Imaging Tips and Tricks in Management of Renal and Urothelial Malignancies

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Abstract

Management of urological malignancies has evolved significantly with continually changing guidelines and treatment options which demand more centralized involvement of radiology than ever before. Radiologists play a pivotal role in interpreting complex cancer scans and guiding clinical teams toward the best management options in the light of clinical profile. Management of complex uro-oncology cases is often discussed in multidisciplinary meetings which are essential checkpoints to evaluate an overall picture and formulate optimal treatment plans.

The aim of this article is to provide a radiological perspective with practical guidance to fellow radiologists participating in uro-oncology multidisciplinary meetings based on commonly encountered case scenarios, updated guidelines, and cancer pathways.

Crucial imaging tips with regards to renal and urinary tract cancers, upon which therapeutic decisions are made, have been condensed in this article after reviewing several complex cases from urology multidisciplinary meetings and European Association of Urology guidelines.

Outline of various diagnostic and management strategies, key staging features, surveillance guidelines, and, above all, what the onco-urologists want to know from radiologists have been succinctly discussed in this article.

Introduction

Diagnostic steps and management pathways of various urological malignancies have been continually evolving and substantially changed over the years. Radiology plays a crucial and pivotal role in management decisions adapted in multidisciplinary meetings, an integral part in all modern cancer care delivery and decision-making pathways. Radiologists chairing uro-oncology multidisciplinary meetings face new challenges at every step, from accurate staging, timely identifying early recurrent disease, assessing treatment response, locating potential sites for tissue sampling to surveillance of patients under long-term care.

This article aims to provide imaging perspective to both general and uro-radiologists in management of urological malignancies.
malignancies with reference to case examples and updated guidelines, without delving into in depth discussion on pathological classification of tumor subtypes or imaging techniques.

We have reviewed challenging uro-oncology cases from multidisciplinary meetings over the last few years, updated European Association of Urology guidelines, and highlighted imaging aspects involved in decision making, limiting our discussion to kidney and urothelial cancers (ureter and bladder origin). We have categorized renal cell and urothelial cancers according to radiological presentation on cross-sectional imaging and discussed salient imaging tips, which directly influence staging and management decisions.

**Discussion**

**Renal Cell Cancer**

Renal cell cancer (RCC) accounts for 3% of cancers in adults and is the most common kidney cancer. Renal masses are usually characterized by pre- and postcontrast image acquisition on computed tomography (CT)/magnetic resonance (MR) with postcontrast sequences acquired at 20 to 70 seconds (corticomediullary phase), 80 to 120 seconds (nephrographic), and delayed excretory phases. Imaging techniques and tips with regard to pathological subtypes of RCCs are summarized in Table 1.

Incidentally detected small renal masses and T1 stage tumors are being increasingly detected with the use of cross-sectional imaging techniques. Small masses can be treated with renal sparing treatments like partial nephrectomy (PN) besides radioablation or cryotherapy to preserve renal function.

**Imaging tips:** Nephrographic phase of renal protocol CT is ideal to evaluate small endophytic masses as these lesions become more conspicuous against a background of homogeneously intensely enhancing renal parenchyma and hence are easier to differentiate from the renal medulla. Exact location of such small masses, distance from renal hilum, and vascular (presence of accessory renal arteries) supply (Fig. 1) are important preoperative information for urologists which are easily confirmed on multiplanar reconstructions.

PN might be unsuitable even for small tumors if there is insufficient volume of postresection remnant parenchyma to maintain proper organ function, hence documenting kidney size, presence of cortical scarring, renal vein thrombosis, unfavorable tumor location (e.g., adherence to renal vessels), and status of contralateral kidney is an important preoperative parameter.

Complicated renal cysts/cystic RCCs are categorized as per Bosniak classification on CT and the criteria have also been validated for use on MR imaging (MRI) as well. The Bosniak category of a cystic lesion might be upgraded on MRI as MRI with superior contrast resolution is likely to demonstrate more septations and nodularity.

**Imaging tips:** Few thin septations (<1 mm) observed in a cystic lesion would be a Bosniak 2 cyst while multiple septations with nodularity a Bosniak 2F cyst. The distinction between perceived and measurable enhancement in septal or wall nodularity is important as the latter group of cystic lesions would classify as Bosniak 3 cysts. Bosniak 3 lesions have approximately 50% chances of harboring potential malignancies and might require surgical excision. On CT, an unequivocal increase in attenuation values by more than 20 HU after administration of contrast is taken as a criterion for measurable enhancement. However, it is often difficult to assess enhancement in small intrarenal masses owing to chances of pseudo-enhancement which may be due to particular reconstruction algorithm and/or incorporated...
MRI with gadolinium enhanced and subtraction imaging is especially helpful in characterizing smaller complex lesions (Fig. 2).\(^2\)

Majority of Bosniak 2F and almost 50% of Bosniak 3 cysts are benign with very low potential to metastasize and hence might be considered suitable for surveillance.\(^5,6\) Surgical options are reconsidered in case of interval growth or appearance of solid elements on follow-up imaging.

Multifocal or bilateral RCCs might be associated with hereditary kidney cancer syndromes like Von Hippel–Lindau disease (Fig. 3) or Lynch syndrome.

**Imaging tips:** Patients with hereditary RCC wherever possible should be considered for MR surveillance to reduce burden of radiation exposure from frequent CT scans. Moreover, superior contrast resolution of MRI allows better assessment of small cystic lesions. Assessment and documentation of all suspicious lesions with size, interval growth, and other visceral lesions are crucial for overall management of such patients.\(^7,8\)

Multifocal or bilateral tumors might benefit from cryoablation or RFA (radiofrequency ablation) to avoid repeated surgical interventions although cystic lesions are ideally not candidates for ablative treatment.\(^8\)

Appropriately timed nephron-sparing approaches are recommended with the exception of hereditary leiomyomatosis and RCC and succinate dehydrogenase syndromes, for which surveillance is recommended until the largest solid tumor reaches 3 cm in diameter, to reduce interventions.\(^8\)

RCCs encountered in patients with end-stage kidney disease might also be multicentric and bilateral. They are generally found in younger patients (mostly male) and tend to be less aggressive.\(^9\)

**Fig. 1** (A) Axial-enhanced CT images demonstrated a right renal interpolar lesion being considered for partial nephrectomy, but close to renal hilum. The mass also shows calcification inside (white arrow), which favors more toward RCC with osteometaplasia. (B) Complex cystic mass in right kidney lower pole with MIP image demonstrating multiple accessory renal arteries (black arrows).

**Fig. 2** (A) CT coronal reformatted images show a complex cystic mass (solid white arrow) with an apparently enhancing nodule (dashed arrow) in left kidney upper pole and another hypodense lesion more inferiorly (circle). (B) Contrast-enhanced MR images downstage the complex cyst in left kidney upper pole (solid white arrow) with thin septation; however, the mural nodule (dashed arrow) turned out to be a separate proteinaceous cyst without any obvious enhancement. The more inferior hypodense lesion is a solid enhancing mass more clearly demonstrated (circle). This information was vital to the surgeon who could spare the cyst and perform partial nephrectomy for the smaller solid lesion. CT, computed tomography; MR, magnetic resonance.
which might otherwise result in local recurrent disease or correctly staged as T3 tumor to prevent inadequate treatment. RCCs (renal cell carcinoma) are among the most common solid tumors and account for more than 70% of the cases. The 

Imaging tips: Baseline split renal function should be estimated using renal scintigraphy preoperatively to determine the feasibility of conserving renal function in patients with solitary kidneys or bilateral tumors. CT or MRI allows accurate diagnosis of RCC in the majority of cases. However, image-guided percutaneous biopsy can provide additional information, especially in indeterminate masses. In patients with metastatic disease, appropriate documentation of all tumoral deposits is critical for successful outcome of surgical debulking or cytoreductive nephrectomy. This includes patients with primary tumor in place and single or oligo-metastatic resectable disease, for palliative treatment options, and to control hematuria.

Imaging tips: RCC metastases are often hypervascular, more easily evident on arterial phases, and can be masked on portal venous phases. Radiologists should be aware of pseudo-progression changes on surveillance scans for metastatic RCCs treated with immunotherapeutic agents and report findings with knowledge of iRECIST criteria. Correct assessment of treatment response and true progression of disease can only be possible after evaluating interim and follow-up scans with background clinical information as there can be deceptive increase in size of tumoral deposits on initial scan owing to immune response.

Locally advanced RCCs are T3 and T4 tumors. Updated TNM (TNM Classification of Malignant Tumors) classification reclassified RCCs with invasion of renal sinus fat and involvement of branch renal veins as stage T3a. Centrally located small RCCs (<4 cm) with renal sinus fat or calyceal invasion should be correctly staged as T3 tumor to prevent inadequate treatment which might otherwise result in local recurrent disease or metastasis. Tumor thrombosis in renal vein or inferior vena cava (IVC) in RCC patients is a significant adverse prognostic factor.

Imaging tips: Knowledge of IVC involvement by tumor thrombus is essential for preoperative planning. MRI with its higher sensitivity and specificity is superior to CT for evaluating the extent of tumor thrombus in doubtful cases. Distinguishing tumoral clot extension along the renal vein from direct invasion of the IVC wall by RCC is important as the later upstages to T3c and requires more extensive surgery and preoperative planning.

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Higher grade tumors require more stringent follow-up, whereas lower grade cancers like chromophobe tumors are eligible for low-risk follow-up. Usually a staging CT of the chest and abdomen is performed for high or intermediate risk cases at 6 months and thereafter annually till 3 years and then every 2 years. CT is done for follow-up at 1 year and then every 2 yearly in low-risk cases.

Imaging postablation: Residual tumor post-RFA is usually demonstrated as any soft tissue enhancement >10 HU on day 7 scan. A noncontrast scan should be included, as it is useful to differentiate residual tumors from blood degradation products. Ideally, complete tumor ablation is achieved if there is nonenhancement at the site of previous tumor with attenuation <10 HU. Postablative halo at the penumbral repair zone might show some enhancement due to an inflammatory reaction at variable duration but usually distinguishable from solid residual tumor on day 7 scan. Further follow-up scans can be subsequently acquired at 6 monthly intervals following RFA treatment. RFA-treated tumors demonstrate variable degree of involution, over a time period, and radiologists should primarily look for enhancing soft tissue to check for recurrences rather than size reduction.

An imaging algorithm of various renal masses with corresponding management strategies is summarized in Fig. 6.

Urothelial Cancers
Urothelial cancers are a heterogeneous spectrum of malignant cancers that can have their origin from any part of the urinary tract from renal pelvis to proximal urethra. While most urothelial cancers are of bladder origin and only 5 to 10% involve upper tracts, there is a notable difference in behavior, management, and prognosis between upper and lower tract cancers. These cancers are notorious for multicentricity and metachronous presentation across the entire urinary tract.

Upper tract urothelial cancer (UTUC): CT urography (CTU) is the imaging modality of choice for evaluating and staging upper-tract transitional cell carcinomas (TCCs). There is a high degree of variation in practice with regard to acquisition of CTUs across several centers, although split bolus, dual-phase CTU is the standard practice in most trusts in England. MR urography has no current role in staging UTUC, however, has its applications for patients allergic to iodinated contrast agents, obstructed system, and in relatively younger individuals, pregnant patients. Retrograde pyelography is reserved for patients with renal insufficiency and hence poor excretion on CTU or to further characterize CTU findings while antegrade nephrotomograms are attempted in patients with an obstructed...
collecting system and difficult-to-catheterize ureteric orifices, pre-existing urinary diversions.20

Imaging tips: Triple-phase CTU for higher grade UTUCs by some studies with urothelial phase images at 60 seconds has added a usefulness technique in detecting flat lesions over combined nephrographic–excretory phase images acquired in split bolus.21

Ureteroscopic biopsy cannot accurately determine depth of upper tract wall invasion, hence preoperative cross-sectional imaging has a central role in deciding nephroureterectomy over kidney sparing surgery.21,22

UTUCs can have a wide spectrum of appearances on CTU ranging from focal filling defects, wall enhancements, en plaque or papillary lesions, to frankly infiltrative or invasive tumors.

Honda et al21 classified ureteric tumors on CTU in mainly six patterns to differentiate T2 or lower stage tumors from T3 or higher stage groups:

1. Circumferential wall thickening with no spiculation.
2. Circumferential wall thickening with spiculation.
3. Intraluminal mass with smooth external surface and no spiculation.
4. Asymmetric circumferential wall thickening with spiculation.
5. Intraluminal mass with smooth external surface and spiculation.
6. Intraluminal mass with irregular external surface and spiculation.

Patterns 1 to 3 have been associated with T2 or lower stage tumors, whereas patterns 4 to 6 have been associated with T3 or higher stage tumors (Fig. 7) with reported sensitivity and specificity for the latter group on preoperative CTU being 87.5 and 92.9%, respectively.21

Imaging tips: Knowledge of lesion location, distortion in normal anatomy, thickness of the urinary wall, and tumor multiplicity in CTU report would highly aid the urologist before ureteropyeloscopy and biopsy. Mass-like urothelial cancers in renal pelvis need differentiating from RCCs with secondary infiltration to renal calyces on imaging owing to their completely different management. While RCC infiltrating into renal pelvis would be a stage 3 tumor requiring nephrectomy, an invasive urothelial cancer of renal pelvic origin would mandate radical nephroureterectomy (RNU). Distortion of renal contour, more distinct demarcation between tumor and renal parenchyma, and pseudo-capsule (associated with expansive growth of RCC compared with infiltrative growth of TCC) might be helpful, although in doubtful cases one should seek help of MRI or percutaneous biopsy21,24 (Fig. 8).

Hydronephrosis, lymph nodal disease at the time of presentation, tumors >2 cm in size, and multifocal disease usually determine high-risk upper tract cancers with poor prognosis.20,21 MR diffusion-weighted imaging has a role in detecting higher cellularity and aggressive tumors and hence predicting prognosis. Some studies have also documented the role of T1 fat-suppressed post-gadolinium images in differentiating T3 and higher stage ureteric tumors (irregular or disruptive enhancing rim) from T2 or lower stage tumors (smooth rim enhancement).21,25

Majority of high-risk UTUCs are treated with RNU with bladder cuff excision as the standard treatment. Bladder cuff and distal ureteric excision alongside nephrectomy is regularly considered beneficial because of high incidence of recurrence in the distal ureter. However, excision of distal ureter might be precluded in patients with chronic fibrotic or adhesive disease process in pelvis from prior interventions or complex surgery. A common site of recurrence in such cases is the distal ureteric stump.26,27

There is a role of neoadjuvant chemotherapy for T3 or higher stage UTUC tumors considering evidence of increased disease-free survival in such group of patients. Hence, accurate T staging on preoperative CTU is important although CTU is limited in the assessment of lower than T2-stage tumors.21,26

Benign conditions which might pose as differentials of UTUC on imaging are inflammatory strictures and ureteric amyloidosis. There are several extra-luminal pathologies like retroperitoneal fibrosis, lymphoma or IgG4 disease, and endometriosis, which can involve ureters extrinsically and can mimic urethral cancers.

Imaging tips: Benign strictures are usually long segmental. Ureteric amyloidosis demonstrates T2 low signal on MR images. Radiological clues like extrinsic soft tissue encasing ureters, bilateral involvement, medialization of ureters might be helpful in classic presentation of retroperitoneal fibrosis (Fig. 9); however, differentiating atypical presentations of such benign entities from malignant strictures can be challenging at times and correlation with urinary cytology, ureteroscopic, or laparoscopic biopsy and follow-up imaging should be sought for in doubtful cases.21,25

Recurrent disease: The rate of bladder recurrence after RNU for UTUC is up to 50%, while recurrence in the contralateral collecting system is 2 to 6%. Bladder recurrence is however not considered as a distant recurrence.25

Imaging surveillance: Follow-up is more frequent and stricter in patients with invasive cancers and who have undergone kidney-sparing treatment compared with RNU. Surveillance includes cystoscopy, urinary cytology, and upper tract assessment by CTU. Usually CTU is recommended 6 monthly for the initial 2 years and then annually for another 3 years. For noninvasive cancers managed with radical surgery, CTU is done annually.20,26

Urothelial carcinomas of bladder origin (UCBs): Approximately 90 percent of bladder cancers are of urothelial origin. Cystoscopy and biopsy at presentation are invaluable for classifying bladder tumors and guiding further management.20 Imaging depends on biopsy findings and treatment intent.

Tumor Subtypes

Nonmuscle invasive bladder cancers constitute majority of UCBs, are usually multifocal, low-grade lesions, but with a higher recurrence rate. However, superficial noninvasive diseases can recur and transform to higher grade muscle invasive bladder cancer (MIBC) and are often considered precursors to higher grade cancers and might even coexist.
Carcinoma in situ (CIS) is a flat, high-grade, noninvasive, multifocal urothelial carcinoma which can be missed or misinterpreted as an inflammatory lesion during cystoscopy if not biopsied.\(^\text{28}\)

Radiology has a limited role in superficial disease (Ta/T1 tumors) which is usually managed by a repeat complete transurethral resection (TURBT [transurethral resection of a bladder tumor]) 2 to 6 weeks after initial cystoscopic resection and biopsy. Superficial lesions in bladder if macroscopically evident on cross-sectional imaging (\(\text{Fig. 10a}\)) can present as either polypoidal filling defect, en-plaque lesions, or focal thickening. Second resection is often required for larger tumors (>1 cm) or high-grade superficial tumors with residual disease observed in 33 to 51% cases.\(^\text{29,30}\)

**Imaging tips:** Patients with proven invasive disease on biopsy and considered fit for radical treatment are usually staged locally with MRI. The main aim of imaging is to assess muscle invasive T3 tumor or extravesical tumor spread (\(\text{Fig. 10b}\)). T2 weighted (T2W) sequence on MRI helps to appreciate the hypointense detrusor muscle line in contrast to T2 intermediate signal tumor. Dynamic contrast enhanced imaging exploits differential enhancement of early-
enhancing bladder tumors from late-enhancing mural layer (enhances late at 60 seconds) in assessing mural invasion. CT is limited in T-staging of bladder tumors and primarily limited to exclude overt extravesical disease, and nodal or distant metastatic lesions.\textsuperscript{31,32}

Baseline CTU to assess ureteric involvement prior to cystectomy offered as a routine investigation for bladder cancer diagnosed on cystoscopy is of questionable significance. It is usually reserved for high-risk tumors (grade 3, multifocal superficial tumors with >3 cm in size, CIS, recurrent or MIBC) because incidence of upper tract involvement in bladder cancer is significantly low (1.8%) but increases to 7.5% for tumors close to trigone.\textsuperscript{33,34} Ureteroscopy is considered in cases suspicion of ureteric involvement on imaging.

Invasive diseases limited to bladder or with minimal extravesical spread are managed by radical cystectomy or radiotherapy. However, radical cystectomy is also considered for high grade, recurrent, BCG (bacillus Calmette-Guérin) refractory or large superficial tumors, unusual urothelial histology, and also for CIS.\textsuperscript{35}

Tumors in bladder diverticulae have a reported incidence of 2 to 10%.\textsuperscript{28} Diverticulae are considered as risk factors to develop tumor due to urinary stasis. Tumor within a narrow-necked diverticulum can be missed on cystoscopy but easily picked up on MRI (\textbullet\textsuperscript{Fig. 10c}).
Imaging tips: Cancer in bladder diverticulum is usually an invasive T3 disease with increased risk for extravesical spread as the muscle layer is absent in bladder diverticulae. Advanced and metastatic tumors: Advanced T4 bladder cancers with involvement of prostate, vagina, and rectosigmoid might present with fistulation, and at times are considered for anterior or complete pelvic exenteration. Extravesical spread of tumor to the abdominal or pelvic wall represents T4b disease. Radiologists should document clear extensions of advanced bladder masses as tumors invading to sacrosciatic notches, lumbosacral plexus, or tumor/nodes encasing external iliac vessels or extending above the level of true pelvis are not candidates for pelvic exenterations. Currently, there is no evidence supporting routine use of positron emission tomography (PET) in nodal staging of UBC. Nodes above the level of aortic bifurcation are considered as metastatic diseases, and are generally more commonly seen with tumors close to the bladder trigone. Multiple regional nodal metastases in true pelvis (N2) and common iliac nodes (N3), if detected on preoperative MRI, preclude orthotopic reconstruction of neo-bladder. Local recurrence can take place as soft-tissues at the original surgical site in the bladder bed or as nodal recurrence in the area of lymph node dissection. UTUCs occur in 1.8 to 6.0% of cases and represent the most common sites of late recurrence. Distant disease seen in up to 50% of patients treated with cystectomy for MIBC involves lymph nodes, lungs, liver, and bones.

Imaging tips: Patients with multifocal disease, MIBC with CIS, or positive ureteral margins are at higher risk of developing late (>3 years) upper tract disease. Monitoring of the upper tracts with CTU for a longer period is mandatory in such cases. Imaging postsurgery: Postinflammatory changes as bladder wall thickening and extravesical fat stranding can often be seen on a CT/MRI, acquired within short-interval post-TURBT (►Fig. 11). Radiologists reading such postintervention scans should be cautious as not to interpret such postbiopsy changes as a T3 disease. A short-interval follow-up scan might often be helpful to clear dilemma in such cases. Ureteroileal anastomotic junction should be evaluated carefully for recurrent lesions in cases with urinary diversion and ileal conduit (►Fig. 12a, b). Patients with a history of recurrent urinary stent exchange following urinary diversion might show inflammatory thickening of upper tracts and a follow-up scan or ureteroscopic biopsy might avoid misinterpreting such inflammatory thickening as a recurrent disease.

**Fig. 11** Post TURBT CT urogram 2 weeks for superficial papillary tumor with preserved muscle on biopsy. (A) Axial image shows extensive bladder wall thickening, perivesical stranding and a suspicious right internal iliac lymph node (arrow). (B) On follow-up CT after 3 months, although bladder inflammatory changes resolve, right internal iliac node (arrow) persists. (C) The node (arrow) demonstrates stable appearances with no significant uptake on a follow-up PET CT and no other evidence of disease elsewhere, hence considered a reactive node. CT, computed tomography; CTU, computed tomography urography; PET, positron emission tomography; TURBT, transurethral resection of a bladder tumor.

**Fig. 12** (A) Postradical cystectomy coronal CTU images in a different patient: recurrent soft tissue (arrow) seen at ureteroileoal anastomosis on postcystectomy surveillance scan. (B) Sagittal CTU maximum intensity projection images. CTU, computed tomography urography.
Mild prominence of collecting systems following cystectomy and incontinent diversions after removal of stents might persist for variable periods of time; however, significant pelvicaliectasis on surveillance scans might be an early indicator of recurrent disease. However, less sinister reasons like parastomal hernia at the urostomy site, causing extrinsic compression, or kinking of the stoma should be sought for.

Imaging surveillance: Current consensus is to follow up patients post definitive management for four-monthly CT scans during the first year, six-monthly until the third year, and annual imaging thereafter. More stringent follow-up could be considered in patients with locally advanced disease or lymph node involvement.

An imaging algorithm of various types of urothelial cancers and management approaches is summarized in Fig. 13.

In conclusion, cancer care pathways continue to evolve with emerging imaging options, and diagnostic and management strategies become more complex. Knowledge about complex uro-oncology case scenarios, guidelines, pitfalls, and expected complications would enable radiologists to deliver pragmatic opinions and contribute toward decision making in multidisciplinary meetings.

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