

Transitional Cell Carcinoma of the Upper Urinary Tract: Spectrum of Imaging Findings¹

CME FEATURE

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LEARNING OBJECTIVES FOR TEST 5

After reading this article and taking the test, the reader will be able to:

- Identify the typical and atypical appearances of upper urinary tract TCC with conventional imaging modalities (EU, RP, US) and emerging CT and MR imaging techniques.
- Describe the comprehensive, multiphase CT and MR imaging techniques for one-stop evaluation of upper urinary tract TCC.
- Discuss the combined radiologic and endourologic approach to staging and follow-up of upper urinary tract TCC.

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Transitional cell carcinoma (TCC) accounts for up to 10% of neoplasms of the upper urinary tract and usually manifests as hematuria. Imaging plays an important role in assessment of upper tract disease, unlike in bladder TCC, diagnosis of which is usually made at cystoscopy. Traditional imaging modalities, such as excretory urography, retrograde pyelography, and ultrasonography, still play pivotal roles in diagnosis of upper tract TCC, in combination with endourologic techniques. The multicentric nature of TCC makes assessment of the entire urothelium essential before treatment. The advent of minimally invasive surgery, which allows renal preservation in selected patients, makes accurate tumor staging mandatory to determine the appropriate therapy; staging is usually performed with computed tomography (CT) or magnetic resonance (MR) imaging. Vigilant urologic and radiologic follow-up is warranted to assess for metachronous lesions and recurrence. The emerging technique of CT urography allows detection of urinary tract tumors and calculi, assessment of perirenal tissues, and staging of lesions; it may offer the opportunity for one-stop evaluation in the initial assessment of hematuria and in follow-up of TCC. Similar MR imaging protocols can be used in patients who are not candidates for CT urography, although detection of urinary tract calcifications may be suboptimal.

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Abbreviations: EU = excretory urography, MIP = maximum intensity projection, RP = retrograde pyelography, TCC = transitional cell carcinoma, 3D = three-dimensional

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Introduction

Transitional cell carcinoma (TCC) is commonly encountered in the urinary bladder and is usually diagnosed at cystoscopy. Five percent of urothelial tumors arise from the ureter or the renal pelvis or calices, accounting for approximately 10% of upper tract neoplasms (1,2). Patients with TCC typically present with hematuria, which may be frank or microscopic. Up to one-third of patients present with flank pain or acute renal colic, symptoms more typically associated with calculi. Occasionally, tumors may manifest with distant metastases or be discovered incidentally at radiologic examination.

Renal TCC most frequently arises in the extrarenal part of the pelvis, followed by the infundibulocaliceal region (3). The distribution is equal between the left and right kidneys, with 2%–4% of cases occurring bilaterally. Twenty-five percent of upper tract tumors occur in the ureter, where 60%–75% of cases are found in the lower third, with no side predominance (2). Tumor spread occurs by mucosal extension or local, hematogenous, or lymphatic invasion. The most common sites for metastases are the liver, bone, and lungs. The tumor stage at diagnosis influences the development of local recurrence and metastases and hence overall survival (1,4). Multicentric TCC is common and is associated with poor survival (4). Synchronous or metachronous tumor of the ipsilateral or contralateral collecting system is also common, necessitating vigilant urologic and radiologic follow-up.

This article reviews the characteristic imaging features of upper tract TCC and outlines the role of imaging in diagnosis, preoperative staging, and follow-up. The appearances at excretory urography (EU), retrograde pyelography (RP), and renal ultrasonography (US) are reviewed. Emphasis is placed on cross-sectional imaging modalities such as computed tomographic (CT) urography, which is fast becoming the investigation of choice in the assessment of patients with suspected TCC. The emerging role of magnetic resonance

(MR) imaging techniques such as gadolinium-enhanced three-dimensional (3D) MR angiography and urography is also discussed.

Pathogenesis

Upper tract TCC typically occurs in the 6th and 7th decades of life, with males affected three times more often than females (3). Besides increasing age and male gender, the most important risk factor is smoking, with smokers being two to three times more likely to develop TCC than nonsmokers (3). 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 (2). These substances are metabolized and excreted in the urine as carcinogenic substances that act locally on the urothelium. Stasis of urine and structural abnormalities such as horseshoe kidney are also associated with increased prevalence (5).

Upper tract TCC is common in families affected with “Balkan endemic nephropathy.” Familial metabolic abnormalities in these patients lead to tubulointerstitial nephritis, renal failure, carcinogenic glomerulotubular toxins, and multiple tumors (2). Analgesic abuse, particularly long-term use of phenacetin, produces capillo-sclerosis and predisposes to a highly invasive type of TCC that preferentially involves the renal pelvis (5). Human papilloma virus and hereditary nonpolyposis colon cancer have also been suggested as risk factors for TCC of the upper tract, and the prevalence is significantly higher in areas where endemic “blackfoot disease” is seen (2).

Pathologic Features

Upper tract TCC is histologically and cytologically similar to bladder TCC (6). Eighty-five percent of upper tract TCCs are low-stage, superficial, papillary neoplasms with a broad base and frondlike morphologic structure (7). These tumors are usually small at diagnosis, grow slowly, and follow a relatively benign course (8). Pedunculated or diffusely infiltrating tumor is less common, accounting for approximately 15% of upper

tract TCCs, but tends to behave more aggressively and be more advanced at diagnosis (9). Infiltrating tumors are characterized by thickening and induration of the ureteric or renal pelvic wall. If the renal pelvis is involved, there is often invasion into the renal parenchyma. However, this infiltrative growth pattern preserves renal contour and differs from renal cell carcinoma, which is typically expansile.

Synchronous bilateral TCC has been reported to occur in 1%–2% of cases of renal lesions and 2%–9% of cases of ureteric lesions. Eleven percent to 13% of patients with upper tract TCC subsequently develop metachronous upper tract tumors (3). Furthermore, up to 50% of patients initially presenting with upper tract TCC will develop metachronous tumors in the bladder, typically developing within 2 years of surgical treatment and seen more commonly with ureteric tumors than with renal tumors (2,10). Two percent of patients with bladder TCC also have synchronous upper tract tumors at presentation, and 6% will develop metachronous upper tract disease (11).

Diagnosis

The evaluation of hematuria requires assessment of the entire urothelium and the renal parenchyma for tumor and of the urinary tract for calculi. The standard work-up for these patients as recommended by the American Urological Association consists of urinalysis and cytologic analysis, cystoscopy, and EU (12,13). The initial diagnosis of TCC is usually made on the basis of findings from urine cytology; the diagnostic yield is improved with selective lavage and collection and with brush biopsies performed at cystoscopy or RP (14,15). However, these techniques are invasive and technically demanding. The limitations of EU in assessing the renal parenchyma usually require the supplemental use of US, CT, or MR imaging to evaluate the kidneys for masses (16–18). Furthermore, additional imaging is often required to clarify indeterminate findings at EU.

Recently, the technique of multiphasic CT urography has emerged as an alternative method of assessing patients with hematuria, offering su-

perior detection of urinary calculi and renal parenchymal masses, and in some studies, improved detection of urothelial lesions. Because surrounding structures can also be assessed, CT urography is rapidly replacing EU as the definitive study for these patients, potentially shortening the duration of diagnostic evaluation. MR imaging, including the newer techniques of MR angiography and MR urography, is also being used, particularly in patients who cannot tolerate iodinated contrast material and in whom multiplanar, vascular, and collecting system imaging is required. Because of the multifocal and metachronous nature of TCC, thorough assessment of the entire urothelium is required before treatment. Therefore, evaluation of the upper tract with EU (or CT urography if equivalent) is indicated in those with newly diagnosed bladder TCC; conversely, patients with upper tract TCC should undergo cystoscopic evaluation.

Excretory Urography

The diagnosis of upper tract TCC is most frequently made at EU in patients undergoing investigation for hematuria. EU remains the noninvasive method of choice for imaging the detailed anatomy of the pelvicaliceal system and ureters (15,17–19), although this is likely to change as CT urography becomes more refined and accepted as a primary diagnostic investigation. The appearances of upper tract lesions at EU are well described. Calcification may be visualized on control radiographs but is uncommon, occurring in 2%–7% of tumors, and, when present, may mimic urinary tract calculi (3). Enlargement of the kidney may be seen with a large infiltrating tumor or a ureteric tumor causing prolonged obstruction.

Renal TCC usually manifests as a filling defect within the contrast-enhanced collecting system, which may be single or multiple and smooth, irregular (Fig 1), or stippled. The stipple sign refers to tracking of contrast material into the interstices of a papillary lesion (Fig 2) (2,3). However, this



Figures 1, 2. (1) TCC of the renal pelvis in a 60-year-old man with painless hematuria. Fifteen-minute EU image shows a large irregular filling defect (arrow) involving the right renal pelvis and extending into the lower pole caliceal system. (2) TCC of the renal pelvis in a 65-year-old man. Fifteen-minute EU image shows a large stippled filling defect involving the collecting system of the right kidney (arrow).

sign may also be seen with blood clot and fungus balls and should be interpreted with caution. Stricture-like lesions of the pelvicaliceal system may be evident and, if multiple, may mimic renal tuberculosis (5). Filling defects within dilated calices may occur secondary to tumor obstruction of the infundibulum and may lead to caliceal “amputation” (Fig 3). Tumor-filled, distended calices have been called “oncocalices.” If these fail to opacify with contrast material, they are known as “phantom calices.”

Ureteric TCC is typically seen as single or multiple ureteric filling defects with or without surface stippling and proximal ureteric dilatation. It is important to remember that long-standing tumor obstruction of the ureteropelvic junction or ureter may lead to generalized hydronephrosis and poor excretion. This is a major disadvantage of EU when compared with CT urography, which allows assessment of nonfunctioning kidneys. Upper tract filling defects may be nonspecific at EU, and obstruction of pelvicaliceal drainage may obscure distal synchronous ureteric tumors, meaning that RP is usually performed to further assess these patients.

Retrograde Pyelography

RP is usually performed during cystoscopy or to further characterize abnormalities detected at EU, in inadequately excreting kidneys, or in cases



Figure 3. TCC of the upper pole collecting system in a 55-year-old woman. Fifteen-minute EU image shows amputation of the upper pole calix (arrow) secondary to TCC.

of contrast material allergy. Although invasive, RP allows confirmation of the radiologic diagnosis while also facilitating ureterorenoscopy with biopsy or brushing and cytologic examination of localized urine collections. As with EU, renal TCC typically appears as an intraluminal filling defect, which may be smooth, irregular, or stippled. Opacification of a tumor-involved calix



Figure 4. Renal TCC in a 67-year-old woman. RP image shows a diffuse infiltrating TCC involving the right lower pole calix with irregularity of the involved mucosa (arrow).

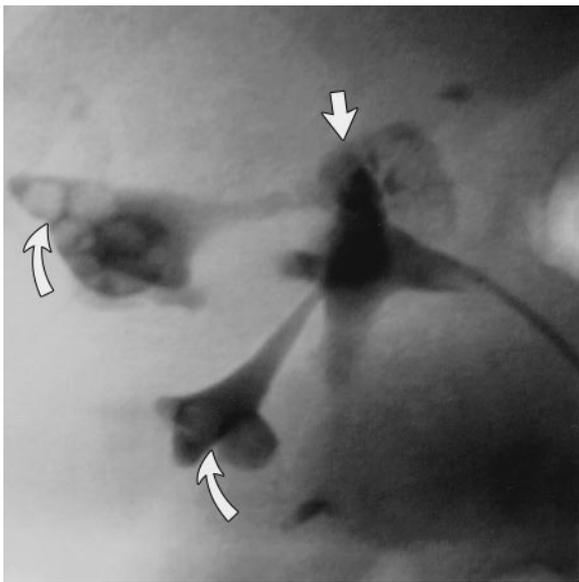


Figure 5. Renal TCC in a 67-year-old man with hematuria. RP image shows amputation of the upper pole calix due to TCC (straight arrow). Multiple calculi are also seen within the lower pole and interpolar calices (curved arrows).

may show irregular papillary or nodular mucosa (Fig 4). If TCC involves an infundibulum, then an “amputated” calix may be seen with or without focal hydronephrosis and calculi secondary to urinary stasis (Fig 5). Tumor-filled, distended calices are known as “oncocalices.”

Ureteric TCC classically appears as a solitary, polypoid filling defect with ureteric dilatation

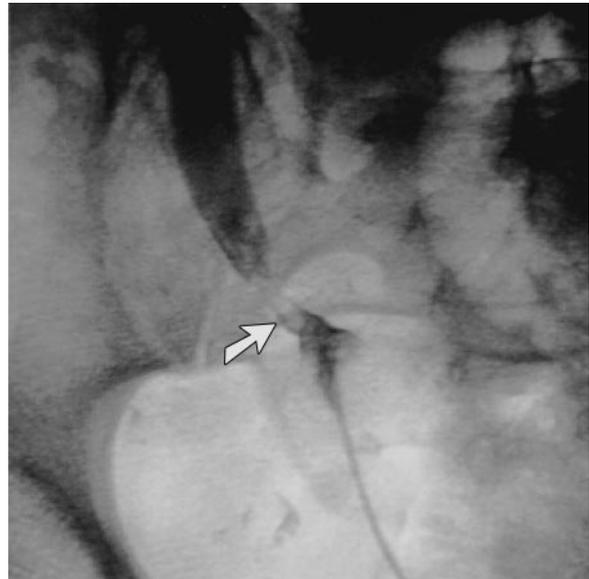


Figure 6. Ureteric TCC in a 62-year-old man. RP image shows an irregular stricture (arrow) with hydronephrosis proximal to the site of the tumor.

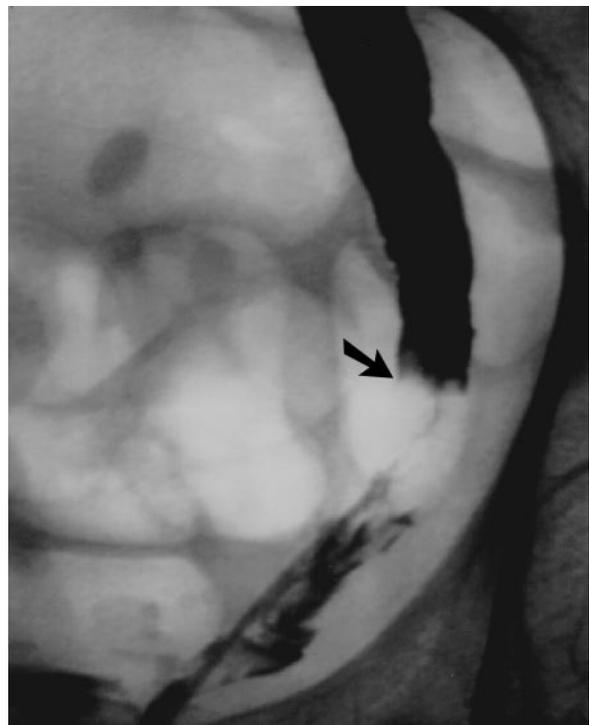


Figure 7. Ureteric TCC in a 68-year-old woman. RP image shows a long irregular stricture of the left distal ureter with proximal hydronephrosis and “shouldering” (arrow).

proximal to the lesion (Fig 6). The ureter itself may occasionally be fixed by diffuse ureteric wall infiltration from an intramural lesion. An “apple core” appearance may be observed with eccentric or encircling ureteric lesions (Fig 7). Malignant



Figure 8. TCC of the pelviureteric junction in a 76-year-old man with painless hematuria. RP image shows concentric narrowing of the pelviureteric junction (arrow) with hydronephrosis. This appearance simulates benign disease but was shown to represent TCC at histologic analysis.

ureteric strictures may be circumferential or eccentric and can occasionally be confused with benign strictures (Fig 8), although ureteric fixation and nontapering margins are suggestive of malignancy (3). At RP, localized ureteric dilatation around and distal to the filling defect may give rise to the “goblet” sign (Fig 9), which occurs due to slow tumor growth with resultant lumen expansion and is not characteristic of more acute causes of obstruction.

Ultrasonography

Currently, renal US is frequently requested in the evaluation of patients with hematuria to assess for renal parenchymal masses. However, US is not as sensitive as CT in identifying or characterizing renal masses (16,20–22); as CT urography emerges as an initial imaging investigation for hematuria, US will likely play a limited diagnostic role in the future. US can be useful in patients with renal functional impairment or allergy to iodinated contrast material, although MR imaging is becoming established as the investigation of choice in these patients. US can also allow assess-

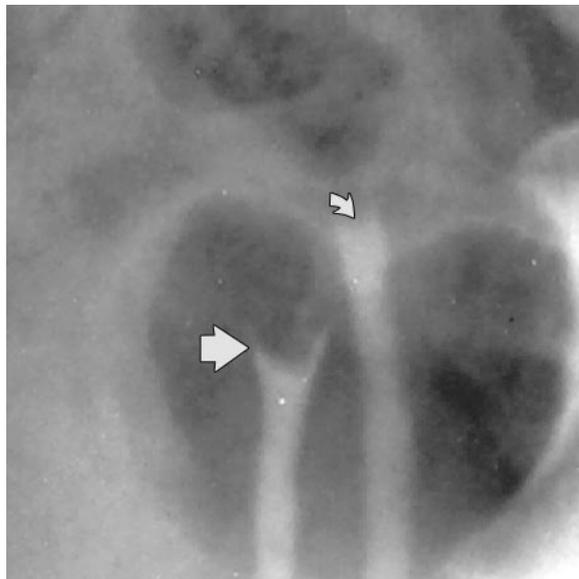


Figure 9. Ureteric TCC in a 58-year-old man. RP image shows a duplex right collecting system. TCC in the midportion of the ureter draining the upper pole moiety produces the characteristic goblet sign (straight arrow). Another tumor is identified in the ureter draining the lower pole moiety (curved arrow).

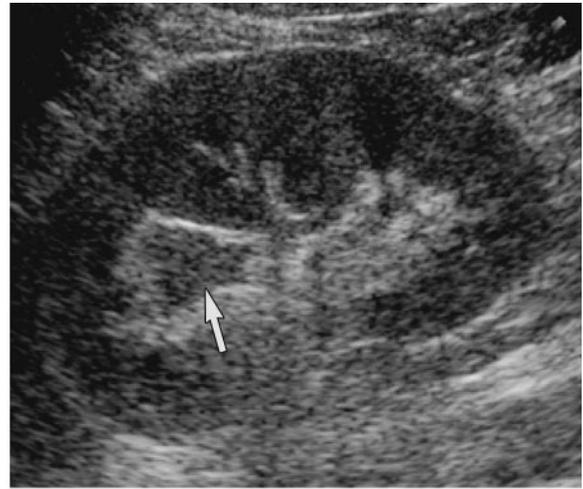
ment of the degree of hydronephrosis and guide interventional procedures in the setting of acute obstruction.

At US, renal pelvic TCC typically appears as a central soft-tissue mass in the echogenic renal sinus, with or without hydronephrosis (Figs 10, 11) (2). TCC is usually slightly hyperechoic relative to surrounding renal parenchyma; occasionally, high-grade TCC may show areas of mixed echogenicity (Fig 12). Infundibular tumors may cause focal hydronephrosis. Although lesions may extend into the renal cortex and cause focal contour distortion, typically TCC is infiltrative and does not distort the renal contour (3).

US has a limited role in the evaluation of ureteric TCC as the ureters are rarely visualized in their entirety, even if dilated. If visualized, these tumors are typically intraluminal soft-tissue masses with proximal distention of the ureter (23). US also allows limited assessment of periureteric tissues. Recent developments in high-resolution endoluminal US performed during ureterorenoscopy have shown promise in the evaluation of upper tract TCC, offering potential advantages over other imaging techniques, and may assume a more prominent role in future diagnosis (2,24).



10.



11.

Figures 10, 11. (10) Renal TCC in a 59-year-old woman. Sagittal US scan shows a tumor (arrows) in the echogenic renal sinus. Tumor tissue is more echogenic than the surrounding renal cortex but less echogenic than renal sinus fat. (11) Renal TCC in a 55-year-old man. Sagittal US scan of the left kidney shows a tumor in the upper pole (arrow).

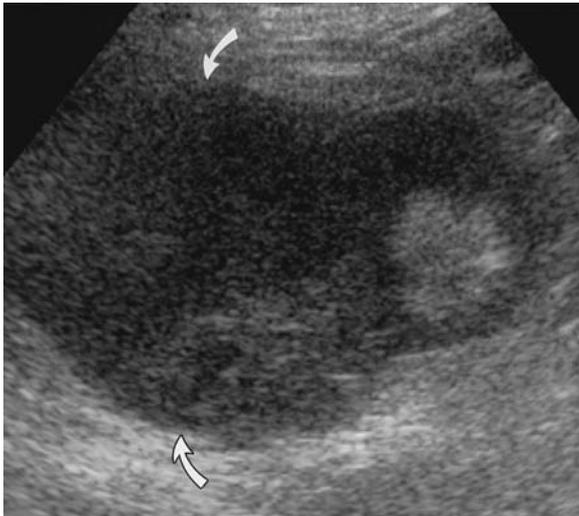


Figure 12. Renal TCC in a 65-year-old woman. Sagittal US scan shows a large mass of mixed echogenicity (arrows) involving the upper pole calix and overlying renal parenchyma. At histologic analysis, the mass was shown to represent high-grade TCC.

Computed Tomography

CT is well established in the preoperative staging and assessment of upper tract TCC. CT has also been shown to be more sensitive than either US or EU in the detection of small renal mass lesions

and urinary tract calculi (15,25–30). The recent advent of CT urography, offering single breath-hold coverage of the entire urinary tract, improved resolution, and the ability to capture multiple phases of contrast material excretion, offers improved diagnostic potential over EU and US in the assessment of patients with hematuria due to calculi or tumor (16,18,29,30). Recent studies have also shown higher detection rates for upper and lower tract urothelial malignancies with CT urography over EU (17,31). Although the American College of Radiology still recommends EU in the investigation of hematuria, as CT urography 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.

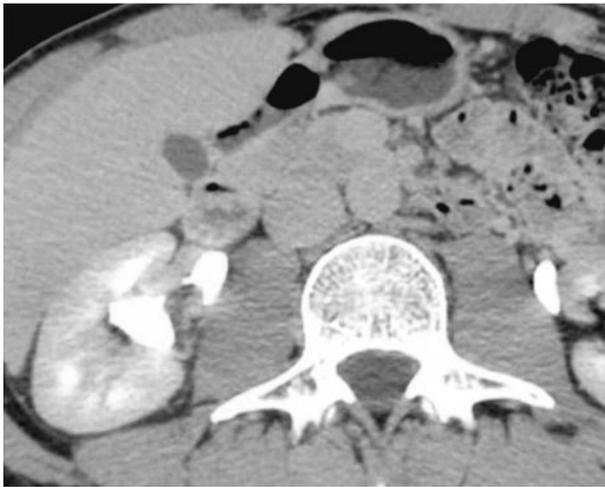
Typically, CT urography consists of a multiphasic helical CT protocol (Fig 13). A pre-enhancement scan is initially performed from the upper pole of the kidney to the lower edge of the symphysis pubis to exclude urinary tract calculi. A late arterial, early corticomedullary phase scan of the kidney and lower pelvis, beginning 15–25 seconds after contrast material infusion, allows



a.



b.



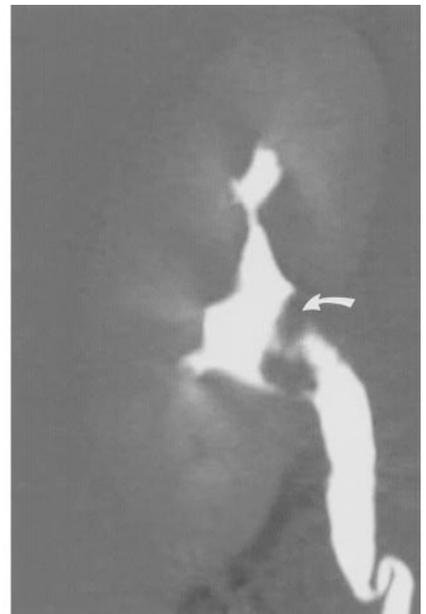
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e.



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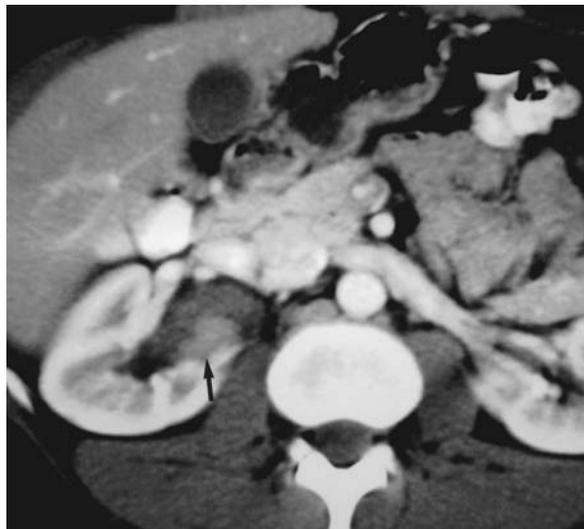


Figure 14. TCC of the renal pelvis in a 66-year-old man with hematuria. Axial nephrographic phase CT scan shows a sessile filling defect (arrow), which is typical of renal pelvic TCC.

evaluation for vascular abnormalities. In the interest of decreasing radiation exposure and time of examination, however, this scan may be omitted unless a vascular abnormality is suspected. A nephrographic phase scan of the kidney, performed 80–140 seconds after contrast material infusion, allows assessment of the renal parenchyma. An excretory phase scan from the upper pole of the kidney to the symphysis pubis, performed 4–8 minutes after contrast material infusion, allows assessment of the urothelium. Some authors advocate a two-phase hematuria protocol where a nephrographic phase is performed only if the initial nonenhanced scan does not demonstrate a satisfactory cause for the patient's hematuria (18).

Three-dimensional reformations typically include thick and thin slab coronal and sagittal MIPs for the kidneys, ureters, and bladder, al-

though other 3D reformation techniques can be used. Coronal reformation in particular demonstrates the longitudinal extent of a lesion, allows assessment for multicentric tumors, and provides urologists with a familiar imaging format (Fig 13). Viewing the opacified system at wider window settings such as bone windows can also aid in identifying and differentiating subtle lesions (Fig 13).

Unlike EU, imaging is not dependent on a functioning kidney and the tract distal to a lesion can be evaluated. CT urography may reveal causes of hematuria other than tumor or calculi, such as papillary necrosis, inflammatory lesions, or infarcts. Precontrast scans are necessary to detect calculi and obtain accurate attenuation values for nonopaque filling defects, whereas postcontrast scans aid in confirming lesion location and extent. On precontrast images, TCC is typically hyperattenuating (5–30 HU) to urine and renal parenchyma (Fig 13) but less attenuating than other pelvic filling defects such as clot (40–80 HU) or calculus (>100 HU).

Renal TCC is typically seen as a sessile filling defect in the excretory phase, which expands centrifugally with compression of the renal sinus fat (Fig 14). Other appearances include pelvicaliceal irregularity, focal or diffuse mural thickening, oncocalix, and focally obstructed calices. Early tumors confined to the muscularis are separated from the renal parenchyma by renal sinus fat or excreted contrast material and have normal-appearing peripelvic fat (Fig 13). Advanced TCC extends into the renal parenchyma in an infiltrating pattern that distorts normal architecture (Figs 15, 16). However, reniform shape is typically preserved (Figs 17, 18), unlike in renal cell carcinoma.

Figure 13. TCC of the renal pelvis in a 43-year-old man with flank pain and hematuria. **(a)** Axial nonenhanced CT scan shows a mass (arrow) in the right renal pelvis. The mass is slightly hyperattenuating relative to the urine and renal parenchyma. **(b)** Axial nephrographic phase CT scan shows that the mass (arrow) has characteristic early enhancement, which is less than that of the surrounding renal parenchyma. **(c)** Axial excretory phase CT scan shows the mass within the renal pelvis with surrounding excreted contrast medium. **(d)** Axial excretory phase CT scan (bone window) shows the lesion more clearly (arrow). **(e)** Coronal maximum intensity projection (MIP) image shows the tumor (arrow) in EU format. **(f)** Detail of a coronal MIP image shows the lesion more clearly (arrow).

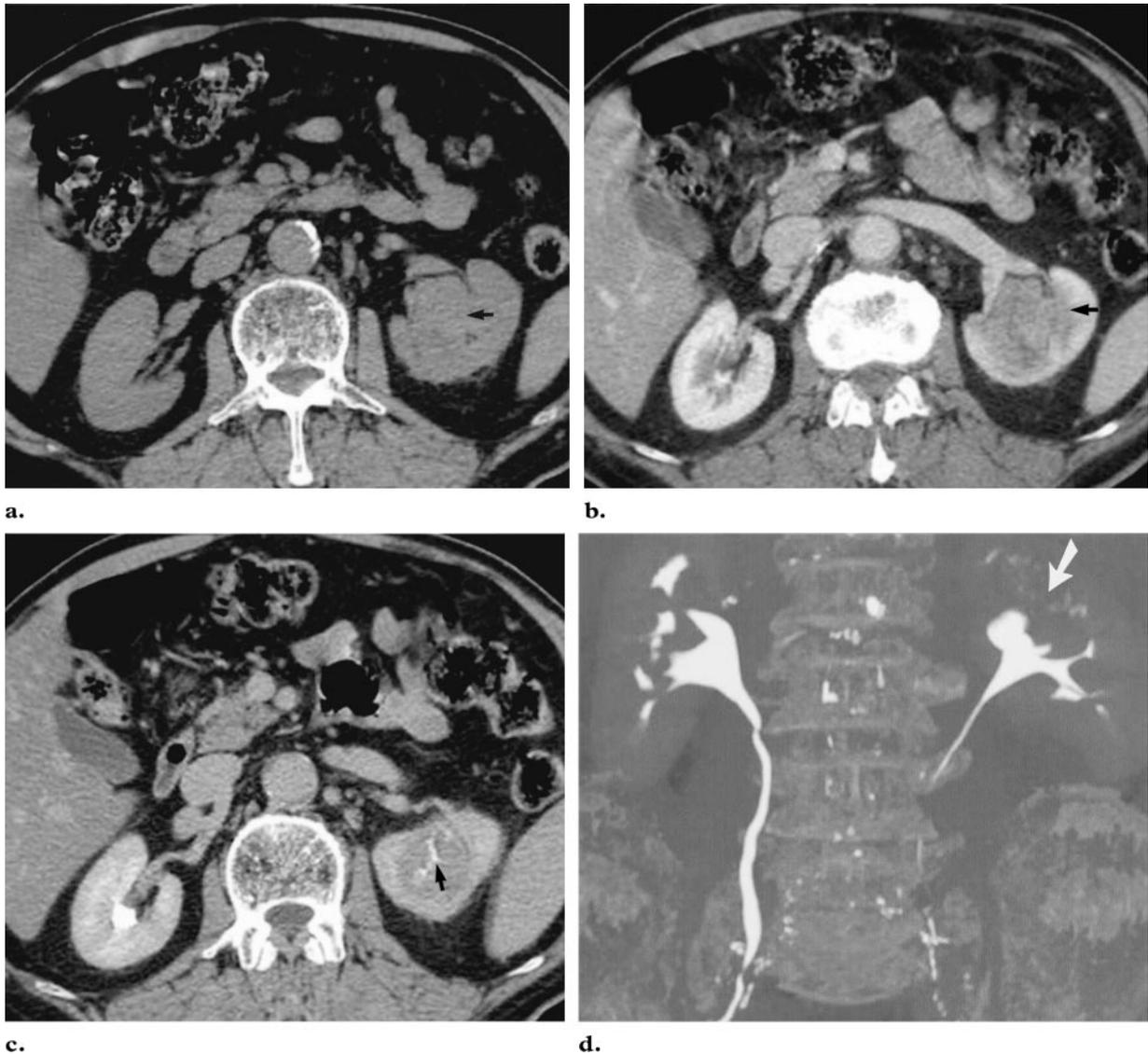


Figure 15. TCC of the upper renal pole in a 61-year-old woman. **(a)** Axial nonenhanced CT scan shows a mass (arrow) in the upper pole calyx of the left kidney. **(b)** Axial nephrographic phase CT scan shows characteristic early enhancement of the tumor with extension into the surrounding upper pole parenchyma (arrow). **(c)** Axial excretory phase CT scan shows the diffuse tumor with a small amount of excreted contrast medium centrally (arrow). **(d)** Coronal MIP image shows the extent of the tumor (arrow) in EU format.

Both TCC and renal cell carcinoma can show early enhancement and de-enhancement after contrast material administration (30). Renal cell carcinoma, being hypervascular, tends to enhance more, although the two tumors often cannot be

differentiated. 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 have these appearances. A large infiltrating renal TCC may occasionally manifest with areas of necrosis and must be differentiated from lymphoma, metastases,



Figure 16. Renal TCC in a 54-year-old man. Axial excretory phase CT scan shows TCC expanding centrifugally from the right renal pelvis. Note the parenchymal invasion with a delay in the cortical nephrogram (arrow).

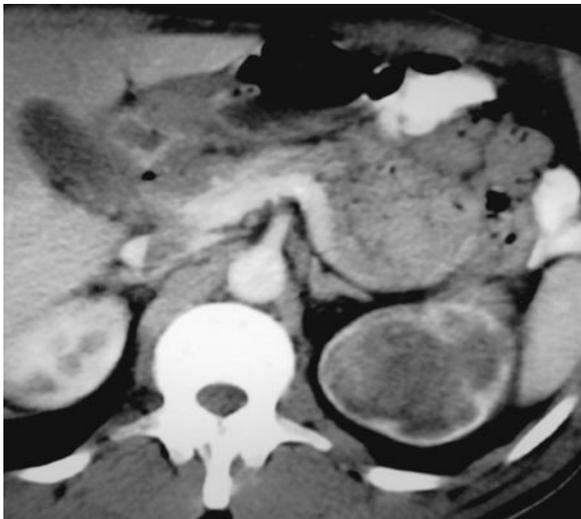


Figure 17. Renal TCC in a 53-year-old man. Axial nephrographic phase CT scan shows diffuse tumor infiltration of the left kidney with preservation of its reniform contour.

and xanthogranulomatous pyelonephritis, which can have a similar appearance (3,5).

Hydronephrosis is the most frequent finding in ureteric TCC and hydroureter can often be seen to the point of obstruction, where Hounsfield unit values for attenuation and enhancement usually

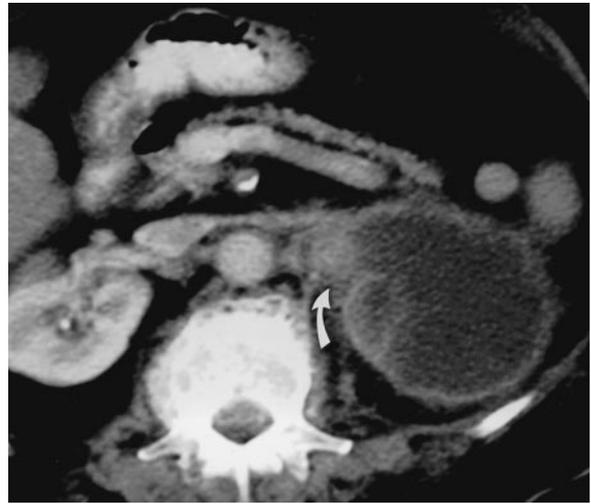


Figure 18. Renal and ureteric TCC in a 76-year-old woman with gross hematuria and flank pain. Axial nephrographic phase CT scan shows extensive involvement of the left kidney and proximal ureter with TCC and perinephric extension of the tumor (arrow). Note the preservation of the reniform contour.

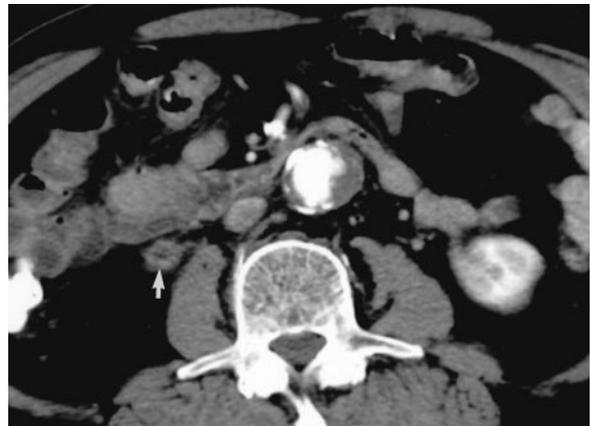
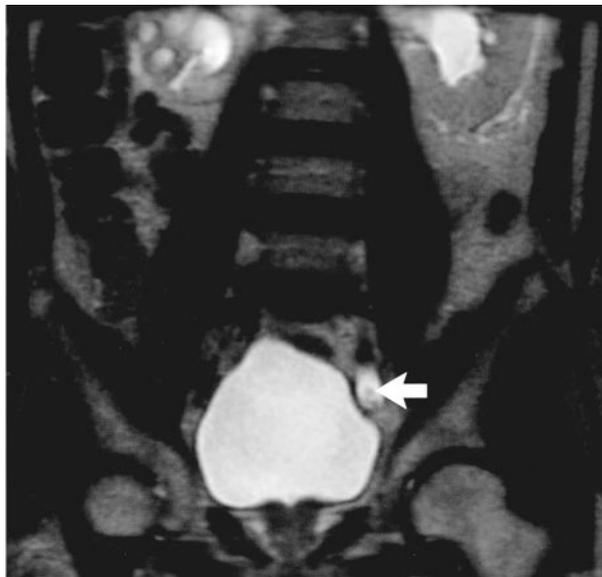
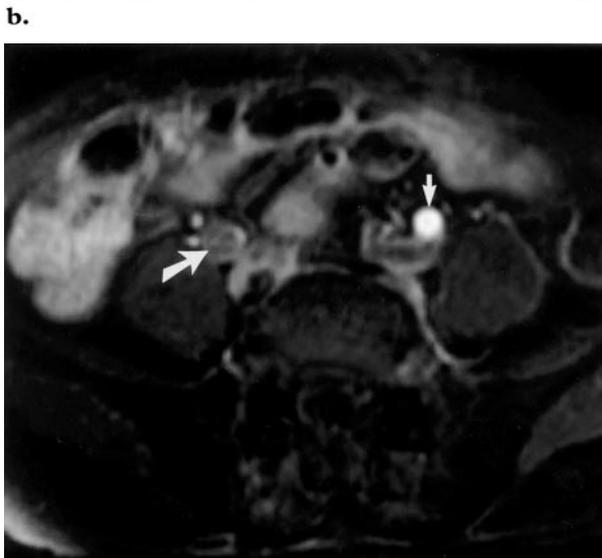


Figure 19. Ureteric TCC in a 62-year-old man with right flank pain. Axial nephrographic phase CT scan shows enhancing TCC in the wall of the right ureter (arrow) with periureteric stranding and tumor extension.

allow differentiation of TCC from calculus and clot. Ureteric wall thickening (eccentric or circumferential), luminal narrowing, or an infiltrating mass are other features of disease (29). A thickened enhancing ureteric wall with periureteric fat stranding is suggestive of extramural spread (Fig 19).



a.
Figure 20. Bilateral ureteric TCC in a 57-year-old woman. **(a, b)** Coronal T2-weighted MR images (repetition time msec/echo time msec = 1655/99.6) show low-signal-intensity tumors in the distal right (arrow in **a**) and distal left (arrow in **b**) ureters. Note the high-signal-intensity urine surrounding the tumors. **(c)** Axial gadolinium-enhanced T1-weighted MR image (616.7/10) obtained with fat saturation shows enhancement of the right ureteric tumor (large arrow). Note the gadolinium contrast material in the left ureter (small arrow) above the tumor.



CT urography allows identification of lesions at an early stage, thereby allowing nephron-sparing surgery. Axial source images also allow assessment of surrounding structures. Adequate distention and opacification are fundamental factors in the thorough evaluation of the urothelium at CT urography. The increased radiation exposure is estimated at only 50%–80% over a complete EU series (30). Although reformatting and review of multiple images with different window settings is time-consuming, CT urography has the potential to stand alone as a comprehensive “one-stop” frontline study for hematuria and therefore detection of TCC.

MR Imaging

MR imaging is infrequently used in the primary assessment of upper tract TCC, and the MR imaging characteristics of this tumor are not well described. In general, MR imaging has not played

a leading role in renal tumor imaging due to limitations in image quality, time-consuming sequences, and susceptibility to artifacts. Recently, however, the development of newer fast sequences has led to increasing use and MR imaging has been shown to equal CT in the detection and diagnosis of renal masses (32–34).

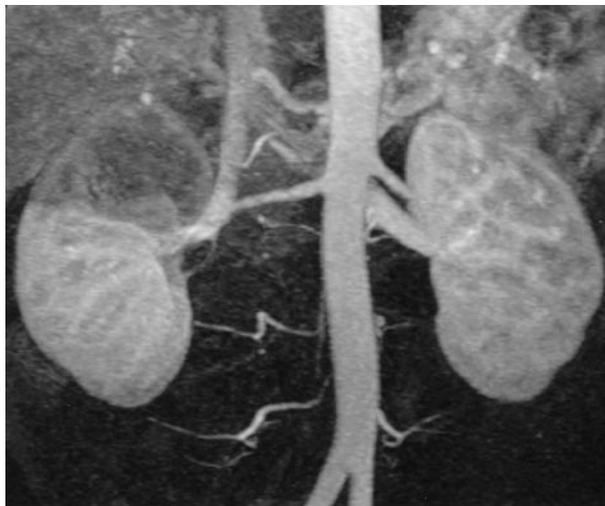
MR imaging offers inherently high soft-tissue contrast, is independent of excretory function, and allows multiplanar imaging, which permits direct image acquisition in the plane of tumor spread. The coronal plane is often advantageous because it allows evaluation of the kidneys, renal vessels, inferior vena cava, and spine in a small number of sections. As with CT, MR imaging can



a.



b.



c.

Figure 21. Renal TCC in a 68-year-old woman. (a, b) Nephrographic phase (a) and excretory phase (b) coronal gadolinium-enhanced 3D fast low-angle shot source MR angiograms (3.64/1.37) show a moderately enhancing TCC (arrow) in the upper pole of the right kidney. (c) Gadolinium-enhanced 3D MIP MR angiogram shows the tumor more clearly. Note the retroaortic segment of the left renal vein.

demonstrate tumor involvement of the renal parenchyma, perinephric tissues, or periureteric tissues and distant metastases (35,36).

TCC has lower signal intensity than the normally high-signal-intensity urine on T2-weighted images, permitting good demonstration of tumor in a dilated collecting system (Fig 20). However, TCC is nearly isointense to renal parenchyma on T1- and T2-weighted images, meaning that gadolinium contrast material is necessary for accurate assessment of tumor extent (3,33). Although TCC is a hypovascular tumor, moderate enhancement is seen with gadolinium contrast material, although not to the same degree as renal parenchyma (37). Postcontrast imaging may be performed by using 3D sequences to allow dynamic evaluation of the kidney (Fig 21). This allows assessment of the renal vasculature in arterial and venous phases and of the renal parenchyma in corticomedullary and nephrographic phases. Vascular invasion of the renal vein or inferior vena cava, although rare, may be demonstrated without gadolinium contrast material by using T2-weighted or gradient-echo flow-sensitive sequences (Fig 22).

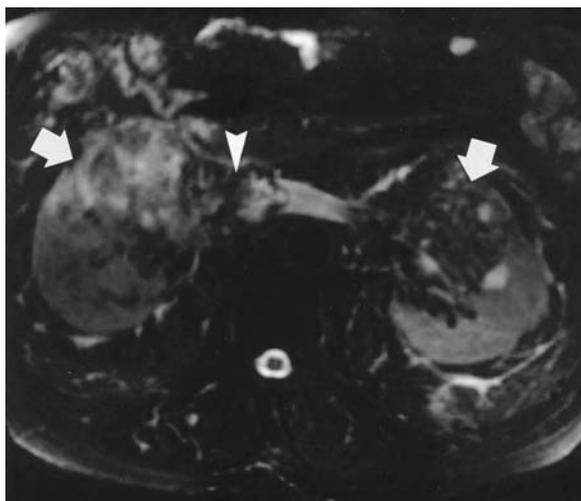


Figure 22. Bilateral renal TCC in a 77-year-old man with hematuria. Axial T2-weighted fast spin-echo MR image (8000/104) obtained with fat saturation shows TCC in the upper poles of both kidneys (arrows) with invasion of the right renal vein and inferior vena cava (arrowhead).

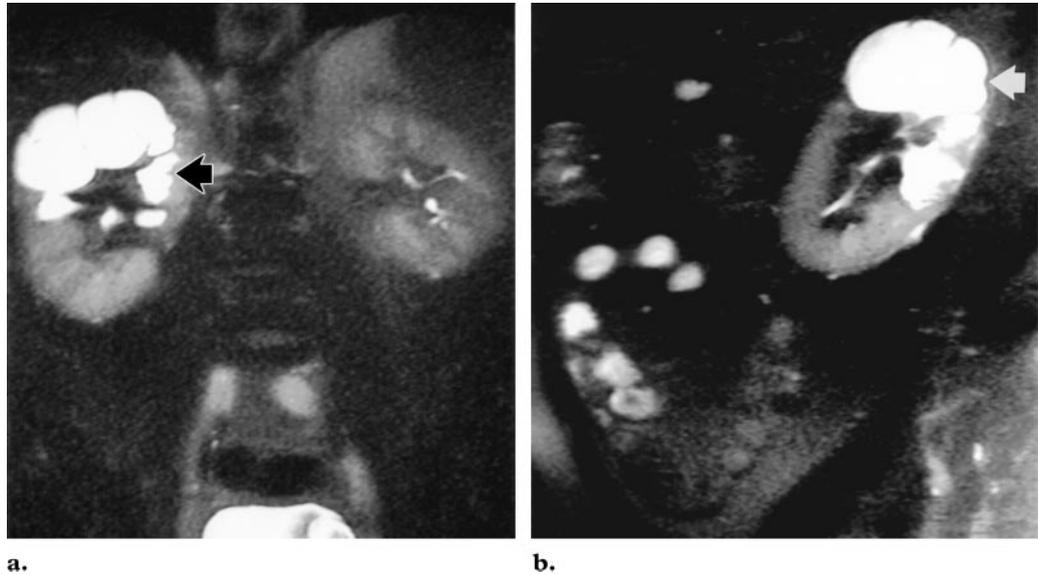


Figure 23. TCC of the renal pelvis in a 65-year-old man. Coronal (**a**) and sagittal (**b**) heavily T2-weighted (half-Fourier rapid acquisition with relaxation enhancement) source MR urograms (1500/116) show focal hydronephrosis and irregularity of the upper pole and interpolar calices of the right kidney (arrow).

MR imaging evaluation of upper tract TCC should include MR urography, which may be static or may be dynamic by using gadolinium contrast material (36). Static MR urography performed by using heavily T2-weighted sequences can permit accurate localization of ureteric obstruction (Fig 23), although imaging of undilated systems may be suboptimal (19,38) (Fig 24). Dynamic gadolinium-enhanced T1-weighted MR urography performed with or without a diuretic overcomes this problem and allows delayed acquisitions at various time intervals depending on the degree and level of obstruction (Fig 25). This technique is helpful in patients in whom urography with iodinated contrast material is not possible. Data postprocessing (eg, MIPs) allows 3D rotation and evaluation of suspected areas of disease without superimposition of other structures. This can be performed for both vessels and the collecting system. The latter images, which resemble conventional EU images, are readily acceptable to clinicians.

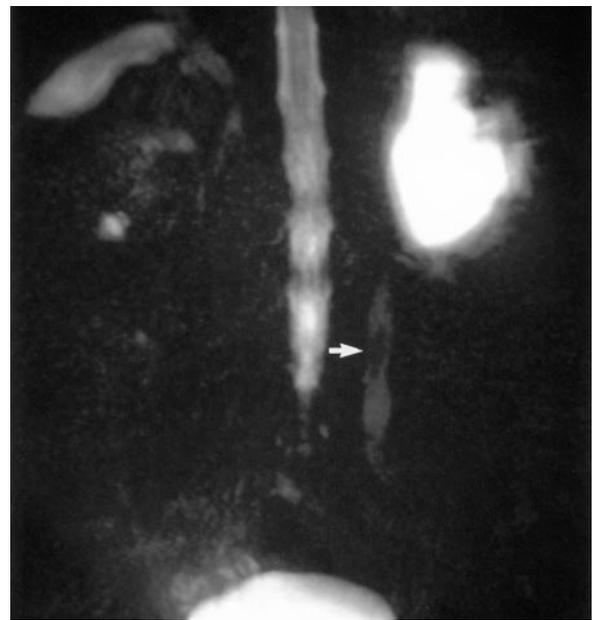


Figure 24. Ureteric TCC in a 56-year-old woman. Coronal MIP half-Fourier rapid acquisition with relaxation enhancement MR urogram (1500/116) shows hydronephrosis and a filling defect due to a tumor in the mid left ureter (arrow). Note the poor demonstration of the nondilated right collecting system.

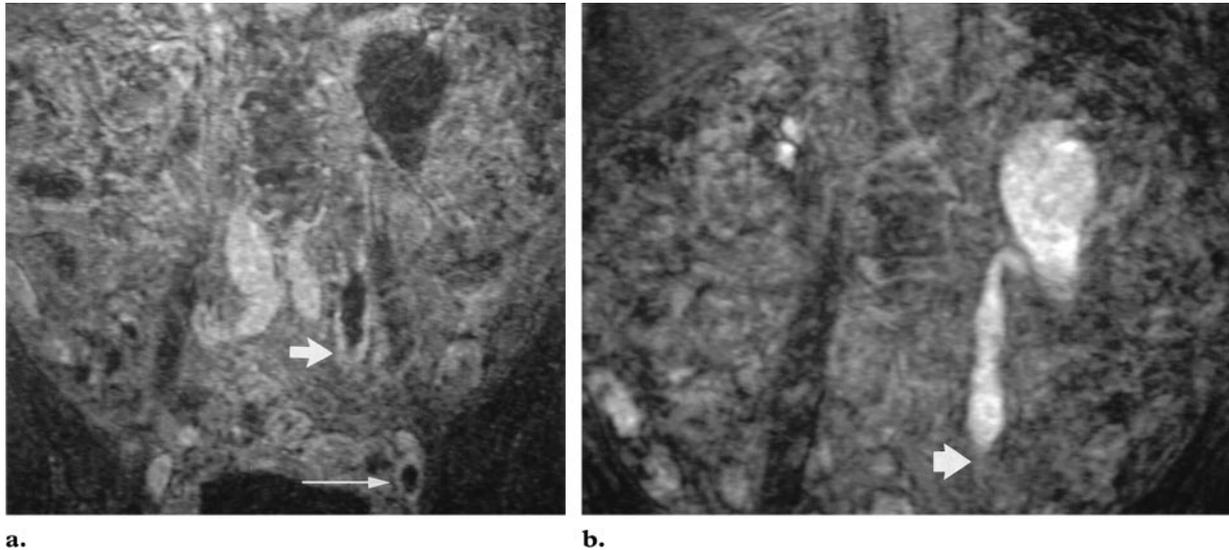


Figure 25. Ureteric TCC in a 68-year-old man with hematuria. **(a)** Coronal gadolinium-enhanced 3D fast low-angle shot MR urogram (3.64/1.37) obtained at 15 minutes shows hydronephrosis and proximal hydroureter to the level of the mid ureter. An enhancing tumor is seen in the ureteric wall at this level (thick arrow). No gadolinium contrast material is seen in the left collecting system. Deep vein thrombosis of the left femoral vein is incidentally noted (thin arrow). **(b)** Coronal gadolinium-enhanced 3D fast low-angle shot MR urogram (3.64/1.37) obtained at 2 hours shows the site of ureteric obstruction due to TCC (arrow).

Ureteric TCC is isointense to muscle on T1-weighted images and slightly hyperintense on T2-weighted images (39). At MR urography, ureteric TCC typically appears as an irregular mass, whereas calculi appear as sharply delineated filling defects, although differentiation between small calculi and tumor may be difficult (19). Tumor enhancement after administration of gadolinium contrast material can also help distinguish it from calculi (Fig 20). Soft-tissue stranding in the periureteric fat is suggestive of periureteric extension, although prior surgery, radiation, and inflammation can also give these appearances. MR imaging may help differentiate these entities, however, as fibrosis will appear hypointense on T2-weighted images, particularly in long-standing cases (39).

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 line to CT, it offers further noninvasive imaging of masses that are not adequately characterized with other imaging mo-

dalities (36). 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 that of intravenous urography or CT urography, making detection of subtle urothelial malignancies less likely (17). Furthermore, complete characterization of renal masses may require multiple time-consuming sequences before and after administration of gadolinium contrast material (17,18).

Staging and Treatment

The tumor stage at diagnosis influences the development of local recurrence and metastases and hence overall survival (1,4). Furthermore, treatment and prognosis are largely determined by the depth of tumor infiltration, the degree of lymph

Table 1
TNM Classification of Renal TCC

Stage	Histopathologic Findings
Tx	Primary tumor cannot be assessed
T0	No evidence of a primary tumor
Ta	Papillary noninvasive carcinoma
Tis	Carcinoma in situ
T1	Tumor invades subepithelial connective tissue
T2	Tumor invades the muscularis
T3	Tumor invades beyond the muscularis into the periureteric fat or renal parenchyma
T4	Tumor invades adjacent organs, the pelvic or 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 in greatest dimension
N2	Metastasis in a single lymph node > 2 cm but ≤ 5 cm in greatest dimension or in multiple lymph nodes ≤ 5 cm in greatest dimension
N3	Metastasis in a lymph node > 5 cm in greatest dimension
Mx	Distant metastasis cannot be assessed
M0	No distant metastasis
M1	Distant metastasis

node and distant metastases, and the histologic tumor type, making exact staging imperative (Tables 1, 2).

Conventional imaging methods such as EU and RP cannot demonstrate extension into the peripelvic or periureteric fat or metastases. Cross-sectional imaging with CT or MR is now routinely employed in the presurgical work-up of these patients. These techniques can demonstrate 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 and biopsy for staging before surgery.

CT has become routine in the further characterization of upper tract lesions demonstrated with other modalities and, despite varying reports on staging accuracy, is currently the preoperative imaging modality of choice (9,15,40) (Table 1). As studies show higher detection rates for urothelial malignancies with CT urography than with EU (29,31), this technique is being advocated as a one-stop diagnostic and staging assessment of suspected urothelial malignancy. Although CT does not allow distinction between stage 0–II tu-

Table 2
Histopathologic Grading of Renal TCC

Grade	Histopathologic Findings
Gx	Grade of differentiation cannot be assessed
G1	Well-differentiated tumor
G2	Moderately differentiated tumor
G3, G4	Poorly differentiated or undifferentiated tumor

mors, it does allow differentiation of early-stage TCC confined to the collecting system wall from advanced disease with local extension or distant metastases, which is important for defining surgical management (8,41). Early-stage tumors (stage 0–II) confined to the muscularis are separated from the renal parenchyma by renal sinus fat or excreted contrast material and have normal-appearing peripelvic fat (Fig 13).

More-advanced tumors infiltrating beyond the muscularis into the peripelvic fat typically show increased, inhomogeneous peripelvic attenuation (Fig 18), although this finding may also be seen with superimposed infection, hemorrhage, or inflammation and should be interpreted with caution to avoid overstaging (39). Metastatic spread

via urinary or hematogenous routes usually manifests as multifocal mucosal nodules or wall thickening, whereas direct invasion produces a short or long stricture (22). Extrarenal spread can occur at or through the renal hilum, and common sites of metastases include the lungs, retroperitoneum, lymph nodes, and bones (40). Rarely, invasion of the renal vein or inferior vena cava is seen and can be well demonstrated with comprehensive CT urography protocols. The overall accuracy of CT in predicting the pathologic stage ranges from 36% to 83% in the literature (2), which means that ureterorenoscopy and biopsy remain essential additional tools.

As with CT, MR imaging can demonstrate tumor involvement of the renal parenchyma, perinephric fat, or periureteric fat and distant metastases. It therefore offers an alternative staging modality and has been shown to allow accurate staging of TCC lesions larger than 2 cm (Fig 22) (37). As with CT, however, limitations exist in detecting superficial invasion of the renal parenchyma and small lesions may be missed because of motion artifacts (2,37). It is the preferred staging examination in patients who cannot tolerate iodinated contrast material and in whom multiplanar and vascular imaging is required for preoperative assessment.

The traditional treatment of upper tract TCC involves total nephroureterectomy with excision of the ipsilateral ureteric orifice and a contiguous cuff of bladder tissue (25). However, the development of endoscopic and minimally invasive surgical techniques allows renal preservation in selected patients, particularly those with a solitary kidney, bilateral tumor, poor renal function, low-grade tumor, or prohibitive surgical risk, with results comparable to those of radical surgery (2,25,42–45). Accurate radiologic detection and staging of tumor is therefore essential to determine appropriate surgical therapy, especially if conservative surgery is being considered, or the intensity of chemotherapy for advanced-stage tumors (25,40).

Follow-up

There is still no widely accepted protocol for the radiologic follow-up of patients with primary TCC of the upper urinary tract. Current data

suggest that routine follow-up imaging strategies should be individually tailored on the basis of primary tumor characteristics (2). Annual EU is recommended, especially in the first 2 years after initial diagnosis (10,19,42). RP should be sought if EU fails to depict or adequately distend the entire upper tract, especially if cystoscopy is being performed to assess the bladder. 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.

Owing 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. In the future, CT urography will likely become the primary radiologic method of TCC follow-up, allowing assessment of the entire urothelium and also facilitating virtual cystoscopy, although conventional cystoscopy is still necessary for direct visualization and biopsy.

Conclusions

Conventional imaging modalities such as EU, RP, and US still play a key role in the assessment of hematuria, in combination with endourologic techniques. However, multiphasic CT urography offers superior detection of calculi, urothelial tumor, and parenchymal tumor over EU and US and allows accurate staging of detected lesions at the same examination. MR imaging, including the newer techniques of MR angiography and MR urography, offers comparable evaluation in patients who cannot tolerate iodinated contrast material and in whom multiplanar, vascular, and collecting system imaging is required. Recognition by the radiologist of the variety of appearances of upper tract TCC with all imaging modalities is necessary to detect and stage tumors accurately. In addition, atypical appearances, particularly in advanced tumors, should be recognized. Synchronous or metachronous tumors of

the urothelium are common, necessitating vigilant urologic and radiologic follow-up. In the future, CT urography will likely become the definitive radiologic examination for diagnosis and follow-up in patients with suspected TCC.

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