountered in the urinary bladder, up to 5% are found in the upper urinary tract. The evaluation of hematuria, however, also requires assessment of the renal parenchyma for masses and the urinary tract for calculi. In addition, the urothelium must be examined in its entirety because of the multicentric nature of TCC. Conventional imaging modalities, such as intravenous urography (IVU), retrograde pyelography (RP), and ultrasound (US), still play a key role in diagnosis in combination with cystoscopy and endourological techniques. Recently, the technique of multiphasic computed tomographic urography (CTU) has evolved as an alternative method of assessing patients with hematuria, offering superior detection of urinary calculi and renal parenchymal masses, and in some studies, improved detection of urothelial lesions. Because surrounding structures can also be assessed, CTU is rapidly becoming the definitive study for these patients, potentially shortening the duration of diagnostic evaluation. Magnetic resonance (MR) imaging, including the newer techniques of MR angiography (MRA) and MR urography (MRU), is also being used, particularly in patients who cannot tolerate iodinated contrast, and in whom multiplanar, vascular, and collecting system imaging is required.

Although there are pathological and imaging features common to TCC occurring anywhere in the urinary tract, certain findings are more typical of tumors of the upper urinary tract. Synchronous or metachronous tumor of either ipsilateral or contralateral collecting system is common, necessitating vigilant urological and radiological follow-up. This chapter reviews the characteristic imaging features of renal TCC and outlines the role of imaging in diagnosis, pre-operative staging, and follow-up.

## 8.2 Incidence

Transitional cell carcinoma of the kidney arises from the urothelium of the renal pelvis or calices overlying the renal parenchyma, and is the most common urothelial malignancy of the urinary tract (Scolieri et al. 2000). Five percent of urothelial tumors arise in the kidney or ureters, accounting for approximately 10% of upper-tract neoplasm

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(Hall et al. 1998; Kirkali and Tuzel 2003). Renal TCC most frequently arises in the extrarenal part of the pelvis, followed by the infundibulocalyceal region.

Distribution is equal between left and right kidneys, with 2–4% occurring bilaterally. Twenty-five percent of upper-tract tumors occur in the ureter, and only 25% of these are found in the upper third (Kirkali and Tuzel 2003)

## 8.3 Etiology

Renal TCC typically occurs in the sixth and seventh decades of life, with men affected three times more often than women. Besides increasing age and male gender, the most important risk factor is smoking, with smokers two to three times more likely to develop renal TCC than non-smokers (Kirkali and Tuzel 2003). Chemical carcinogens (aniline, benzidine, aromatic amine, azo dyes), cyclophosphamide therapy, and heavy caffeine consumption are also associated with TCC, and all predispose to synchronous and metachronous tumor development (Kirkali and Tuzel 2003). These substances are metabolized and excreted in the urine as carcinogenic substances that act locally on the urothelium. Because urine is in contact with mucosa in the bladder reservoir for a longer time and because the surface area of the bladder is larger than other parts of the urinary tract, bladder carcinomas are 30–50 times more common than tumors of the upper tract (Wong-You-Cheong et al. 1998). Stasis of urine and structural abnormalities, such as horseshoe kidneys which predispose to stasis, are therefore also associated with increased prevalence. Renal TCC is very common in families affected with "Balkan endemic nephropathy." Familial metabolic abnormalities in these patients lead to tubulointerstitial nephritis, renal failure, carcinogenic glomerular–tubular toxins and multiple tumors (Kirkali and Tuzel 2003). Analgesic abuse, particularly long-term use of phenacetin, produces capillosclerosis and predisposes to a highly invasive type of TCC that preferentially involves the renal pelvis (Lee et al. 1997). Human papilloma virus and hereditary non-polyposis colon cancer have also been suggested as risk factors for renal TCC, and the incidence is also significantly higher in areas where endemic "blackfoot disease" is seen (Kirkali and Tuzel 2003).

## 8.4 Presentation

Patients with renal TCC typically present with hematuria, which may be frank or microscopic. Up to a third of patients with ureteric lesions may present with flank pain or acute renal colic. The gradual expansion of the ureteral lumen around these slow-growing tumors, however, makes these symptoms, which are more commonly associated with calculi, less likely than may be expected. Occasionally, tumors may be discovered incidentally during radiological investigations performed for unrelated symptomatology. Tumor spread occurs by mucosal extension or local, hematogenous, or lymphatic invasion. Occasionally, patients may present with distant metastases usually to the liver, bone, and lungs (Chan et al. 2002).

## 8.5 Pathophysiology

Approximately 80% of TCC is low-stage, superficial, papillary neoplasm with a broad base and frond-like morphologic structure (Barentsz et al. 1996). These tumors are usually small at time of diagnosis, grow slowly, and follow a relatively benign course (Urban et al. 1997a).

Pedunculated or diffusely infiltrating tumor accounts for approximately 20% of TCC and tends to behave more aggressively and be more advanced at diagnosis (Buckley et al. 1996). Infiltrating tumors are characterized by thickening and induration of the renal pelvic wall, often with invasion into the renal parenchyma. This infiltrative growth pattern, however, preserves renal contour and differs from renal cell carcinomas (RCC), which are largely expansile.

Synchronous bilateral TCC has been reported to occur in 1–2% of cases of renal lesions. Eleven to 13% of patients with upper-tract TCC subsequently develop metachronous upper-tract tumor (Wong-You-Cheong et al. 1998). Furthermore, up to 50% of patients initially presenting with upper-tract TCC develop metachronous tumor in the bladder, typically developing within 2 years of surgical treatment and seen more commonly with ureteral than renal tumors (Keeley et al. 1997; Kirkali and Tuzel 2003). On the other hand, 2% of patients with bladder TCC have synchronous upper-tract tumor at time of evaluation (Herranz-Amo et al. 1999). In patients

with bladder cancer, metachronous upper-tract disease occurs in up to 6%, invariably seen in patients with cystoscopic evidence of recurrent bladder tumor, typically occurring within 3 years and carrying a relatively poor prognosis (Hession et al. 1999; Kirkali and Tuzel 2003). The incidence is higher with multifocal or high-grade tumor, distal ureteric involvement, or vesicoureteral reflux (Kirkali and Tuzel 2003; Wong-You-Cheong et al. 1998).

## 8.6 Diagnosis

The standard work-up of patients with hematuria as recommended by the American Urological Association consists of urinalysis and cytology, cystoscopy, and IVU (Grossfeld et al. 2001; O'Malley et al. 2003). The initial diagnosis of TCC is usually made on the basis of urine cytology and diagnostic yield is improved with selective lavage and collection, and brush biopsies performed at cystoscopy or retrograde ureteropyelography; however, these techniques are invasive and technically demanding. The limitations of IVU in assessing the renal parenchyma usually requires the supplemental use of US, CT, or MR imaging to evaluate the kidneys for masses (Gray Sears et al. 2002; Kawashima et al. 2003; Maher et al. 2004). Furthermore, additional imaging is also often required to clarify indeterminate findings on IVU. Computed tomographic urography offers the potential to diagnose calculi, urothelial tumors, and renal parenchymal tumors as a single investigation, although further studies are required before it becomes the standard first-line investigation for hematuria. Cystoscopy remains the gold standard for the diagnosis and follow-up of carcinoma of the bladder, and is therefore performed in all patients presenting with hematuria in whom tumor is suspected (Lang et al. 2003; O'Malley et al. 2003).

### 8.6.1 Intravenous Urography

The diagnosis of renal TCC is most frequently made on IVU in patients undergoing investigation for hematuria or flank pain. Intravenous urography remains the non-invasive method of choice for imaging the detailed anatomy of the pelvicalyceal system and ureters (Kawashima et al. 2003; O'Malley et al. 2003; Scolieri et al. 2000; Yousem et al. 1988), although this is likely to change as CTU becomes more refined and accepted as a primary diagnostic investigation. The appearances of renal lesions on IVU are well described. Calcification may be visualized on preliminary radiographs but is uncommon, occurring in 2–7% of tumors, and, when present, may mimic urinary tract calculi (Fig. 8.1;

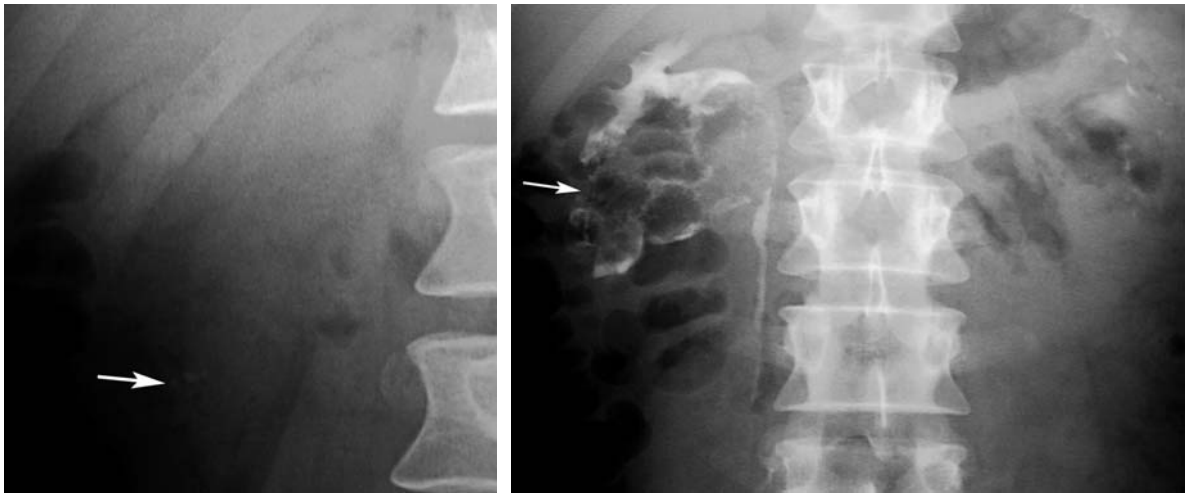


**Fig. 8.1a,b.** Transitional cell carcinoma of the renal pelvis in a 65-year-old man. **a** Oblique intravenous urography (IVU) scout film reveals microscopic calcification (*arrow*) overlying the lower pole of the right kidney, subsequently shown to represent transitional cell carcinoma. **b** Anteroposterior IVU 15-min film reveals a large stippled filling defect involving the collecting system of the right kidney. Calcification in the periphery is again noted and discerned from contrast by reference to the scout film (*arrow*).

Wong-You-Cheong et al. 1998). Renal enlargement is seen only with very large tumors. On IVU renal TCC usually manifests as a filling defect within the contrast-enhanced renal collecting system. Filling defects may be single or multiple and smooth, irregular (Fig. 8.2), or stippled. The stipple sign refers to tracking of contrast into the interstices of a papillary lesion (Fig. 8.1b; Kirkali and Tuzel 2003; Wong-You-Cheong et al. 1998). This sign, however, may also be seen with blood clot and fungus balls, and should be interpreted with caution. Stricture-like lesions of the pelvicalyceal system may be evident and, if multiple, may mimic renal tuberculosis. Filling defects within dilated calices may occur secondary to tumor obstruction of the infundibulum, and may lead to calyceal amputation (Fig. 8.3). Tumor-filled, distended calices have been called "oncocalices/phantom calices" which fail to opacify with contrast. It is important to remember that longstanding tumor obstruction of the uretero-pelvic junction or ureter may lead to generalized hydronephrosis and poor excretion. In this case alternative imaging modalities are often required for diagnosis. This is a major disadvantage of IVU when compared with CTU, which allows assessment of non-functioning kidneys. Because pelvicalyceal filling defects may be non-specific and urinary obstruction may obscure distal synchronous ureteric tumors, RP is often required to clarify the diagnosis.

### 8.6.2 Retrograde Pyelography

Retrograde pyelography is usually performed during cystoscopy or to further characterize abnormalities detected on IVU, in inadequately excreting kidneys, or in cases of contrast allergy. Retrograde pyelography, although invasive, can confirm the radiological diagnosis while also facilitating ureterorenoscopy with biopsy/brushings and cytological examination of localized urine collection. As with IVU, renal TCC typically appears as an intraluminal filling defect, which may be smooth, irregular, or stippled (Figs. 8.4–8.6). Opacification of a tumor-involved calyx may show irregular papillary or nodular mucosa (Figs. 8.7, 8.8). If TCC involves an infundibulum, then an "amputated" calyx may be seen with/without focal hydronephrosis and "oncocalyx" (Fig. 8.9). If renal lesions extend into the upper ureter, ureteric fixation may occur secondary to diffuse mural infiltration.

### 8.6.3 Ultrasound

At present, renal US is frequently used for patients with hematuria to assess for renal parenchymal masses. Ultrasound, however, is not as sensitive as

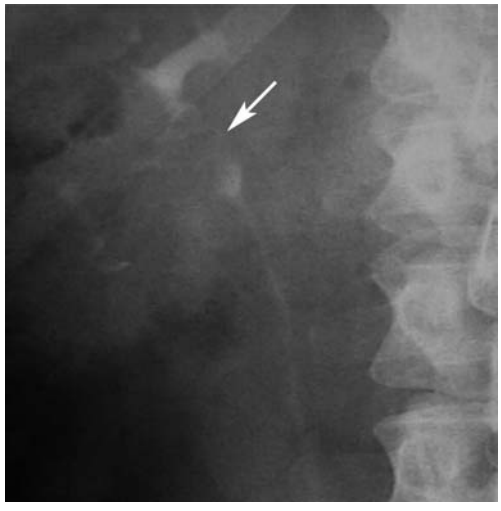


**Fig. 8.2.** Transitional cell carcinoma of the renal pelvis in a 60-year-old man with painless hematuria. Oblique IVU 15-min film demonstrates a large irregular filling defect (*arrow*) involving the right renal pelvis and extending into the lower-pole calyceal system due to transitional cell carcinoma.

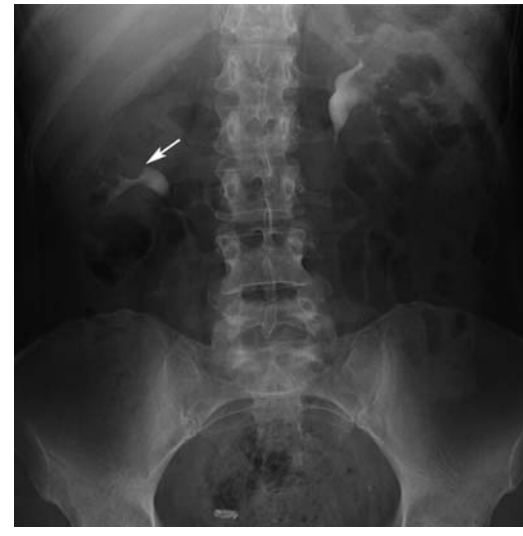


**Fig. 8.3.** Transitional cell carcinoma of the upper-pole collecting system in a 58-year-old woman. Anteroposterior IVU 15-min film shows amputation of the upper-pole calyx secondary to transitional cell carcinoma (*arrow*).

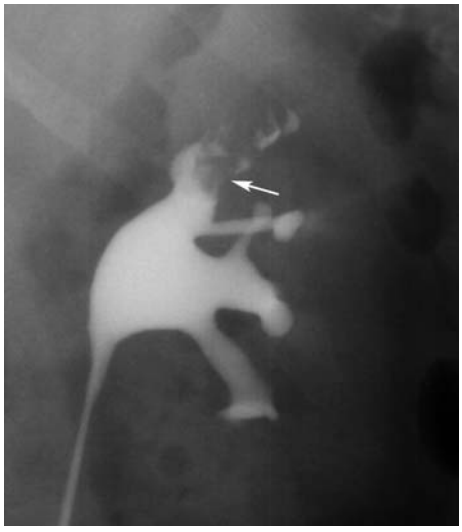


**Fig. 8.4.** Transitional cell carcinoma of the upper pole in a 70-year-old man. Anteroposterior retrograde pyelography (RP) view shows distortion and an irregular filling defect involving the left upper-pole calyx (*arrow*).

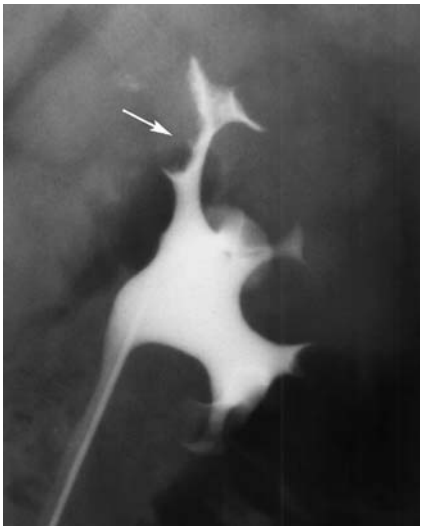


**Fig. 8.5.** Transitional cell carcinoma of the upper pole of left kidney in a 67-year-old man. Anteroposterior RP view shows a large, irregular filling defect involving the upper-pole calyx (*arrow*).

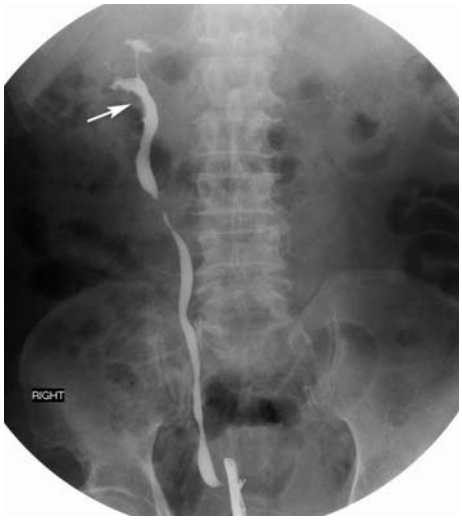



**Fig. 8.6.** Transitional cell carcinoma of the lower pole of right kidney in a 70-year-old man. Anteroposterior RP view shows a large, irregular mass arising from and distorting the lower-pole collecting system (*arrow*).

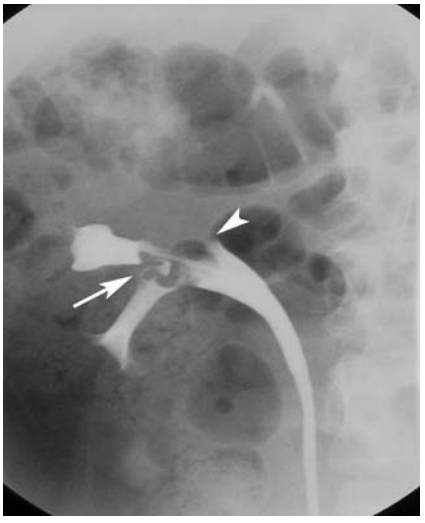


**Fig. 8.7.** Transitional cell carcinoma in a 72-year-old man. Anteroposterior RP view shows an irregular, papillary filling defect of the lower/mid-pole calyces due to transitional cell carcinoma (*arrow*). Complete amputation of the upper pole calyx is seen (*arrowhead*).

CT in identifying or characterizing renal masses (Gray Sears et al. 2002; Joffe et al. 2003; Kim and Cho 2003; Perlman et al. 1996), and as CTU emerges as an initial imaging investigation of hematuria, US will also likely play only a limited diagnostic role in the future. Ultrasound can be useful in patients with renal impairment or iodinated contrast allergy, although MR imaging is becoming established as the investigation of choice in these patients. Ultrasound can also assess the degree of hydronephrosis and guide interventional procedures in the setting of acute obstruction. The US features of renal pelvic TCC are non-specific, but usual appearances are of a central soft tissue mass in the echogenic renal sinus, with or without hydronephrosis (Figs. 8.10–8.12). Infundibular tumors may cause focal hydronephrosis (Fig. 8.13). Transitional cell carcinoma is usually iso- or hypoechoic relative

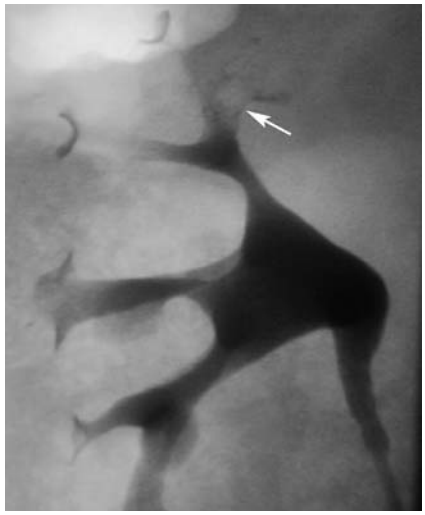
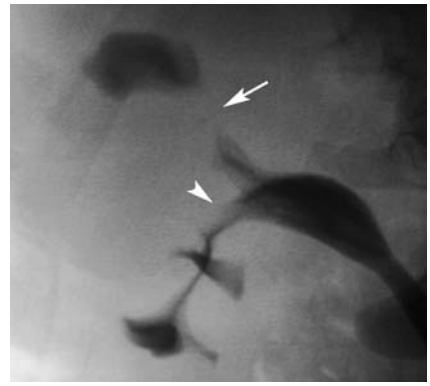


**Fig. 8.8.** Transitional cell carcinoma in a 61-year-old woman. Anteroposterior RP view shows a diffuse infiltrating transitional cell carcinoma involving the right upper-pole calyx with nodular irregularity of the involved mucosa (*arrow*).



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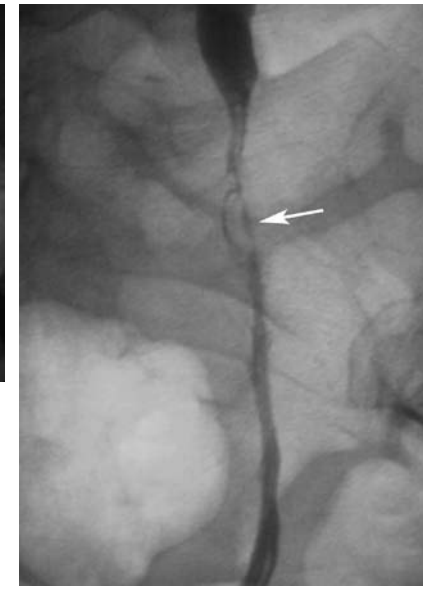
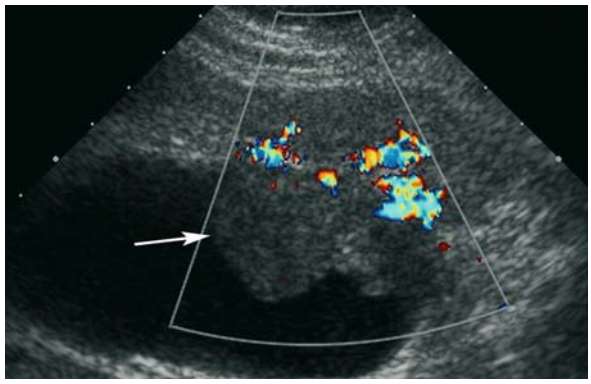


**b**

**Fig. 8.9a,b.** Multifocal transitional cell carcinoma in an 83-year-old woman. **a** Anteroposterior RP view of the right kidney demonstrates amputation of the interpolar calyx (*arrowhead*) and stricture of the upper pole infundibulum (*arrow*) with local upper-pole hydronephrosis and "oncocalyx" due to multifocal transitional cell carcinoma. **b** Anteroposterior RP view of the left ureter shows diffuse infiltration of the lower ureter with mural irregularity, intraluminal filling defects (*arrow*) and proximal dilatation.



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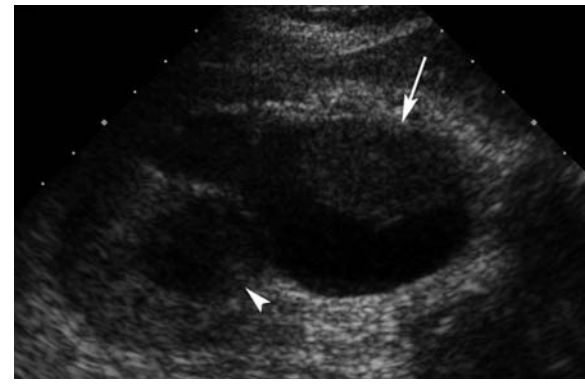


**b**

**Fig. 8.10a,b.** Transitional cell carcinoma in a 62-year-old man with gross hematuria. **a** Longitudinal Doppler US image shows gross hydronephrosis of the right kidney secondary to a large transitional cell carcinoma (*arrow*) arising from the anterior aspect of the renal pelvis. Note the moderate Doppler flow within the lesion. **b** Longitudinal US image again shows transitional cell carcinoma (*arrow*), with further tumor identified within the mid-pole calyx (*arrowhead*).

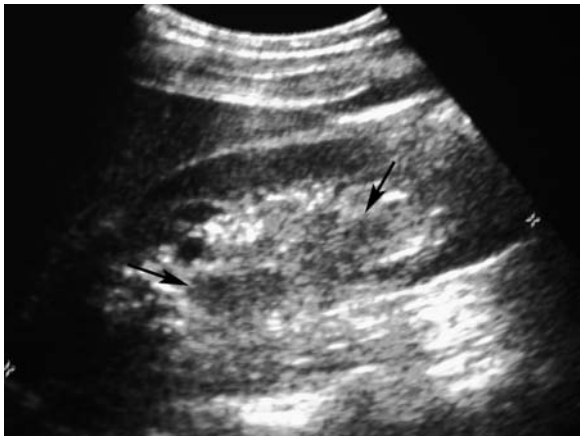


**Fig. 8.11.** Transitional cell carcinoma of renal pelvis in a 58-year-old woman. Longitudinal US image shows large mass (*arrows*) in the echoic right renal sinus. The tumor itself is isoechoic to renal parenchyma.

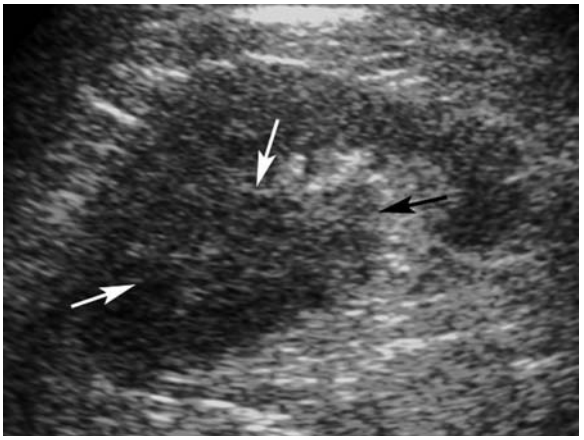
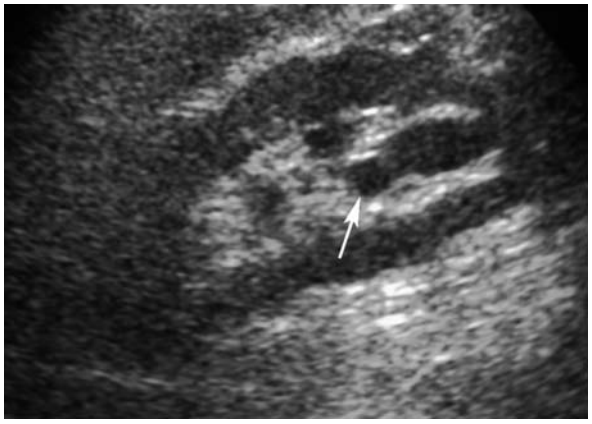


**Fig. 8.12.** Transitional cell carcinoma of left kidney in a 67-year-old woman. Longitudinal US image shows large lesion, isoechoic to renal parenchyma (*arrows*). The renal sinus fat is obliterated in the upper pole suggestive of parenchymal invasion.



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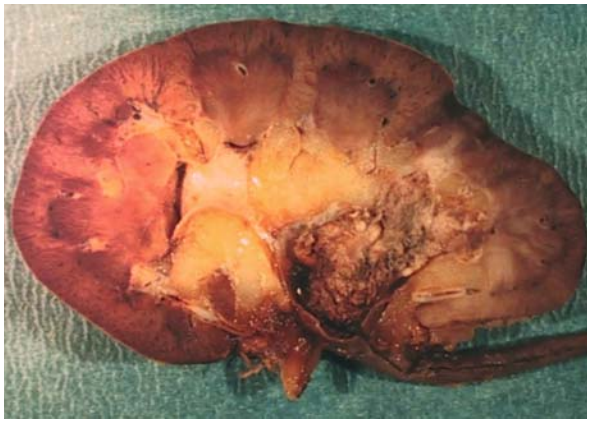

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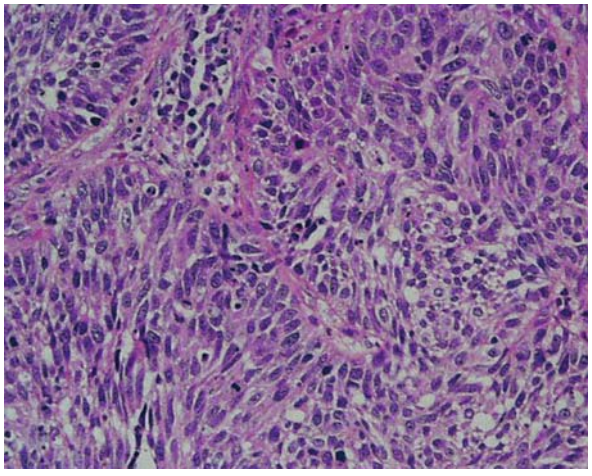

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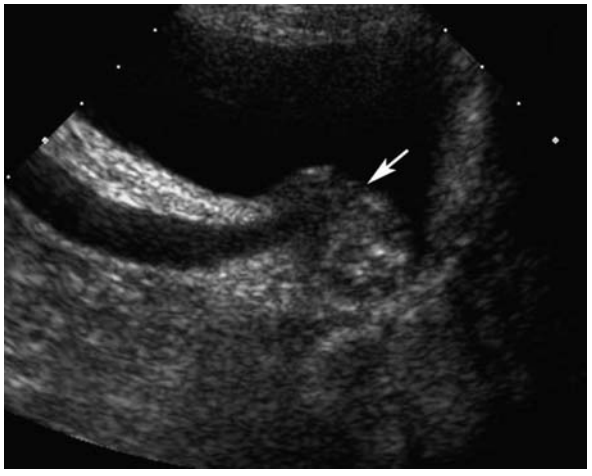


**d**

**Fig. 8.13a-d.** Multifocal transitional cell carcinoma in a 78-year-old man. **a** Longitudinal US image shows focal mid- and lower-pole hydronephrosis (*arrow*) secondary to transitional cell carcinoma. **b** Gross pathological section shows tumor in the renal pelvis with extension to involve the lower-pole calyx. **c** Microscopic pathological section of tumor (hematoxylin and eosin stain; original magnification, ×100). **d** Longitudinal US image of the contralateral vesicoureteric junction demonstrates transitional cell carcinoma (*arrow*) with proximal hydroureter.

to surrounding renal parenchyma, but occasionally high-grade TCC may show areas of mixed echogenicity (Fig. 8.14). Ultrasound can sometimes help differentiate tumor from radiolucent calculi, which appear more echogenic and cause a greater degree of acoustic shadowing. Although lesions may extend into the renal cortex and cause focal contour distortion, typically TCC is infiltrative and does not distort the renal contour. Recent developments in high-resolution endoluminal US performed during ureterorenoscopy have shown promise in the evaluation of renal TCC, offering potential advantages over other imaging techniques, and may assume a more prominent role in future diagnosis (Hadas-Halpern et al. 1999).

### 8.6.4 Computed Tomography

Computed tomography is well established in the preoperative staging and assessment of upper-tract TCC. Computed tomography is more sensitive than either US or IVU in the detection of small renal mass lesions and urinary tract calculi (Caoili et al. 2002; Fielding et al. 1999; Lang et al. 2003; Scolieri et al. 2000; Silverman et al. 1994; Szolar et al. 1997; Tawfiek and Bagley 1997; Warshauer et al. 1988). The recent advent of CTU, offering single breath-hold coverage of the entire urinary tract, improved resolution and the ability to capture multiple phases of contrast, offers improved diagnostic potential over IVU and US in the assessment of patients with hematuria due to calculi or tumor (Caoili et al. 2002; Corrie and Thompson 1987; Gray Sears et al. 2002; Lang et al. 2003; Maher et al. 2004). Recent studies have also shown higher detection rates for upper- and lower-tract urothelial malignancies by CTU over IVU (Kawashima et al. 2003; McCarthy and Cowan 2002; Newhouse et al. 2000). Although the American College of Radiology still recommends IVU in the investigation of hematuria, as CTU becomes more prevalent it is likely to become the investigation of choice, as the urothelium, renal parenchyma, and perirenal tissues can be assessed at a single examination. Typically, CTU consists of a multiphasic helical CT protocol comprising four sequences:

1. A pre-enhancement helical CT scan from the upper pole of the kidney to the lower edge of the symphysis, to exclude urinary tract calculi.
2. A late arterial, early corticomedullary phase helical CT scan of the kidney and lower pelvis, beginning 15–25 s after infusion of 150 ml of nonionic contrast medium, to evaluate for vascular abnormalities.
3. A nephrographic phase helical CT scan of the kidney, 80–140 s after contrast infusion, to assess renal parenchyma.
4. An excretory phase helical CT scan from the upper pole of the kidney to the symphysis pubis 4–8 min after contrast infusion, to detect urothelial disease.

In the interest of decreasing radiation exposure and time of examination, many protocols omit the late arterial, early corticomedullary phase scan, unless a vascular abnormality is suspected (Fig. 8.15). In fact, some authors advocate a two-phase protocol where a nephropyelographic phase scan is performed if the initial non-contrast phase does not demonstrate a satisfactory cause for the patient's hematuria. This involves two contrast infusions with a delay of 10–15 min between them, allowing assessment of the renal parenchyma in the nephrographic phase and the entire collecting system in the pyelographic phase simultaneously. Saline is infused after the first bolus to distend the ureters. Other authors have utilized abdominal compression, prone scanning, and diuretics to obtain optimum distension and opacification (Joffe et al. 2003; Kawashima et al. 2003; Maher et al. 2004). Oral contrast is omitted to facilitate three-dimensional (3D) reformats, which typically include thick- and thin-slab coronal and sagittal maximum intensity projections (MIPs) for kidneys, ureters, and bladder, although other 3D reconstruction techniques can be used. These pro-

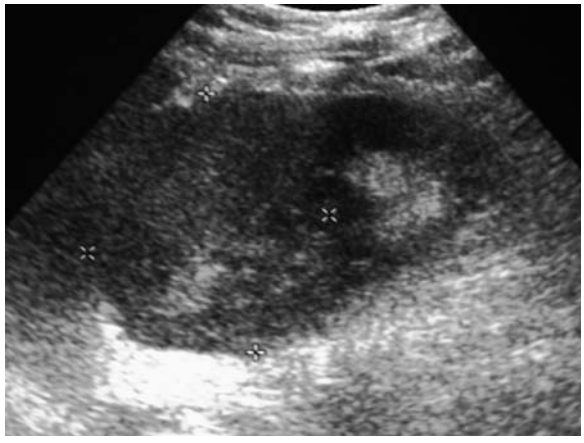


**Fig. 8.14.** Transitional cell carcinoma of the right upper pole in a 63-year-old woman. Longitudinal US image shows large mixed echoic lesion with obvious parenchymal invasion and distortion.

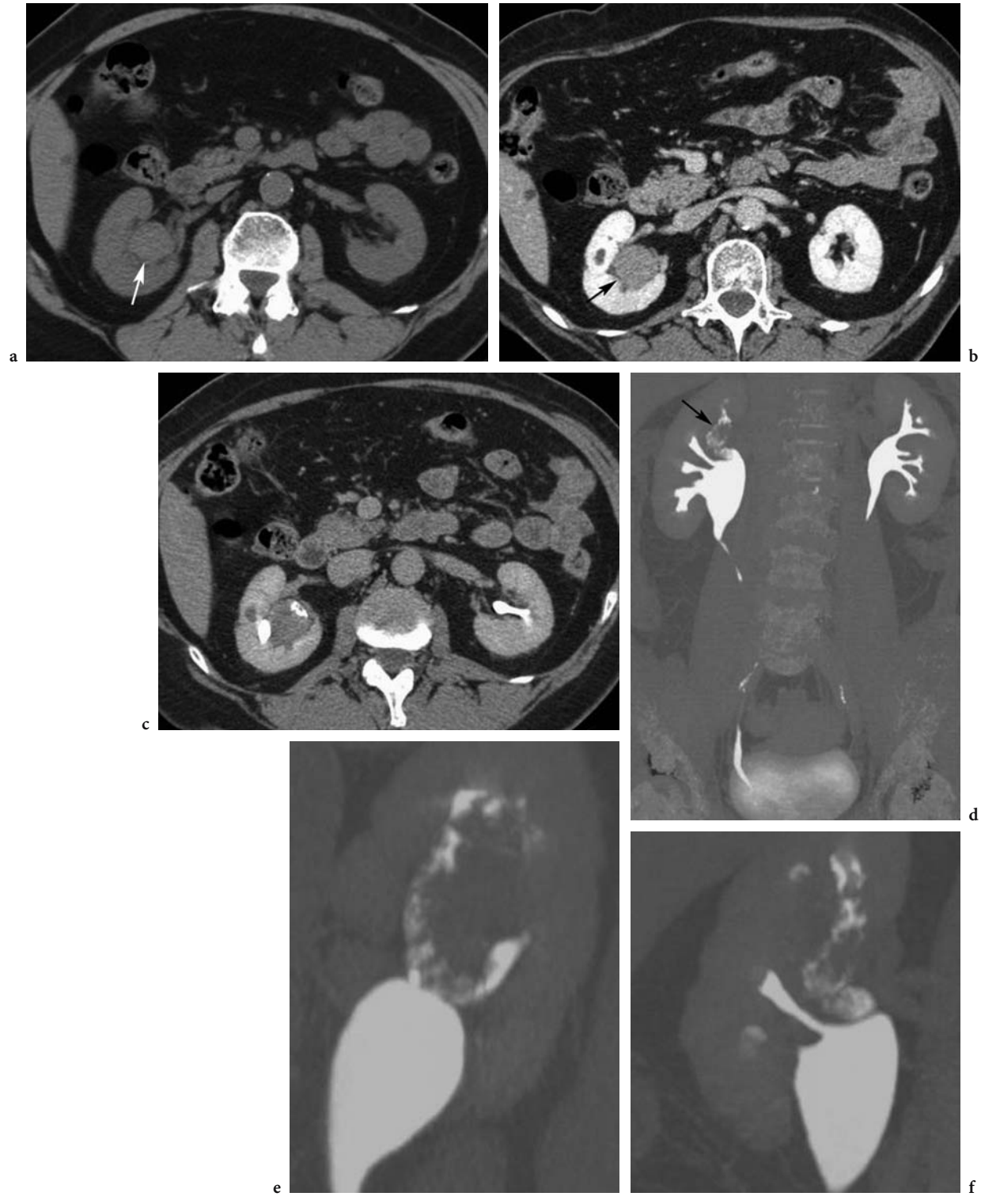



**Fig. 8.15a-f.** Upper-pole transitional cell carcinoma on CT urography in a 59-year-old man. **a** Axial pre-enhancement CT scan shows mass (*arrow*) in the right upper-pole calyx slightly hyperdense relative to the renal parenchyma. **b** Axial nephrographic phase-contrast-enhanced CT scan demonstrates characteristic early enhancement of the mass (*arrow*) which is less than surrounding renal parenchyma. **c** Axial excretory phase-contrast-enhanced CT scan confirms tumor within the upper-pole calyx with surrounding excreted contrast medium. **d** Coronal maximum intensity projection (MIP) reformatted image displaying the upper pole tumor (*arrow*) in IVU format. **e** Sagittal and **f** coronal MIP reformatted images further demonstrate the lesion.

vide urologists with a familiar imaging format while still demonstrating small filling defects, although most radiologists diagnose primarily from the axial images, using the planar images to confirm or better display an abnormality. Coronal reconstructions in particular demonstrate the longitudinal extent of a lesion and assess for multicentric tumor (Fig. 8.15d). Viewing the opacified system at wider window settings, such as bone windows, can aid in identifying and differentiating subtle lesions. Unlike IVU, imaging is not dependent on a functioning kidney and the tract distal to a lesion can be evaluated. Pre-contrast scans are necessary to obtain accurate density values and differentiate tumor from other non-opaque filling defects, whereas post-contrast scans aid in confirming lesion location and extent. On pre-contrast imaging TCC is typically hyperdense (5–30 HU) to urine and renal parenchyma (Fig. 8.16) but less dense than other pelvic filling defects such as clot (40–80 HU), papillary necrosis (20–40 HU), or calculus (>100 HU). Calcified TCC may occasionally be difficult to distinguish from calculi, in which case enhancement of the non-calcified portions of the tumor should be sought.

Short-interval follow-up is occasionally required to differentiate between clot and tumor (McNicholas et al. 1998; Urban et al. 1997a). Post-contrast early enhancement and de-enhancement, although more typical of RCC, is also seen with TCC (Garant et al. 1998). Computed tomographic urography may also reveal other causes of hematuria such as calculi, papillary necrosis, inflammatory lesions, or infarcts. Renal TCC is characteristically seen as a filling defect in the excretory phase, which expands centrifugally with compression of the renal sinus fat (Figs. 8.17–8.19). Other appearances include pelvicalyceal irregularity, focal or diffuse mural thickening, oncocalyx, and focally obstructed calices. Early tumors confined to the muscularis are separated from the renal parenchyma, either by renal sinus fat or excreted contrast, and have normal-appearing peripelvic fat. Advanced TCC extends into the renal parenchyma in an infiltrating pattern which distorts normal architecture (Fig. 8.20). Reniform shape is typically preserved, however, unlike RCC (Fig. 8.21). Renal cell carcinoma, being hypervascular, also tends to enhance more, although the two tumors often cannot be differentiated. Transitional

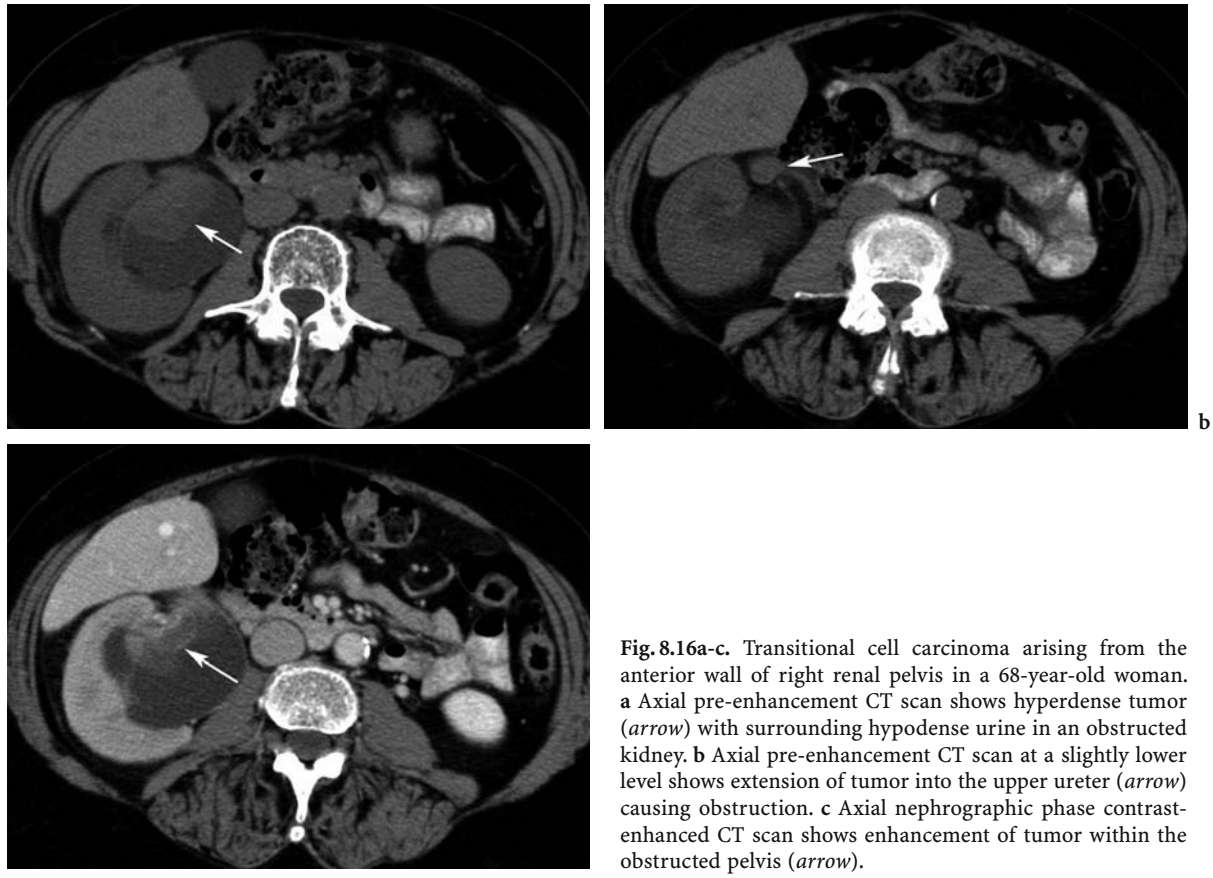



**Fig. 8.16a-c.** Transitional cell carcinoma arising from the anterior wall of right renal pelvis in a 68-year-old woman. **a** Axial pre-enhancement CT scan shows hyperdense tumor (*arrow*) with surrounding hypodense urine in an obstructed kidney. **b** Axial pre-enhancement CT scan at a slightly lower level shows extension of tumor into the upper ureter (*arrow*) causing obstruction. **c** Axial nephrographic phase contrast-enhanced CT scan shows enhancement of tumor within the obstructed pelvis (*arrow*).

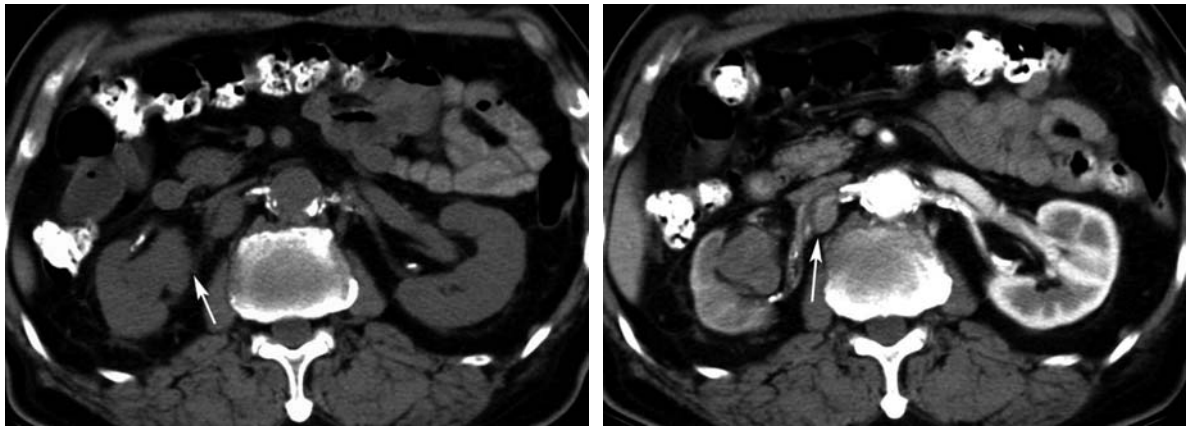


**Fig. 8.17a-c.** Right renal pelvis transitional cell carcinoma in a 43-year-old woman. **a** Axial pre-enhancement CT scan shows tumor of the right renal pelvis, with extension to parapelvic tissues (*arrow*). **b** Axial nephrographic phase contrast-enhanced CT scan shows typical early moderate enhancement (34–54 HU). Note also that enhancement in local tumor involved retrocaval lymph node (*arrow*). **c** Axial excretory phase-contrast-enhanced CT scan shows extent of tumor in the pelvis with a small amount of surrounding contrast visualized.

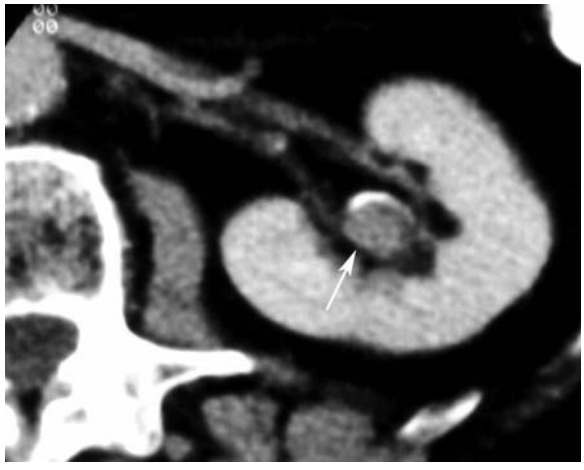


**Fig. 8.18.** Transitional cell carcinoma of the left upper pole in a 75-year-old woman. Axial excretory phase-contrast-enhanced CT scan shows focal mass (*arrow*) with surrounding contrast anteriorly within the collecting system.

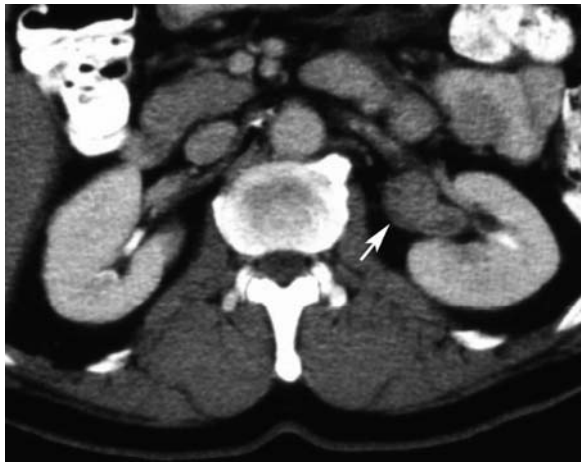


**Fig. 8.19.** Transitional cell carcinoma in a 72-year-old man with gross hematuria. Axial excretory phase-contrast-enhanced CT scan shows transitional cell carcinoma of the mid-pole calyx with extension into the renal pelvis (*arrow*).

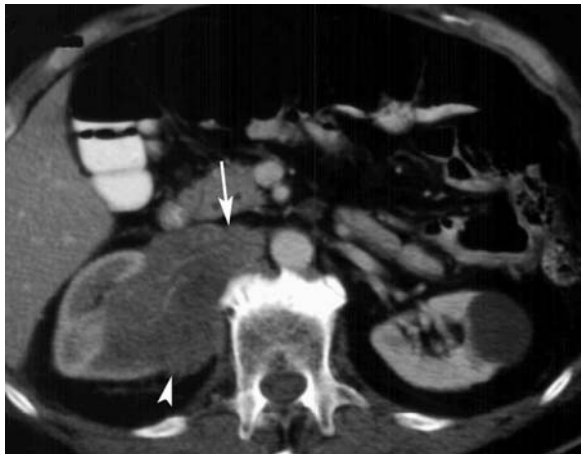
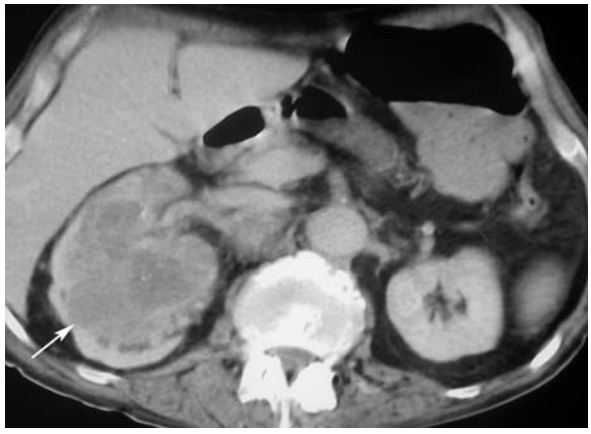


**Fig. 8.20.** Large transitional cell carcinoma in a 66-year-old man with frank hematuria and right flank mass. Axial contrast-enhanced CT scan shows a large transitional cell carcinoma of the right renal pelvis with perinephric/parapelvic extension (*arrowhead*) and invasion of the right renal vein and IVC (*arrow*).

cell carcinoma may appear nodular, especially on post-contrast imaging (Lang et al. 2003). Parenchymal invasion may be seen as a focal delay in all or part of the cortical nephrogram, although superimposed pyelonephritis or obstruction alone can also give these appearances (Fig. 8.22). Large infiltrating renal TCC may occasionally present with areas of necrosis and must be differentiated from lymphoma, metastases, and xanthogranulomatous pyelonephritis (XGP; Garant et al. 1998). Retention of contrast material in obstructed tubules may result in accentuated delayed enhancement of the renal parenchyma surrounding larger lesions.

Computed tomographic urography is capable of identifying lesions at an early stage, thereby allowing nephron-sparing surgery. It also allows demonstration of surrounding structures by reference to the source images. Adequate distension and opacification are fundamental factors in the thorough evaluation of the urothelium with CTU. The increased radiation exposure is estimated at only 50–80% over a complete IVU series (Lee et al. 1997). Although



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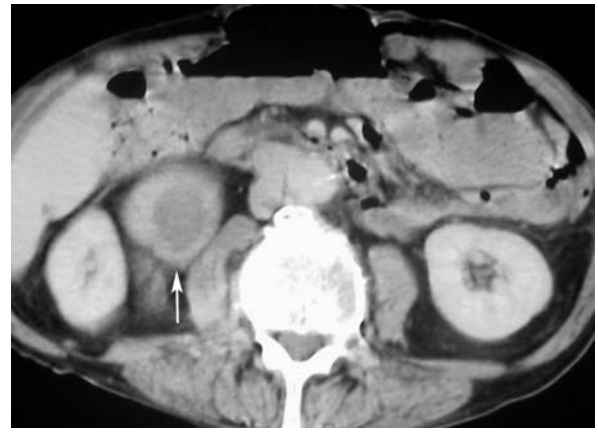

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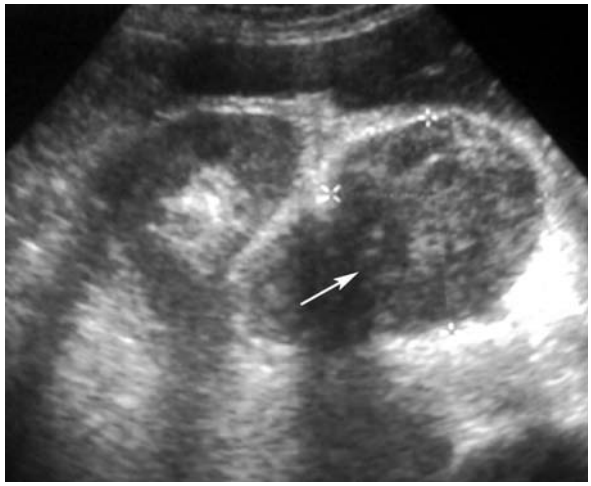

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**Fig. 8.21a-c.** Transitional cell carcinoma of the right kidney in a 61-year-old man. **a** Axial contrast-enhanced CT scan shows large, enhancing soft tissue mass involving the pelvis of the right kidney with extension to involve the renal parenchyma (*arrow*) and perinephric tissues. The tumor expands centrifugally from the renal pelvis but there is preservation of the reniform contour. **b** Axial contrast-enhanced CT scan at a lower level demonstrates tumor extension into the proximal ureter with diffuse mural thickening and enhancement (*arrow*) and central clot. **c** Transverse US image at this level also shows diffuse tumor involvement of the ureter (*arrow*).

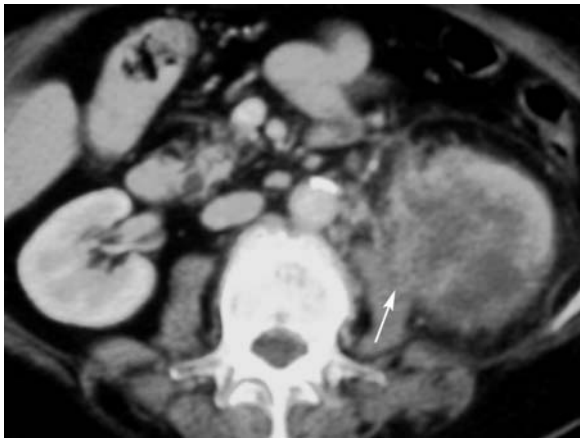


**Fig. 8.22.** Transitional cell carcinoma of the left kidney in a in a 67-year-old man. Axial contrast-enhanced CT scan shows tumor involving the upper pole of the left kidney with diffuse parenchymal infiltration and extension to involve the perinephric tissues and left psoas muscle (*arrow*).

reformatting and review of multiple images on different window settings is time consuming, CTU has the potential to stand alone as a comprehensive "one-stop" front-line study for hematuria and therefore detection of TCC.

### 8.6.5 Angiography

Angiography is not employed in the routine assessment of renal TCC but can distinguish TCC from RCC, which is often associated with neovascularization and tumoral arteriovenous shunting on angiography. Transitional cell carcinoma is typically hypovascular, occasionally demonstrating fine tortuous neovascularity or tumor blush. Encasement of vessels and a reduced intensity of the capillary nephrogram may be seen if TCC infiltrates the renal parenchyma. In rare cases where renal vein/IVC involvement is suspected, CT or duplex US are usually employed. Flow-sensitive MR imaging sequences have also been used in this role recently.

### 8.6.6 Magnetic Resonance Imaging

Magnetic resonance imaging is infrequently used in the primary diagnosis and assessment of renal TCC, and the MR imaging characteristics of this tumor are not well described. Magnetic resonance imaging, in general, has not played a leading role in renal tumor imaging, due to limitations in image quality, time-consuming sequences, and artifact susceptibility.Recently, however, the development of newer fast sequences has led to increased use. Magnetic resonance imaging has been shown to equal CT in the detection and diagnosis of renal masses (Cholankeril et al. 1986; Lang et al. 2003; Walter et al. 2003). Magnetic resonance imaging offers inherently high soft tissue contrast, is independent of excretory function, and multiplanar imaging permits direct image acquisition in the plane of tumor spread. The coronal plane is often advantageous because it allows evaluation of both kidneys, the renal vessels, the inferior vena cava, and the spine in a small number of slices.

Transitional cell carcinoma is of lower signal intensity than the normally hyperintense urine on T2-weighted sequences, permitting good demonstration of tumor in a dilated collecting system. Renal TCC, however, appears nearly isointense to renal parenchyma on T1-weighted and T2-weighted sequences, necessitating the use of contrast for accurate assessment of tumor extent (Kreft et al. 1997). Although TCC is a hypovascular tumor, moderate enhancement is seen post-gadolinium, although not to the same degree as the surrounding renal parenchyma (Figs. 8.23, 8.24). Differentiation between small renal calculi and tumor may occasionally be difficult unless definite gadolinium enhancement is seen in the tumor (Walter et al. 2003). Post-gadolinium imaging may be performed using 3D sequences to allow dynamic evaluation of the kidney. This allows assessment of renal vasculature in arterial and venous phases and the renal parenchyma in corticomedullary and nephrographic phases. Vascular invasion of renal vein/inferior vena cava (IVC), although rare, may also be demonstrated without gadolinium administration on T2-weighted or gradient-echo flow-sensitive sequences (Fig. 8.25). As with CT, however, limitations exist in detecting superficial invasion of the renal parenchyma, and small lesions may be missed because of motion artifacts (Kirkali and Tuzel 2003; Yousem et al. 1988). The MR imaging protocols to evaluate renal TCC should also include MRU, which may be static, or dynamic using gadolinium. Static MRU utilizing heavily T2-weighted sequences can permit accurate localization of obstruction (Fig. 8.26), although imaging of undilated systems may be suboptimal (Pretorius et al. 2000; Yousem et al. 1988). This technique is helpful in patients with impaired renal function, where iodinated contrast-enhanced urography is not possible. Contrast-enhanced T1-

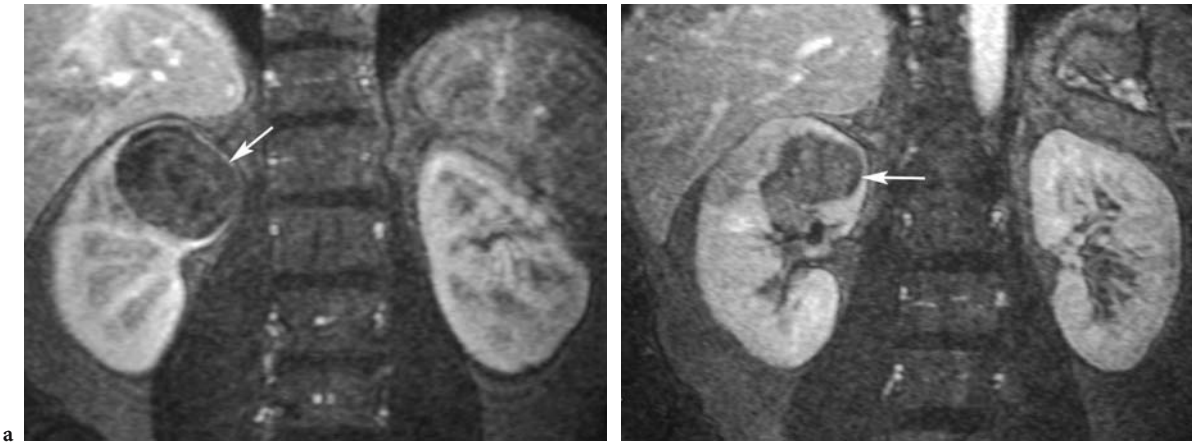


**Fig. 8.23a,b.** Renal transitional cell carcinoma in a 68-year-old woman. **a, b** Coronal contrast-enhanced 3D fast low-angle shot (FLASH) MRA source images in early phase of dynamic acquisition (TR=3.64 ms, TE=1.37 ms) demonstrate mildly enhancing tumor in the right renal pelvis and upper-pole calyx (*arrow*) with extension to involve upper-pole parenchyma but not the perirenal tissues.

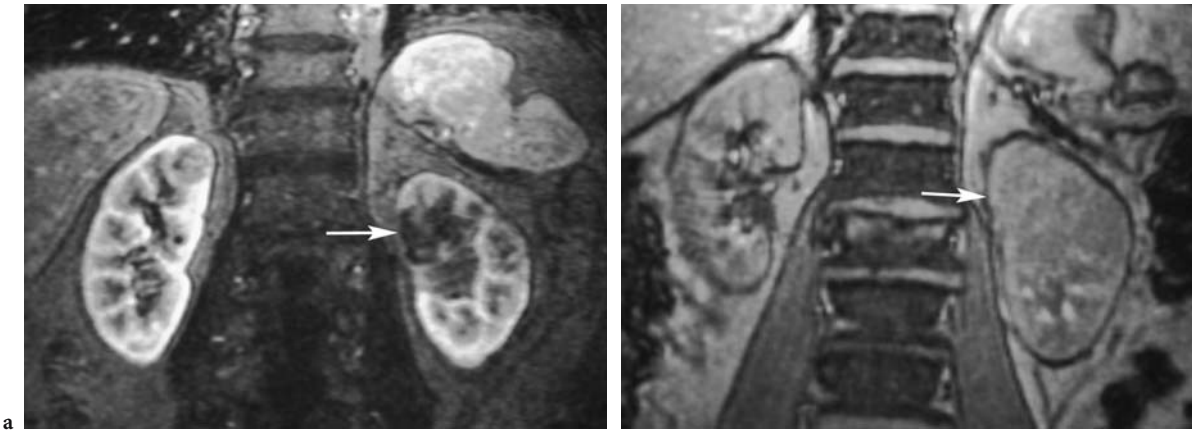


**Fig. 8.24a,b.** Renal transitional cell carcinoma in a 68-year-old woman. Coronal contrast-enhanced 3D fast low-angle shot (FLASH) MRA source images in **a** early and **b** late phases of dynamic acquisition (TR=3.64 ms, TE=1.37 ms) demonstrate moderately enhancing left upper-pole transitional cell carcinoma tumor (*arrow*).

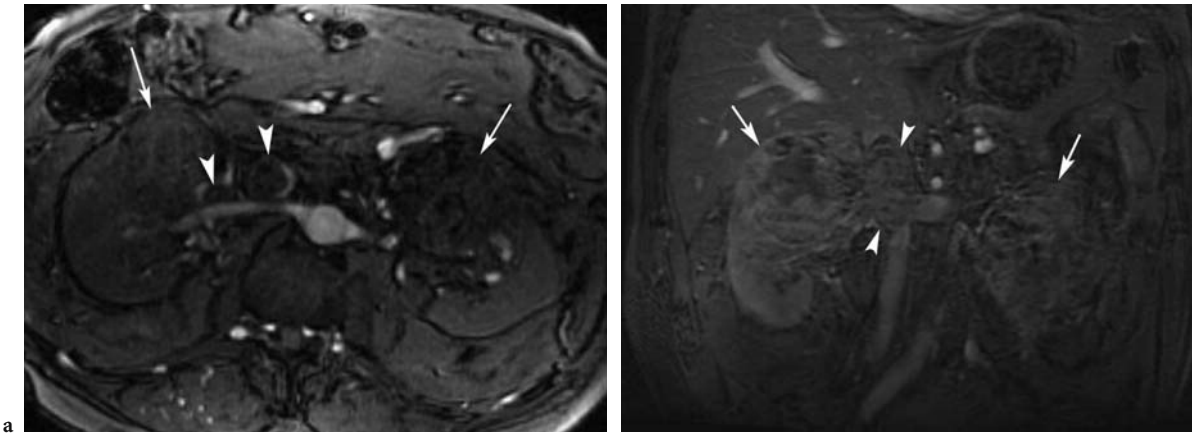
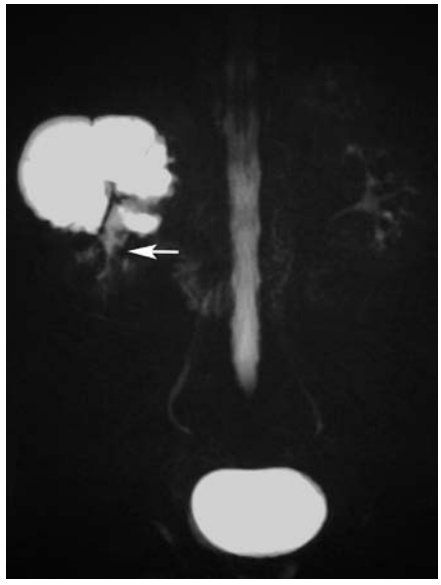


**Fig. 8.25a,b.** Transitional cell carcinoma in a 77-year-old man with hematuria. **a** Axial fat-suppressed fast-spin-echo T2-weighted (TR=8000 ms, TE=104 ms) and **b** coronal gradient-recalled acquisition in the steady state (GRASS; TR=30 ms, TE=8 ms) MR images demonstrate bilateral upper-pole transitional cell carcinoma (*arrows*) with right renal vein and inferior vena cava invasion (*arrowheads*).



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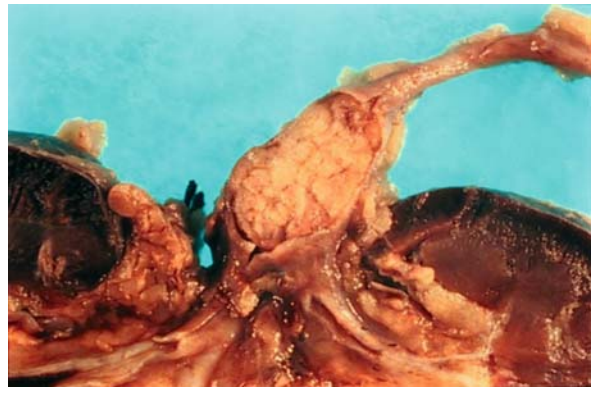

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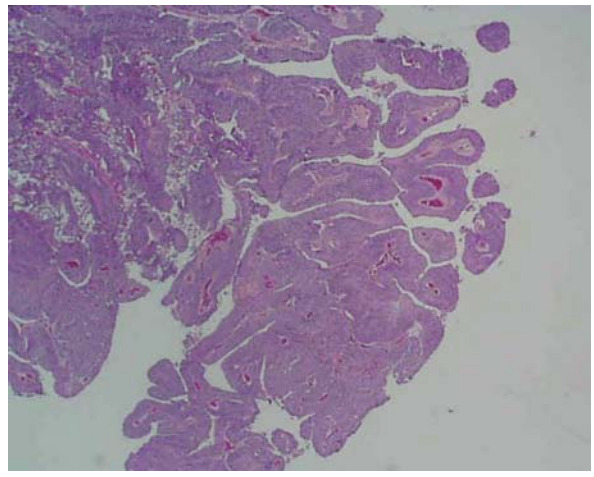

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**Fig. 8.26a-c.** Renal pelvis transitional cell carcinoma in a 65-year-old man. **a** Coronal heavily half-Fourier acquisition single-shot turbo spin-echo (HASTE) T2-weighted MRU (TR=1500 ms, TE=116 ms) MIP image shows focal hydronephrosis of the right upper-pole calyx and irregularity of the pelvis and mid-calyx (*arrow*), consistent with transitional cell carcinoma. **b** Gross pathological section shows tumor in the right renal pelvis and proximal ureter. **c** Microscopic pathological section of tumor (hematoxylin and eosin stain; original magnification, ×40).

weighted MRU with/without diuretic provides dynamic imaging of the entire urinary tract and delayed acquisitions can be obtained at various time intervals depending on degree and level of obstruction. Dynamic MRU also allows an estimate of renal function to be made. Post-processing of the data set to yield MIPs allows 3D rotation and viewing of suspected areas of disease without superimposition of other anatomic structures. This can be performed for both vascular structures and the collecting system; the latter, resembling conventional IVU studies, is readily acceptable to clinicians.

These comprehensive MR protocols can image all the anatomic components of the urinary tract in a single test and offer advantages over other techniques including lack of iodinated contrast medium and radiation exposure. Although MR imaging remains second to CT, it offers further non-invasive imaging of renal masses, which are not adequately characterized by other imaging modalities (Weeks et al. 1995). The main disadvantage of MR imaging is the inability to reliably detect urinary tract calcifications, calculi, and air, which limits its use as a first-line test in the investigation of hematuria. Although the sensitivity of renal parenchymal MR imaging with gadolinium for assessing renal masses and abnormalities of the nephrogram is considered similar to that of CT, spatial resolution is poor compared with IVU or CTU, making it less likely to detect subtle urothelial malignancies (Milestone et al. 1990). Furthermore, the complete characterization of renal masses may require multiple, time-consuming sequences pre- and post-gadolinium administration (Kawashima et al. 2003).

## 8.7 Staging

Tumor stage at diagnosis influences the development of local recurrence and metastases, and hence overall survival (Maher et al. 2004; Hall et al. 1998). Furthermore, treatment and prognosis are largely determined by the depth of tumor infiltration, the degree of lymph node and distant metastases, and the histological tumor type, making exact staging imperative (Table 8.1). Conventional imaging meth-

ods, such as IVU and RP, cannot detect extension into the peripelvic fat or metastases. Cross-sectional imaging with dynamic contrast-enhanced CT or MR imaging is now routinely employed in the pre-surgical work-up of these patients. These techniques can determine intra- and extrarenal local extension of tumor and the presence of nodal or distant metastases with a high degree of accuracy. They are used in conjunction with ureterorenoscopy for staging prior to surgery. In most cases of renal TCC, CT has become routine in the further characterization of lesions demonstrated by other modalities and, despite varying reports on staging accuracy, is currently the preoperative imaging modality of choice (Tables 8.1, 8.2; Buckley et al. 1996; Chan et al. 2002; Scolieri et al. 2000; Urban et al. 1997a). As studies show higher detection rates for urothelial malignancies by CTU over IVU (Caoili et al. 2002), this technique is being advocated as a one-stop diagnostic and staging assessment of suspected urothelial malignancy. Although CT cannot distinguish between stages T0–TII tumor, it can differentiate early-stage TCC confined to the collecting system wall from advanced disease with local extension or distant metastases, which is important to define surgical management (McCarthy and Cowan 2002; Urban et al. 1997b). More advanced tumors infiltrating beyond the muscularis into the peripelvic fat typically show increased, inhomogeneous peripelvic density and stranding, although this finding may also be seen with superimposed infection, hemorrhage, or inflammation, and should be interpreted with caution to avoid overstaging (McCoy et al. 1991). Metastatic spread via urinary or hematogenous routes usually manifests as multifocal mucosal nodules or wall thickening, whereas direct invasion into the upper ureter generates a short or long stricture (Rothpearl et al. 1995). Extrarenal spread can occur at or through the renal hilum, and common sites of metastases include the lungs, retroperitoneum, lymph nodes, and bones. Renal vein or IVC invasion is occasionally seen and can be well demonstrated by comprehensive CTU protocols. The overall accuracy of CT in predicting the pathological stage ranges from 36 to 83% in the literature (Kim and Cho 2003), meaning ureterorenoscopy and biopsy remain essential additional tools for presurgical assessment.

As with CT, MR imaging can detect tumor involvement of the renal parenchyma, perinephric fat, and distant metastases. It therefore offers an alternative staging modality and has been shown to stage TCC lesions greater than 2 cm well (Kirkali and Tuzel 2003). T1-weighted images are used to determine tumor infiltration into the perirenal fat, and to show the endoluminal component. T1-weighted images are also good for detecting nodes, although an abnormal node can only be defined by size. T2-weighted images are used to determine the depth of tumor infiltration into the renal parenchyma and adjacent organs. Magnetic resonance imaging can help in differentiating perirenal changes, as fibrosis appears hypointense on T2-weighted sequences, particularly in long-standing cases (Pretorius et al. 2000). It is the preferred staging examination in patients who cannot tolerate iodinated contrast, and in whom multiplanar and vascular imaging is required for preoperative assessment.

**Table 8.1.** The TNM classification of renal transitional cell carcinoma

| TNM | Histopathological findings |
|---|---|
| Tx | Primary tumor cannot be assessed |
| T0 | No evidence of primary tumor |
| Ta | Papillary non-invasive carcinoma |
| Tis | Carcinoma in situ |
| T1 | Tumor invades subepithelial connective tissue |
| T2 | Tumor invades the muscularis |
| T3 | Tumor invades beyond muscularis into periureteric fat or the renal parenchyma |
| T4 | Tumor invades adjacent organs, pelvic/abdominal wall, or through the kidney into perinephric fat |
| Nx | Regional lymph nodes cannot be assessed |
| N0 | No regional lymph node metastasis |
| N1 | Metastasis in a single lymph node >2 cm or less in greatest dimension |
| N2 | Metastasis in a single lymph node >2 cm but not >5 cm in greatest dimension, or multiple lymph nodes, none >5 cm in greatest dimension |
| N3 | Metastasis in a lymph node >5 cm in greatest dimension |
| Mx | Distant metastases cannot be assessed |
| M0 | No distant metastasis |
| M1 | Distant metastasis |

**Table 8.2.** Histopathological grading of renal transitional cell carcinoma

| Grade | Histopathological grading |
|---|---|
| Gx | Grade of differentiation cannot be assessed |
| G1 | Well differentiated |
| G2 | Moderately differentiated |
| G3–G4 | Poorly differentiated/undifferentiated |

## 8.8 Treatment

Because of the multifocal and metachronous nature of TCC, thorough assessment of the entire urothelium is required prior to treatment. Newly diag-

nosed renal lesions therefore require evaluation of the contralateral kidney and both ureters, usually with IVU and RP, and cystoscopic evaluation of the bladder (Rothpearl et al. 1995). The traditional treatment of renal TCC involves total nephroureterectomy with excision of the ipsilateral ureteral orifice and a contiguous cuff of bladder tissue (Yousem et al. 1988); however, the development of endoscopic and minimally invasive surgical techniques allows renal preservation in some patients, particularly those with a solitary kidney, bilateral tumor, poor renal function, low-grade tumor, or prohibitive operative risk, with results comparable to those of radical surgery (Chen and Bagley 2000; Keeley et al. 1997; Kirkali and Tuzel 2003; Tawfiek and Bagley 1997). Accurate radiological detection and tumor staging is therefore essential to determine appropriate surgical therapy, especially if conservative surgery is being considered, or the intensity of chemotherapy for advanced-stage tumors (Elliott et al. 2001; Tawfiek and Bagley 1997).

## 8.9 Follow-up

There is still no widely accepted protocol for the radiological follow-up of patients with primary TCC of the kidney (Hession et al. 1999; Urban et al. 1997a). Current data suggest that routine follow-up imaging strategies should be individually tailored based on primary tumor characteristics. In general, annual IVU and, if needed RP, is recommended, especially in the first 2 years after initial diagnosis (Herranz-Amo et al. 1999). As recurrent tumor may not be identified radiologically, RP and ureterorenoscopy should be sought if IVU fails to depict or adequately distend the entire upper tract, especially if cystoscopy is being performed or if there is a high index of suspicion. This vigilance is justified in order to detect early recurrence after conservative surgery or, in patients who have only one remaining kidney, to detect contralateral lesions at an early stage when local excision may be feasible. Due to the high rate of metachronous tumor in the bladder, frequent cystoscopy should also be performed. At our institution this is performed every 3 months for the first year, every 6 months for the second year, and yearly thereafter. If a metachronous bladder lesion is identified, a thorough assessment of the upper tracts is made and the cystoscopy cycle returns to that of every 3 months.

The advent of CTU as a diagnostic tool offers a potential alternative follow-up in these patients allowing assessment of the entire urothelium and also facilitating virtual cystoscopy to assess the bladder. Computed tomographic tomography will likely become the primary radiological method of follow-up in these patients who require assessment of the entire urothelium, although cystoscopy is still necessary for direct bladder visualization and biopsy.

## 8.10 Conclusion

Transitional cell carcinoma is a common urological malignancy and in up to 5% of cases occurs in the kidney. The multicentric nature of TCC makes assessment of the entire urothelium essential prior to treatment. Vigilant urological and radiological follow-up is also warranted post-treatment to assess for metachronous lesions and recurrence. Conventional imaging modalities, such as IVU, RP, and US, still play a pivotal role in the assessment of hematuria in conjunction with endourological techniques. The recent advent of minimally invasive surgery that allows renal preservation makes accurate staging, usually with CT or MR imaging, mandatory to determine appropriate therapy. The technique of CTU has recently developed and offers superior detection of urinary tract tumors and calculi, as well as the ability to assess perirenal tissues and stage lesions, as a single comprehensive study. In the future, it is probable that CTU will become the standard investigation in the initial assessment and follow-up of patients with suspected TCC. Similar MR imaging protocols can also be used in patients not suitable for CTU, although detection of calculi may be suboptimal.

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