

ACR Appropriateness Criteria[®]

Pretreatment Staging of Urothelial Cancer: 2024 Update

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Abstract

Urothelial cancer is the second most common cancer, and cause of cancer death, related to the genitourinary tract. The goals of imaging for pretreatment staging of urothelial cancer are to evaluate for both local and distant spread of the cancer and assessing for synchronous sites of urothelial cancer in the upper tracts and bladder. For pretreatment staging of urothelial carcinoma, patients can be stratified into one of three groups: 1) nonmuscle invasive bladder cancer; 2) muscle invasive bladder cancer; and 3) upper urinary tract urothelial carcinoma. This document is a review of the current literature for urothelial cancer and resulting recommendations for pretreatment staging imaging.

The American College of Radiology Appropriateness Criteria are evidence-based guidelines for specific clinical conditions that are reviewed annually by a multidisciplinary expert panel. The guideline development and revision process support the systematic analysis of the medical literature from peer reviewed journals. Established methodology principles such as Grading of Recommendations Assessment, Development, and Evaluation or GRADE are adapted to evaluate the evidence. The RAND/UCLA Appropriateness Method

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Disclaimer: The ACR Committee on Appropriateness Criteria and its expert panels have developed criteria for determining appropriate imaging examinations for diagnosis and treatment of specified medical condition(s). These criteria are intended to guide radiologists, radiation oncologists and referring physicians in making decisions regarding radiologic imaging and treatment. Generally, the complexity and severity of a patient's clinical condition should dictate the selection of appropriate imaging procedures or treatments. Only those examinations generally used for evaluation of the patient's condition are ranked. Other imaging studies necessary to evaluate other co-existent diseases or other medical consequences of this condition are not considered in this document. The availability of equipment or personnel may influence the selection of appropriate imaging procedures or treatments. Imaging techniques classified as investigational by the FDA have not been considered in developing these criteria; however, study of new equipment and applications should be encouraged. The ultimate decision regarding the appropriateness of any specific radiologic examination or treatment must be made by the referring physician and radiologist in light of all the circumstances presented in an individual examination.

User Manual provides the methodology to determine the appropriateness of imaging and treatment procedures for specific clinical scenarios. In those instances where peer reviewed literature is lacking or equivocal, experts may be the primary evidentiary source available to formulate a recommendation.

Key Words: Appropriateness Criteria, appropriate use criteria, AUC, muscle invasive bladder cancer (MIBC), nonmuscle invasive bladder cancer (NMIBC), pretreatment staging, transitional cell carcinoma, upper tract urothelial carcinoma (UTUC), Urothelial carcinoma

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ACR Appropriateness Criteria® Pretreatment Staging of Urothelial Cancer: 2024 Update. [Variants 1 to 3](#) and [Tables 1 and 2](#).

Variant 1. Adult. Nonmuscle invasive bladder cancer. Pretreatment staging.

Procedure	Appropriateness Category	Relative Radiation Level
MRI pelvis without and with IV contrast	Usually Appropriate	○
MRU without and with IV contrast	Usually Appropriate	○
CT abdomen and pelvis with IV contrast	Usually Appropriate	⊕⊕⊕
CTU without and with IV contrast	Usually Appropriate	⊕⊕⊕⊕
US pelvis (bladder)	May Be Appropriate	○
MRI abdomen and pelvis without and with IV contrast	May Be Appropriate	○
MRI abdomen and pelvis without IV contrast	May Be Appropriate	○
MRI pelvis without IV contrast	May Be Appropriate	○
MRU without IV contrast	May Be Appropriate	○
CT chest with IV contrast	May Be Appropriate	⊕⊕⊕
CT abdomen and pelvis without and with IV contrast	May Be Appropriate	⊕⊕⊕⊕
US kidneys and bladder retroperitoneal	Usually Not Appropriate	○
Radiography chest	Usually Not Appropriate	⊕
Radiography intravenous urography	Usually Not Appropriate	⊕⊕⊕
MRI abdomen without and with IV contrast	Usually Not Appropriate	○
MRI abdomen without IV contrast	Usually Not Appropriate	○
MRI head without and with IV contrast	Usually Not Appropriate	○
MRI head without IV contrast	Usually Not Appropriate	○
Bone scan whole body	Usually Not Appropriate	⊕⊕⊕
CT abdomen and pelvis without IV contrast	Usually Not Appropriate	⊕⊕⊕
CT abdomen with IV contrast	Usually Not Appropriate	⊕⊕⊕
CT abdomen without IV contrast	Usually Not Appropriate	⊕⊕⊕
CT chest without and with IV contrast	Usually Not Appropriate	⊕⊕⊕
CT chest without IV contrast	Usually Not Appropriate	⊕⊕⊕
CT pelvis with IV contrast	Usually Not Appropriate	⊕⊕⊕
CT pelvis without IV contrast	Usually Not Appropriate	⊕⊕⊕
FDG-PET/MRI skull base to mid-thigh	Usually Not Appropriate	⊕⊕⊕

(continued)

Variant 1. Continued

Procedure	Appropriateness Category	Relative Radiation Level
CT abdomen without and with IV contrast	Usually Not Appropriate	☼☼☼☼
CT pelvis without and with IV contrast	Usually Not Appropriate	☼☼☼☼
FDG-PET/CT skull base to mid-thigh	Usually Not Appropriate	☼☼☼☼

Variant 2. Adult. Muscle invasive bladder cancer. Pretreatment staging.

Procedure	Appropriateness Category	Relative Radiation Level
Radiography chest	Usually Appropriate	☼
MRI abdomen and pelvis without and with IV contrast	Usually Appropriate	○
MRI pelvis without and with IV contrast	Usually Appropriate	○
MRU without and with IV contrast	Usually Appropriate	○
MRU without IV contrast	Usually Appropriate	○
CT abdomen and pelvis with IV contrast	Usually Appropriate	☼☼☼
CT chest with IV contrast	Usually Appropriate	☼☼☼
CTU without and with IV contrast	Usually Appropriate	☼☼☼☼
FDG-PET/CT skull base to mid-thigh	Usually Appropriate	☼☼☼☼
US pelvis (bladder)	May Be Appropriate	○
MRI abdomen and pelvis without IV contrast	May Be Appropriate	○
MRI pelvis without IV contrast	May Be Appropriate	○
Bone scan whole body	May Be Appropriate	☼☼☼
CT chest without IV contrast	May Be Appropriate	☼☼☼
FDG-PET/MRI skull base to mid-thigh	May Be Appropriate	☼☼☼
CT abdomen and pelvis without and with IV contrast	May Be Appropriate (Disagreement)	☼☼☼☼
US kidneys and bladder retroperitoneal	Usually Not Appropriate	○
Radiography intravenous urography	Usually Not Appropriate	☼☼☼
MRI abdomen without and with IV contrast	Usually Not Appropriate	○
MRI abdomen without IV contrast	Usually Not Appropriate	○
MRI head without and with IV contrast	Usually Not Appropriate	○
MRI head without IV contrast	Usually Not Appropriate	○
CT abdomen and pelvis without IV contrast	Usually Not Appropriate	☼☼☼
CT abdomen with IV contrast	Usually Not Appropriate	☼☼☼
CT abdomen without IV contrast	Usually Not Appropriate	☼☼☼
CT chest without and with IV contrast	Usually Not Appropriate	☼☼☼
CT pelvis with IV contrast	Usually Not Appropriate	☼☼☼
CT pelvis without IV contrast	Usually Not Appropriate	☼☼☼
CT abdomen without and with IV contrast	Usually Not Appropriate	☼☼☼☼
CT pelvis without and with IV contrast	Usually Not Appropriate	☼☼☼☼

Variant 3. Adult. Upper urinary tract urothelial cancer. Pretreatment staging.

Procedure	Appropriateness Category	Relative Radiation Level
Radiography chest	Usually Appropriate	☼
MRI abdomen and pelvis without and with IV contrast	Usually Appropriate	○
MRU without and with IV contrast	Usually Appropriate	○
CT chest with IV contrast	Usually Appropriate	☼☼☼
CTU without and with IV contrast	Usually Appropriate	☼☼☼☼
MRI abdomen and pelvis without IV contrast	May Be Appropriate	○
MRU without IV contrast	May Be Appropriate	○
CT abdomen and pelvis with IV contrast	May Be Appropriate	☼☼☼
CT chest without IV contrast	May Be Appropriate	☼☼☼
FDG-PET/MRI skull base to mid-thigh	May Be Appropriate	☼☼☼
CT abdomen and pelvis without and with IV contrast	May Be Appropriate	☼☼☼☼
FDG-PET/CT skull base to mid-thigh	May Be Appropriate	☼☼☼☼
US kidneys and bladder retroperitoneal	Usually Not Appropriate	○
US pelvis (bladder)	Usually Not Appropriate	○
Radiography intravenous urography	Usually Not Appropriate	☼☼☼
MRI abdomen without and with IV contrast	Usually Not Appropriate	○
MRI abdomen without IV contrast	Usually Not Appropriate	○
MRI head without and with IV contrast	Usually Not Appropriate	○
MRI head without IV contrast	Usually Not Appropriate	○
MRI pelvis without and with IV contrast	Usually Not Appropriate	○
MRI pelvis without IV contrast	Usually Not Appropriate	○
Bone scan whole body	Usually Not Appropriate	☼☼☼
CT abdomen and pelvis without IV contrast	Usually Not Appropriate	☼☼☼
CT abdomen with IV contrast	Usually Not Appropriate	☼☼☼
CT abdomen without IV contrast	Usually Not Appropriate	☼☼☼
CT chest without and with IV contrast	Usually Not Appropriate	☼☼☼
CT pelvis with IV contrast	Usually Not Appropriate	☼☼☼
CT pelvis without IV contrast	Usually Not Appropriate	☼☼☼
CT abdomen without and with IV contrast	Usually Not Appropriate	☼☼☼☼
CT pelvis without and with IV contrast	Usually Not Appropriate	☼☼☼☼

Table 1. Appropriateness category names and definitions

Appropriateness Category Name	Appropriateness Rating	Appropriateness Category Definition
Usually Appropriate	7, 8, or 9	The imaging procedure or treatment is indicated in the specified clinical scenarios at a favorable risk-benefit ratio for patients.
May Be Appropriate	4, 5, or 6	The imaging procedure or treatment may be indicated in the specified clinical scenarios as an alternative to imaging procedures or treatments with a more favorable risk-benefit ratio, or the risk-benefit ratio for patients is equivocal.
May Be Appropriate (Disagreement)	5	The individual ratings are too dispersed from the panel median. The different label provides transparency regarding the panel's recommendation. "May be appropriate" is the rating category and a rating of 5 is assigned.
Usually Not Appropriate	1, 2, or 3	The imaging procedure or treatment is unlikely to be indicated in the specified clinical scenarios, or the risk-benefit ratio for patients is likely to be unfavorable.

Table 2. Relative radiation level designations

RRL	Adult Effective Dose Estimate Range (mSv)	Pediatric Effective Dose Estimate Range (mSv)
0	0	0
⊕	<0.1	<0.03
⊕⊕	0.1-1	0.03-0.3
⊕⊕⊕	1-10	0.3-3
⊕⊕⊕⊕	10-30	3-10
⊕⊕⊕⊕⊕	30-100	10-30

Note: Relative radiation level (RRL) assignments for some of the examinations cannot be made, because the actual patient doses in these procedures vary as a function of a number of factors (eg, region of the body exposed to ionizing radiation, the imaging guidance that is used). The RRLs for these examinations are designated as "varies."

SUMMARY OF LITERATURE REVIEW

Introduction/Background

The American Cancer Society estimates that in 2023, there will be 82,290 new cases of bladder cancer and 16,710 deaths from the disease in the United States [1]. Bladder cancer has a high tendency toward multifocality at presentation and recurrence after treatment [2]. Urothelial carcinoma (UC) (previously known as transitional cell carcinoma) of the bladder is overwhelmingly the most common histologic type of bladder cancer in industrialized nations, accounting for >90% of all cases [3]. The median age of patients at diagnosis with bladder cancer in the United States is 73 years. Almost 85% of patients with bladder cancer present with hematuria, which is either gross or microscopic and is usually painless and intermittent [4].

UC is a very common tumor, quoted as overall the sixth most common tumor (fourth in male individuals), with the majority of cases arising in the bladder. Primary lesions

arising in the upper tract are relatively uncommon at approximately 5% to 10% [1]. The hallmark of UC is multiplicity and recurrence, with nearly 2% to 4% of patients with bladder cancer developing upper tract UC (UTUC). In addition, 40% of patients with UTUC develop UC of the bladder [5]. UTUC has often been grouped with other renal cancers in the literature, making the true incidence of UTUC difficult to evaluate. Pelvic/ureteral location is twice as common for UTUC as ureteral location, with estimates suggesting that approximately 15% of renal tumors are actually UC [5]. The incidence of UTUC has been increasing recently, which may be related to overall improved survival of patients with UC of the bladder and the associated risk of developing metachronous UTUC in those patients [5].

UC of the bladder spreads by local extension from the urothelium, through the lamina propria, into the muscularis propria or detrusor muscle layer, then to the perivesical fat. It has been estimated that 70% to 85% of UC of the

bladder is nonmuscle invasive at presentation [3]. Invasion of the muscularis propria and beyond, termed muscle-invasive bladder cancer (MIBC), increases the risk for more distant spread. The most common metastatic sites for MIBC include lymph nodes, bone, lung, liver, and peritoneum [6]. UTUC disseminate via lymphatic and hematogenous spread as well as direct extension. The most common sites of metastases for UTUC are lungs, liver, bones, and lymph nodes.

A greater proportion of UTUCs are invasive at diagnosis, compared with UC of the bladder, at approximately two-thirds, and multifocal disease has been reported in approximately 25% to 30% of UTUCs at the time of diagnosis [7,8]. UTUC is approximately twice as common in men than women [5] compared with bladder cancer, which is 4 times as common in men. Presenting complaint in 75% to 95% of patients with UTUC is hematuria. Risk factors for developing UC of the bladder and UTUC are similar, contributing to the field exposure principle.

Bladder lymph node mapping has demonstrated the complexity and extent of bladder lymphatic drainage. Drainage extends beyond the external iliac vessels and obturator fossa, included in a limited pelvic nodal dissection, to also involve the internal iliac and common iliac vessels up to the uretero-iliac crossing and occasionally extending to the inferior mesenteric artery [9]. Traditionally, lymph nodes have been considered suspicious based on increased size; however, newer MRI techniques and fluorine-18-2-fluoro-2-deoxy-D-glucose (FDG)-PET/CT can improve malignancy detection in subcentimeter-sized nodes [10-12].

UC is staged by its extent at presentation and graded as either low grade or high grade. The standard staging system is the Tumor, Node, Metastasis (TNM) system, which encompasses the status of the primary tumor (T), lymph nodes (N), and metastases (M). The eighth edition of the American Joint Committee on Cancer Staging Manual is still currently applicable for TNM staging of UCs [13].

Radical cystectomy with pelvic lymphadenectomy remains the reference standard treatment for MIBC [14]. Neoadjuvant cisplatin-based combination chemotherapy is increasingly being used in these patients and has been shown to improve disease-specific and overall survival compared with surgery alone [15,16]. Alternatively, bladder preservation with concurrent chemoradiotherapy and maximal transurethral resection of bladder tumor (TURBT) is also now included as a category 1 recommendation for localized MIBC in National Comprehensive Cancer Network guidelines [17]. Moving forward, immune-checkpoint inhibitors and molecular-profiling technologies hold the potential to fundamentally change management of bladder cancer [18]. For patients

with UTUC with nonmetastatic disease and a normal contralateral kidney, traditionally, standard treatment was an open radical nephroureterectomy with bladder cuff excision. More recent systemic evidence review shows equivalent oncologic outcomes for open and minimally invasive (laparoscopic, hand-assisted laparoscopic, robot-assisted laparoscopic) approaches [8,19]. In a subset of carefully selected patients, less invasive approaches such as kidney sparing surgery or ablation may be suitable alternatives [8,20].

The principal task of imaging is to characterize the site of known UC in addition to evaluating for additional secondary sites in the ureters or bladder, extravesical/ureteral spread, and nodal and distant metastases [21]. Many patients may have already had imaging during the workup of hematuria.

Some local practice patterns do not routinely administer intravenous (IV) contrast to renal transplant patients. In this document, it is presumed that patients have no contraindications to IV contrast agents.

Special Imaging Considerations

CT urography (CTU) is an imaging study that is tailored to improve visualization of both the upper and lower urinary tracts. Protocols most often include unenhanced images followed by IV contrast-enhanced images, including both nephrographic and excretory phases acquired at least 5 minutes after contrast injection. In some institutions in subsets of patients (ie, less than 40 years of age or lower risk), a split-bolus technique is employed. This uses an initial dose of IV contrast and then obtains a combined nephrographic-excretory phase after a second IV contrast dose is given. Thin-slice acquisition is used with some places using reconstruction methods, commonly including maximum intensity projection or 3-D volume rendering. For the purposes of this document, we make a distinction between CTU and CT abdomen and pelvis without and with IV contrast protocols not specifically tailored for the evaluation of the upper and lower urinary tracts.

MR urography (MRU) is an imaging study also tailored to improve visualization of the urinary system. Unenhanced MRU relies upon heavily T2-weighted imaging (much like magnetic resonance cholangiopancreatography imaging) of the intrinsic high signal intensity from urine. Contrast-enhanced MRU includes IV contrast administration to provide additional information regarding obstruction, urothelial thickening, and focal lesions. Postcontrast-enhanced T1-weighted series should include the corticomedullary, nephrographic, and excretory phase. Thin-slice acquisition and multiplanar imaging should be obtained. For the purposes of this document, we make a distinction between

MRU and MRI abdomen and pelvis without and with IV contrast protocols not specifically tailored for evaluation of the upper and lower urinary tracts.

DISCUSSION OF PROCEDURES BY VARIANT

Variant 1: Adult. Nonmuscle invasive bladder cancer. Pretreatment staging

The goal of imaging in a known nonmuscle invasive bladder cancer (NMIBC) is primarily to evaluate for synchronous sites of UC in the upper tracts and bladder. There is overall a low likelihood of nodal or metastatic disease in NMIBC [22,23]. With the information from imaging, this will initiate the appropriate treatment plan sooner and can improve patient outcome by reducing length of illness. This will ideally help to reduce delaying the appropriate treatment and hasten the patient's recovery.

Bone Scan Whole Body. There is no relevant literature to support the use of whole-body bone scan in the evaluation of NMIBC.

CT Abdomen and Pelvis With IV Contrast. It is common practice in many medical centers to perform abdominal imaging with IV contrast along with pelvis/bladder imaging to fully stage bladder cancer. For further information on detecting bladder cancer, please see the ACR Appropriateness Criteria® topics on "Hematuria" [24] and "Post-Treatment Surveillance of Bladder Cancer" [25].

The overall accuracy of local bladder cancer staging in the literature is variable. A retrospective study looked at 778 patients from 3 academic centers over a 19-year time period who had undergone a radical cystectomy and compared clinical to pathologic stage [26]. In these patients, pathologic upstaging occurred in 42% of patients, and pathologic downstaging occurred in 22%. However, given the 20-year time period that data were collected, the advances in CT technique and imaging prevalence may have affected results. To improve local staging, various techniques including CT cystograms and CT urograms have been investigated. Paik et al [27] found an overall accuracy of 55%, with a 39% understaging and a 21% false-negative for extravesical spread. In a retrospective review of 276 patients, Tritschler et al [28] found the accuracy of CT in predicting pathological tumor stage was 49% and the accuracy for predicting lymph node metastases was 54%. They concluded that multidetector CT had little impact on decision making for local treatment of MIBC during radical cystectomy. Another study by the same group [29] found that there was significant interobserver variability in CT findings, which might contribute to the limited accuracy of CT in the detection of extravesical tumor

spread, infiltration of extravesical organs, and lymph node involvement.

In addition to multidetector CT, various imaging techniques such as multiplanar reformation, 3-D reconstruction, and virtual cystoscopy have been evaluated for local bladder cancer staging. Wang et al [6] demonstrated an overall accuracy of 88% for CT staging of bladder cancer using multiplanar reformation. The accuracy was specifically 77% for T1 to T2 lesions and 95% for T3 to T4 lesions. Multiplanar reformation was found to be effective in evaluating the origin and extent of extravesical invasion as well as the tumor's relationship to the ureter. None of the patients with NMIBC had metastases detected by CT imaging.

CT Abdomen and Pelvis Without and With IV Contrast. Although there is no relevant literature to support the use of CT abdomen and pelvis without and with IV contrast (separate from CTU) in the evaluation of NMIBC, it may be useful in some clinical situations. However, CTU and MRU are of greater usefulness because they allow for a more comprehensive evaluation of the genitourinary tract, as well as assessment of retroperitoneal and pelvic lymph nodes (see CTU and MRU sections).

CT Abdomen and Pelvis Without IV Contrast. There is no relevant literature to support the use of CT abdomen and pelvis without IV contrast (separate from CTU) in the evaluation of NMIBC.

CT Abdomen With IV Contrast. It has been suggested that abdominal CT can be obtained simultaneously with pelvic CT in a single scan, but its usefulness in detecting abdominal lymphadenopathy and metastases in patients with NMIBC may be limited due to the low risk of distant metastasis. In a study by Rajesh et al [30], a CT whole-body staging was performed in 201 patients with biopsy-proven bladder cancer to evaluate distant metastatic disease at the time of diagnosis. Of these patients, 6% had distant metastasis, with retroperitoneal lymph nodes being the most common site of metastasis. None of the patients with NMIBC had metastases detected by CT imaging.

CT Abdomen Without and With IV Contrast. There is no relevant literature to support the use of CT abdomen without and with IV contrast (separate from CTU) in the evaluation of NMIBC.

CTU and MRU are of greater usefulness because they allow for the comprehensive evaluation of the genitourinary tract, as well as the assessment of retroperitoneal and pelvic lymph nodes (see CTU and MRU sections).

CT Abdomen Without IV Contrast. There is no relevant literature to support the use of CT abdomen without

IV contrast (separate from CTU) in the evaluation of NMIBC.

CT Chest With IV Contrast. Although chest CT is generally recommended for patients with MIBC [31,32], the necessity of chest CT in patients with NMIBC is not clearly established. The study by Juri et al [33] suggests that the risk of chest metastasis in patients with Ta or T1 NMIBC is low, and chest CT may not be necessary in these patients unless there is upstaging during follow-up. However, it is important to note that this was a retrospective study, and further prospective studies are needed to confirm these findings and establish clear guidelines for chest imaging in NMIBC. In general, the decision to perform chest imaging should be individualized based on the patient's risk factors and clinical presentation. CT chest with IV contrast is preferred over CT chest without IV contrast when evaluating for metastatic disease and lymphadenopathy.

CT Chest Without and With IV Contrast. There is no relevant literature to support the use of CT chest without and with IV contrast in the evaluation of NMIBC.

CT Chest Without IV Contrast. Although chest CT is generally recommended for patients with MIBC [31,32], the necessity of chest CT in patients with NMIBC is not clearly established. The study by Juri et al [33] suggests that the risk of chest metastasis in patients with Ta or T1 NMIBC is low, and chest CT may not be necessary in these patients unless there is upstaging during follow-up. However, it is important to note that this was a retrospective study, and further prospective studies are needed to confirm these findings and establish clear guidelines for chest imaging in NMIBC. In general, the decision to perform chest imaging should be individualized based on the patient's risk factors and clinical presentation. CT chest with IV contrast is preferred over CT chest without IV contrast when evaluating for metastatic disease and lymphadenopathy.

CT Pelvis With IV Contrast. There is no relevant literature to support the use of CT pelvis with IV contrast in the evaluation of NMIBC.

CTU and MRU are of greater usefulness because they allow for the comprehensive evaluation of the genitourinary tract, as well as the assessment of retroperitoneal and pelvic lymph nodes (see CTU and MRU sections).

CT Pelvis Without and With IV Contrast. There is no relevant literature to support the use of CT pelvis without and with IV contrast in the evaluation of NMIBC.

CTU and MRU are of greater usefulness because they allow for the comprehensive evaluation of the genitourinary

tract, as well as the assessment of retroperitoneal and pelvic lymph nodes (see CTU and MRU sections).

CT Pelvis Without IV Contrast. There is no relevant literature to support the use of CT pelvis without IV contrast in the evaluation of NMIBC.

CTU and MRU are of greater usefulness because they allow for the comprehensive evaluation of the genitourinary tract, as well as the assessment of retroperitoneal and pelvic lymph nodes (see CTU and MRU sections).

CTU Without and With IV Contrast. CT, particularly CTU, is the most used imaging modality worldwide for the diagnosis and staging of urothelial malignancies [2]. CTU is commonly used for localizing, locoregional staging, and detecting distant metastases [34]; however, in NMIBC, the usefulness is primarily to identify synchronous UCs. According to a recent review by Mirmomen et al [35], CTU demonstrated a 91% diagnostic accuracy in detecting UCs. Studies have indicated that CTU is similarly sensitive overall to cystoscopy (CTU up to 87% sensitive, 99% specific; cystoscopy 87% sensitive, 100% specific), but it may miss very small or flat lesions that are more easily detected by cystoscopy [23]. If cystoscopy is performed first, CTU is used to detect isolated or concurrent upper tract lesions, because approximately 2% to 4% of patients with bladder cancer may have concurrent UTUC. One study evaluating CTU in detecting bladder cancer in patients with hematuria or surveillance showed 13 of 710 false-negatives and 47 of 710 false-positives [36]. Of the false-negatives, 11 of 13 were due to limitations of the technique because the lesions were not visible in retrospect, whereas cystoscopy showed carcinoma in situ or urothelial erythema. Two false-negatives were related to technical factors, one case was related to a large postvoid residual with suboptimal opacification of the bladder, and one case was related to bilateral hip arthroplasties with artifacts obscuring the bladder. False-positive results were due to interpretation errors, most caused by benign prostatic hypertrophy mimicking a bladder lesion, followed by bladder trabeculation, post-treatment changes, and intravesical blood clots.

According to experts in the field, a small percentage of patients with bladder cancer will also develop UTUC, necessitating a comprehensive examination of the urothelium [5]. One effective approach to detecting UTUC is the use of an abdomen-pelvis CTU protocol. In recent years, CTU and MRU have largely replaced IV urography (IVU) for evaluating the renal collecting systems and ureters [37,38]. These cross-sectional techniques offer several advantages, such as the ability to visualize small masses, which may be obscured on excretory urography due to contrast

material or bowel gas, identify focal wall thickening, and distinguish enhancing tumors from nonenhancing calculi or blood clots [5,37]. Additionally, CTU and MRU can evaluate nonfunctioning/obstructed kidneys that would not excrete the contrast medium required for excretory urography. Based on these strengths, Jinzaki et al [37] suggest that CTU should be the initial examination for high-risk patients, whereas Cohan et al [39] concluded that CTU can detect more bladder cancers than excretory urography.

A recent retrospective analysis by Chen et al [40] of 168 patients with pathologically confirmed NMIBC who underwent preoperative CTU were divided into low-, medium-, high-, and very-high-risk groups based on the European Society of Urology guidelines [22] and then further analyzed based on tumor size, location, number, and various tumor characteristics including size of base and perivesical stranding at diagnosis [40]. These data were then used to attempt to stratify patients at higher risk for recurrences, which is important because these recurrences can become MIBC and metastasize [41]. This was a preliminary study that demonstrated the feasibility of using preoperative CTU features to predict the risk stratification of NMIBC, but further validation in a larger population is needed. Combinations of CT features and other characteristics may further improve the performance of the model and provide more accurate information for patient evaluation.

FDG-PET/CT Skull Base to Mid-Thigh. FDG-PET/CT is not ideal for evaluating the urinary collecting system because FDG is excreted through urine, but it can be useful in detecting distant metastases. Studies suggest that FDG-PET/CT may not be necessary for staging NMIBC because of a low likelihood of nodal or metastatic disease [22,23].

FDG-PET/MRI Skull Base to Mid-Thigh. A potential novel approach to bladder cancer imaging is FDG-PET/MRI, which combines the strengths of both modalities: the superior contrast resolution and multiparametric assessment with MRI and the metabolic assessment with PET. A pilot study with 22 FDG-PET/MRI examinations [42] found that FDG-PET/MRI had a higher accuracy than MRI alone for detecting bladder tumors (86% versus 77%), metastatic pelvic lymph nodes (95% versus 76%), and nonnodal pelvic malignancies (100% versus 91%). FDG-PET/MRI changed suspicion for bladder tumors in 36% of cases (50% increased, 50% decreased), for pelvic lymph nodes in 52% of cases (36% increased, 64% decreased), and for nonnodal pelvis in 9% of cases (100% increased). Another recent study using FDG-PET/MRI [43] demonstrated similar performance of FDG-PET/MRI

(sensitivity 80%, specificity 56%) compared with CT (sensitivity 91%, specificity 43%) in detecting primary bladder tumors. However, evaluation of nodal status was limited, because of the lack of patients with true pathologic lymph nodes. Civelek et al [44] determined the clinical benefit of FDG-PET/MRI for surveillance and restaging of patients with locally advanced metastatic MIBC compared with conventional imaging methods. FDG-PET/MRI identified 82 metastatic malignant lesions involving lymph nodes, liver, lung, soft tissue, adrenal glands, prostate, and bone, with a resultant advantage of 36% for lesion visibility in comparison with CT. The researchers concluded that FDG-PET/MRI can detect metastatic lesions, which cannot be identified on conventional CT, and this can allow for better treatment planning and improve disease monitoring during therapy. Studies suggest that FDG-PET/MRI may not be necessary for staging NMIBC due to a low likelihood of nodal or metastatic disease [22,23].

MRI Abdomen and Pelvis Without and With IV Contrast. Although there is no relevant literature to support the use of MRI abdomen and pelvis without and with IV contrast (separate from MRU) in the evaluation of NMIBC, it may be useful in some clinical situations. However, CTU and MRU are of greater usefulness because they allow for the comprehensive evaluation of the genitourinary tract, as well as the assessment of retroperitoneal and pelvic lymph nodes (see CTU and MRU sections).

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MRI Abdomen Without IV Contrast. There is no relevant literature to support the use of MRI abdomen without IV contrast (separate from MRU) in the evaluation of NMIBC.

MRI Head Without and With IV Contrast. Neurological complications arising from bladder cancer are uncommon and typically arise from local extension of the tumor. According to a study on metastatic patterns of MIBC, brain metastases were found in only 5% of

patients [45], ranking it as the ninth most common site of metastasis. Consequently, MRI of the brain is not recommended for routine use in asymptomatic patients and should only be considered on an individual basis [46].

MRI Head Without IV Contrast. There is no relevant literature to support the use of MRI head without IV contrast in the evaluation of NMIBC.

MRI Pelvis Without and With IV Contrast. There is some literature discussing the use of imaging, in particular MRI pelvis, in differentiating NMIBC from MIBC; however, most institutions are currently performing that differentiation at TURBT and histologic evaluation. MRI is particularly useful for detecting bladder cancer invasion of the detrusor muscle, perivesical tissues, and nearby organs [5,47,48]. Klein and Pollack [49] noted that MRI has a better sensitivity and specificity than CT for local staging, with the most significant advantage being its ability to distinguish between superficial and deep invasion of the bladder detrusor muscle. For deeply infiltrating tumors (stages T3b-T4b), they concluded that MRI is the most accurate staging technique, making CT unnecessary when MRI is available. Beyersdorff et al [21] concluded that MRI is superior to CT for assessing the depth of invasion in the bladder wall, although both techniques may have difficulty differentiating between tumor and inflammation from previous transurethral biopsy. However, recent studies suggest that adding diffusion-weighted imaging (DWI) to conventional pelvic MRI may aid in distinguishing treatment response and detecting residual/recurrent disease [50].

Some studies have demonstrated the sensitivity and specificity of MRI in distinguishing NMIBC from MIBC ranging from 78% to 98% and 82% to 100% and the sensitivity and specificity for distinguishing organ-confined from non-organ-confined bladder tumors ranging from 90% to 94% and 60% to 94%, respectively [51-54]. Multiparametric MRI, which combines dynamic contrast-enhanced imaging with DWI and T2-weighted imaging, is likely the most optimal MRI technique for local staging of bladder cancer [48,55].

The standardization of bladder cancer staging with multiparametric MRI is facilitated by the Vesical Imaging-Reporting and Data System (VI-RADS) scoring system, which was introduced in 2018 [56]. The VI-RADS uses a 5-point scoring system to estimate the likelihood of detrusor muscle invasion, a poor prognosis indicator that requires radical surgery. Wang et al [57] assessed the ability of VI-RADS score to detect MIBC in a group of patients who had multiparametric MRI before surgery. They concluded that VI-RADS effectively predicts the likelihood of detrusor muscle invasion in bladder cancer and should be considered for evaluation before surgery. Kufukihara et al [58]

compared the diagnostic accuracy of VI-RADS scoring with cystoscopy and found that VI-RADS had superior performance in detecting detrusor muscle invasion, especially in tumors located at the bladder neck/trigone/dome/posterior and anterior wall, but inferior performance in detecting tumors located on the lateral wall or ureteral orifice. Makboul et al [59] evaluated the usefulness of multiparametric MRI in differentiating MIBC from NMIBC with the accuracy of the VI-RADS scoring system. They found that multiparametric MRI is a comprehensive and effective tool for determining muscle invasion in bladder cancer and that VI-RADS can accurately differentiate between MIBC and NMIBC. Hagen et al [60] assessed the clinical applicability of preoperative multiparametric MRI using the 5-point VI-RADS scoring system to stage bladder cancer and compared it with dual-phase contrast-enhanced CT (CECT). Both CECT and multiparametric MRI correctly identified tumor stages as either MIBC or NMIBC, but T stages bordering the histopathologic limits of muscle invasiveness resulted in overestimation of muscle invasion in 43% of cases for the multiparametric MRI image data sets and underestimation of muscle invasion in up to 55.5% of cases for the CECT data.

In addition to its use in detecting muscle invasion, MRI has also been studied as a predictor of bladder cancer progression and prognosis. Yajima et al [41] conducted a study to evaluate the significance of the “inchworm sign” on DWI for the recurrence and progression of T1 bladder cancer. The absence of an inchworm sign on DWI was found to be a significant prognostic factor for progression of T1 bladder cancer, suggesting that morphological evaluation of DWI signals may be a helpful addition to preoperative assessment of the bladder cancer’s aggressiveness.

MRI Pelvis Without IV Contrast. There is little literature to support the use of MRI pelvis without IV contrast in the evaluation of NMIBC. The addition of gadolinium contrast agent on MRI has been found to improve the accuracy of local staging for bladder cancer. In a prospective study by Daneshmand et al [61], 122 patients were examined using contrast-enhanced MRI, which had an 88% sensitivity, a 48% specificity, and a 74% accuracy in distinguishing organ-confined from non-organ-confined bladder cancer and a 41% sensitivity, a 92% specificity, and an 80% accuracy in detecting positive nodal disease. Moderate interobserver agreement was found for T and N staging, consistent with other studies [53,54]. Other studies demonstrated the sensitivity and specificity of MRI in distinguishing NMIBC from MIBC ranging from 78% to 98% and 82% to 100% and the sensitivity and specificity for distinguishing organ-confined from non-organ-confined bladder tumors ranging from 90% to 94% and

60% to 94%, respectively [51-54]. Multiparametric MRI, which combines dynamic contrast-enhanced imaging with DWI and T2-weighted imaging, is likely the most optimal MRI technique for local staging of bladder cancer [48,55].

MRU Without and With IV Contrast. Abdominal MRI, specifically MRU, can be used to stage bladder cancer by evaluating nodal, upper tract, and metastatic involvement along with dedicated pelvic imaging to assess local staging. MRU is a viable alternative for CTU in the evaluation of upper tract disease. The main benefit of MRU over CTU is the inherent higher contrast resolution [62]. When the entire upper tract is not visualized or degraded by motion artifact, MRU sequences can be repeated multiple times without fear of added radiation risk. Inherent higher contrast resolution of MRU is particularly beneficial for small tumor detection. An MRU examination with and without IV contrast provides a more comprehensive evaluation than an MRU without IV contrast examination.

MRU Without IV Contrast. Noncontrast MRU is an option for assessing the renal collecting systems and ureters using a heavily T2-weighted sequence [63]. MRU may be performed for nodal, synchronous bladder, and metastatic staging. The main benefit of MRU over CTU is inherent higher contrast resolution [62]. When the entire upper tract is not visualized or degraded by motion artifact, MRU sequences can be repeated multiple times without fear of added radiation risk. Inherent higher contrast resolution of MRU is particularly beneficial for small tumor detection.

Radiography Chest. Although chest imaging is generally recommended for patients with MIBC [31,32], the necessity of chest imaging in patients with NMIBC is not clearly established. The study by Juri et al [33] suggests that the risk of chest metastasis in patients with Ta or T1 NMIBC is low, and chest imaging may not be necessary in these patients unless there is upstaging during follow-up. However, it is important to note that this was a retrospective study, and further prospective studies are needed to confirm these findings and establish clear guidelines for chest imaging in NMIBC. In general, the decision to perform chest imaging should be individualized based on the patient's risk factors and clinical presentation.

Radiography Intravenous Urography. Excretory urography, previously used for urothelium evaluation in the renal collecting systems and ureters, has now been replaced by CTU and MRU. Excretory urography has a lower sensitivity of 50% to 70% for detecting upper urinary tract lesions, compared with CTU [37]. In fact, a study comparing the accuracy of CTU and excretory urography for detecting and localizing upper urinary tract cancer showed that

CTU had higher sensitivity, specificity, and overall accuracy rates of 93.5%, 94.8%, and 94.2%, respectively, compared with 80.4%, 81.0%, and 80.8%, respectively, for excretory urography [37]. Therefore, once bladder cancer is diagnosed, CTU or MRU is preferred for staging and treatment planning, and routine IVU is typically unnecessary.

US Kidneys and Bladder Retroperitoneal. There is no relevant literature to support the use of ultrasound (US) kidneys and bladder retroperitoneal in the evaluation of NMIBC.

US Pelvis (Bladder). US is not commonly used for bladder cancer staging, because transabdominal grayscale US can lead to overstaging of superficial tumors in 48% to 49% of cases and understaging of invasive tumors in 5% to 11% of cases [64]. However, US can be useful in evaluating hematuria. In a study of 1,007 patients with gross hematuria [65], US had a sensitivity of 63% and a specificity of 99% in detecting bladder cancer. Another study by Fang et al [66] evaluated 214 new cases of bladder cancer with pathological correlation, reporting an overall accuracy of 79% for local staging with transabdominal US, with 10% overstaging and 12% understaging. However, transabdominal US is less accurate for detecting stage T3 and T4 disease compared with T1 and T2 disease [64]. Some researchers have correlated sonographically determined tumor height-to-length ratio with depth of tumor invasion on transabdominal US [67]. A height-to-length ratio of <0.605 was found to be a useful cutoff value for differentiating NMIBC from MIBC.

Three-dimensional US rendering is a new diagnostic tool that shows potential in discriminating NMIBC from MIBC [68]. It allows for retrieval and manipulation of volume data in multiple planes, increasing objectivity and improving the primary bladder tumor diagnosis rate (100% with 3-D US versus 88.9% with 2-D US) when identifying T3b disease [69]. However, the technique has limitations, including difficulty in visualizing the entire tumor, particularly in flat or plaque-like tumors, the presence of coexistent calcification, a rigid abdominal wall, or central obesity [70]. Contrast-enhanced US has also been shown to better differentiate MIBC from NMIBC [71]. In a study of 34 patients who underwent both grayscale and contrast-enhanced US before TURBT [71], contrast-enhanced US performance was similar to the reference standard of TURBT in differentiating MIBC from NMIBC. Ge et al [72] also found that preoperative contrast-enhanced US is highly efficient in discriminating Ta to T1 or low-grade bladder cancer from stage T2 or high-grade bladder cancer. Contrast-enhanced US shows a high sensitivity, specificity, and diagnostic accuracy, making it a promising

method for distinguishing T staging and grading of bladder cancer. Li et al [73] demonstrated that the combined use of contrast-enhanced US and DWI-MRI is more accurate in diagnosing bladder cancer than either method alone, making it a feasible and effective diagnostic approach for bladder cancer.

Variant 2: Adult. Muscle invasive bladder cancer. Pretreatment staging

The goals of imaging in a known MIBC include primarily assessing for synchronous sites of UC in the upper tracts and bladder in addition to evaluating for nodal and distant metastases. Local T staging can also be confirmed on imaging in patients with diagnosed MIBC. With the information from imaging, this will initiate the appropriate treatment plan sooner and can improve patient outcome by reducing length of illness. This will ideally help to reduce delaying the appropriate treatment and hasten the patient's recovery.

Bone Scan Whole Body. In patients with MIBC before radical cystectomy, there is conflicting evidence for the use of whole-body bone scan to evaluate for bone metastases. The incidence of metastases in patients with bladder cancer increases with tumor stage at the time of diagnosis [74]. However, studies on the usefulness of routine preoperative bone scans for bladder carcinoma demonstrate conflicting results. One study found a 4.6% positive rate in 458 bone scan studies with a true-positive rate of only 2.8%, leading to the conclusion that bone scans have no place in routine preoperative staging of bladder carcinoma [75]; however, the T stage of bladder cancer in these patients is not specified. Another study concluded that routine preoperative bone scans are usually unable to identify patients with bladder cancer of stage $\geq T2$ who will not be cured by total cystectomy unless additional investigations such as MRI are performed [76].

For patients with MIBC, the probability of positive bone scans increases, as does its importance in guiding proper management and avoiding unnecessary radical surgery [77]. One study found that 14.5% of patients with bladder cancer had bone metastasis at presentation, with deep muscle invasion being the most common factor associated with metastatic disease [78]. Thus, the authors advocate the routine use of bone scans in patients with MIBC.

However, false-positive bone scans can occur, leading to the need for additional studies. Moreover, the routine use of bone scans in the staging of MIBC often leads to the need for additional downstream studies, resulting in treatment delays [79]. Furrer et al [80] concluded that routine staging bone scintigraphy has limited benefit in the staging of

invasive bladder cancer and does not support its routine use. Overall, baseline bone scintigraphy led to a change in the intended management in only 1.7% of patients, with additional imaging being performed in 4% of patients.

CT Abdomen and Pelvis With IV Contrast. As part of comprehensive staging, many centers perform abdominal imaging with IV contrast in combination with pelvis/bladder imaging. For more information on detecting bladder cancer, please refer to the ACR Appropriateness Criteria® topics on “Hematuria” [24] and “Post-Treatment Surveillance of Bladder Cancer” [25].

CT plays an important role in bladder cancer staging, detecting multifocal disease, extravesical extension, adenopathy, and metastases [2]. It can effectively identify bulky thickening of the bladder wall, perivesical tumor extension, lymphadenopathy, and distant metastases [34]. However, it is more effective for detecting T3b and T4 disease for local staging of bladder cancer. Invasion beyond the serosa is identified as nodularity and stranding along the bladder surface, although inflammation and desmoplastic reaction can appear similar, especially after biopsy [39]. Although CT is not the preferred method for local staging up to T3a and differentiating NMIBC ($\leq T1$) from MIBC ($\geq T2$) compared with MRI, CT is still useful in differentiating tumors staged up to T3a from higher-staged T3b and T4 bladder cancers [81]. According to a study of CT staging of bladder cancer conducted by Mirmomen et al [35], the accuracy in detecting perivesicular invasion with tumors staged $\geq T3$ ranges from 49% to 93%. Early models using machine learning show promise in stratifying tumors into stage $< T2$ and stage $\geq T2$, which may enhance the usefulness of CT in local staging in the future [82]. However, further research and validation are necessary before these models can be clinically implemented and accepted.

CT is commonly used to determine nodal involvement, but relying on size alone is not reliable because small nodes may be metastatic and large nodes may be reactive [83]. CT cannot detect microscopic tumor metastases in nonenlarged lymph nodes [5]. CT accuracy for lymph node evaluation ranges from 73% to 92%, with a tendency to understage nodal involvement, particularly when based on short-axis nodal enlargement criteria of 1 cm [84]. Pelvic nodes are more challenging to recognize than paraaortic nodes, especially in thin patients, although asymmetry can be a useful sign [85]. The accuracy of CT for extravesical extension ranged from 40% to 92% with a mean of 74% in the study by Paik et al [27], and for predicting pathological tumor stage and lymph node metastases, accuracy was 49% and 54%, respectively, in the study by Tritschler et al [28]. Interobserver variability in CT

findings contributes to the limited accuracy of CT in detecting extravesical tumor spread, infiltration of extravesical organs, and lymph node involvement [29]. Yuan et al [86] demonstrated that CT could help surgeons determine the extent of pelvic lymph node dissection, with lower-stage tumors requiring less extensive nodal dissection, reducing the risk of complications. However, Horn et al [87] found that the sensitivity of CT imaging for the detection of lymph node metastases was low, whereas the specificity was relatively high.

Studies have examined the use of multiplanar reformation, 3-D reconstruction, and virtual cystoscopy in addition to multidetector CT. Wang et al [6] reported an overall accuracy of 88% of CT for bladder cancer staging using multiplanar reformation, with a 77% accuracy for T1 to T2 lesions and a 95% accuracy for T3 to T4 lesions. Multiplanar reformation was also found to be useful in evaluating the origin and extent of extravesical invasion and the tumor's relationship with the ureter.

Rajesh et al [30] conducted a study on 201 patients with bladder UC who underwent CT whole-body staging at the time of diagnosis to evaluate distant metastatic disease. Results showed that 6% of patients had distant metastatic spread, with retroperitoneal lymph nodes being the most common site. None of the patients with NMIBC had distant metastases. Peritoneal metastases were observed in 7.6% to 16% of cases, with a higher frequency in cases of atypical variant histology. One study reported CT findings of peritoneal metastases in 8 out of 105 patients, which were associated with poor prognosis [88]. In another study, peritoneal metastasis was observed in 24 out of 150 patients, occurring more frequently in those with atypical histology, including squamous cell carcinoma, adenocarcinoma, small cell carcinoma, and undifferentiated tumors [45].

CT Abdomen and Pelvis Without and With IV Contrast. There is no relevant literature to support the use of CT abdomen and pelvis without and with IV contrast (separate from CTU) in the evaluation of MIBC. There is no relevant literature documenting the additional benefit of CT without and with IV contrast, relative to CT with IV contrast in this setting.

CTU and MRU are of greater usefulness because they allow for the comprehensive evaluation of the genitourinary tract, as well as the assessment of retroperitoneal and pelvic lymph nodes (see CTU and MRU sections).

CT Abdomen and Pelvis Without IV Contrast. There is no relevant literature to support the use of CT abdomen and pelvis without IV contrast (separate from CTU) in the evaluation of MIBC.

CT Abdomen With IV Contrast. There is no relevant literature to support the use of CT abdomen with IV contrast (separate from CTU) in the evaluation of MIBC.

CT Abdomen Without and With IV Contrast. There is no relevant literature to support the use of CT abdomen without and with IV contrast (separate from CTU) in the evaluation of MIBC.

CT Abdomen Without IV Contrast. There is no relevant literature to support the use of CT abdomen without IV contrast (separate from CTU) in the evaluation of MIBC.

CT Chest With IV Contrast. It is recommended that all patients with MIBC undergo pulmonary evaluation [30]. Patients with MIBC who have abnormal chest radiograph findings or are at high risk should undergo chest CT, consistent with other guidelines [31,32]. However, there is currently a lack of original research directly comparing the diagnostic usefulness of chest radiographs versus chest CT in this patient population. CT chest with IV contrast is preferred over CT chest without IV contrast when evaluating for metastatic disease and lymphadenopathy.

CT Chest Without and With IV Contrast. There is no relevant literature to support the use of CT chest without and with IV contrast in the evaluation of MIBC. There is no additional benefit to support performing CT chest without and with contrast over imaging either without or with contrast alone.

CT Chest Without IV Contrast. It is recommended that all patients with MIBC undergo pulmonary evaluation [30]. Patients with MIBC who have abnormal chest radiograph findings or are at high risk should undergo chest CT, consistent with other guidelines [31,32]. However, there is currently a lack of original research directly comparing the diagnostic usefulness of chest radiographs versus chest CT in this patient population. CT chest with contrast is preferred over CT chest without IV contrast when evaluating for metastatic disease and lymphadenopathy.

CT Pelvis With IV Contrast. There is no relevant literature to support the use of CT pelvis with IV contrast (separate from CTU) in the evaluation of MIBC.

CTU and MRU are of greater usefulness because they allow for the comprehensive evaluation of the genitourinary tract, as well as the assessment of retroperitoneal and pelvic lymph nodes (see CTU and MRU sections).

CT Pelvis Without and With IV Contrast. There is no relevant literature to support the use of CT pelvis without and with IV contrast (separate from CTU) in the evaluation of MIBC.

CTU and MRU are of greater usefulness because they allow for the comprehensive evaluation of the genitourinary tract, as well as the assessment of retroperitoneal and pelvic lymph nodes (see CTU and MRU sections).

CT Pelvis Without IV Contrast. There is no relevant literature to support the use of CT pelvis without IV contrast (separate from CTU) in the evaluation of MIBC.

CTU and MRU are of greater usefulness because they allow for the comprehensive evaluation of the genitourinary tract, as well as the assessment of retroperitoneal and pelvic lymph nodes (see CTU and MRU sections).

CTU Without and With IV Contrast. A recommended practice during primary evaluation and surgical treatment of urothelial bladder carcinoma is to image the upper tract if not previously done [5]. Synchronous upper tract tumors occur in 2% of patients at presentation, and 6% develop a metachronous lesion [89]. An abdomen-pelvis CTU protocol can help to detect upper urinary tract disease. Cross-sectional techniques such as CTU and MRU are superior to IVU for evaluating the renal collecting systems and ureters [37,38]. Advantages of CTU and MRU include the ability to visualize small masses directly, identify focal wall thickening, and distinguish nonspecific filling defects such as enhancing tumor versus nonenhancing calculi or blood clots. Additionally, CTU and MRU can assess nonfunctioning/obstructed kidneys that would not excrete contrast medium required for excretory urography [5,37]. Based on these strengths, Jinzaki et al [37] concluded that CTU should be considered as the initial examination for the evaluation of patients at high risk for upper urinary tract UC, and Cohan et al [39] concluded that CTU can detect many more bladder cancers than excretory urography.

FDG-PET/CT Skull Base to Mid-Thigh. FDG-PET/CT is not ideal for evaluating the urinary collecting system due to FDG excretion in urine but can effectively assess nodal and metastatic disease. A study by Goodfellow et al [90] involving 233 patients found that CT had a sensitivity and specificity of 45% and 98%, respectively, in detecting pelvic lymph node metastases. FDG-PET/CT increased sensitivity to 69%, with a slight reduction in specificity to 95%. In a prospective study of 25 patients by Nayak et al [91], FDG-PET/CT had a sensitivity of 78% compared with CT, with a sensitivity of 44% in detecting positive lymph nodes for metastases on histopathology. Other studies have reported the sensitivity of FDG-PET/CT for lymph node metastasis detection ranging from 47% to 56% and the specificity ranging from 93% to 98%, with specificity usually slightly lower than for CT [92]. Pichler et al [93] retrospectively analyzed 70 patients with bladder cancer staged with FDG-PET/CT before radical

cystectomy and found that using an 8-mm cutoff, CT had a specificity of 92%, whereas FDG-PET alone had a sensitivity, specificity, and accuracy of 55%, 90%, and 84%, respectively. Combining FDG-PET/CT resulted in a nonsignificant increase in diagnostic accuracy using an 8-mm cutoff for lymph node evaluation (64%, 86%, and 83%, respectively). Girard et al [94] proposed using the maximum standardized uptake value associated with axial-based lymph node size to improve the detection of regional lymph node metastasis in 61 patients with clinically localized MIBC, showing that combining maximum standardized uptake value and axial-based lymph node size criteria using FDG-PET/CT can improve the diagnostic accuracy for preoperative lymph staging in patients with MIBC.

A meta-analysis showed a combined sensitivity of 82% and a specificity of 89% for detecting metastatic lesions from bladder cancer with FDG-PET [95]. Goodfellow et al [90] compared FDG-PET with CT in detecting metastatic disease outside of the pelvis from bladder cancer and found a higher sensitivity for FDG-PET at 54%, compared with 41% for CT, whereas both imaging modalities had similar specificities of 97% and 98%, respectively. Kibel et al [96] conducted a prospective study of FDG-PET/CT for MIBC in patients with no evidence of metastatic disease through traditional staging methods. In this study, FDG-PET/CT had a sensitivity of 70%, a specificity of 94%, a positive predictive value (PPV) of 78%, and a negative predictive value of 91%.

FDG-PET/CT can have a significant impact on the clinical decisions for patients with bladder cancer. A clinical impact analysis conducted by Apolo et al [97], which analyzed the patients with bladder cancer through the National Oncology PET registry, found that FDG-PET/CT results changed the treatment plan in 68% of patients. Even after accounting for the possibility that a different imaging test may have led to the same management strategy, FDG-PET/CT still altered treatment plans in 47% of patients. Kollberg et al [98] prospectively assessed 103 patients with high-risk MIBC who underwent FDG-PET/CT in addition to CT and found that FDG-PET/CT led to an altered provisional treatment plan in 27% of patients. Similarly, a study by Mertens et al [99] of 96 consecutive patients with bladder cancer found that FDG-PET/CT provided additional staging information that modified the treatment of MIBC in almost 20% of cases. Voskuilen et al [100] evaluated the incremental benefit of FDG-PET/CT after standard conventional staging with a retrospective analysis of 711 consecutive patients having MIBC and found that FDG-PET/CT potentially influenced the treatment of almost one-fifth of patients, similar to the study by Mertens et al [99]. Bertolaso et al [101] assessed the

accuracy of FDG-PET/CT for lymph node staging and found that treatment decisions were altered according to FDG-PET/CT results in almost a quarter of patients with MIBC.

Currently, 11C-choline PET is primarily an experimental imaging modality. When compared with CT, it shows promise for increased accuracy in lymph node staging and may help avoid false-positive results for lymph nodes due to reactive hyperplasia [102]. According to current literature, 11C-choline PET/CT has a sensitivity of 42% to 59% and a specificity of 84% to 90% in detecting nodal disease [103,104]. In a study by Golan et al [105], 11C-choline PET/CT was compared with FDG-PET/CT in 20 consecutive patients with bladder cancer, with a total of 51 lesions. The PPVs for all detected lesions were 85% for 11C-choline PET/CT and 91% for FDG-PET/CT. The corresponding PPVs for extravesical lesions were 79% and 88%, respectively. FDG-PET/CT correctly identified 4 extravesical metastases missed by 11C-choline PET/CT. They concluded that 11C-choline PET/CT did not offer any advantage over FDG-PET/CT in detecting distant metastasis in bladder cancer.

FDG-PET/MRI Skull Base to Mid-Thigh. A potential novel approach to bladder cancer imaging is FDG-PET/MRI, which combines the strengths of both modalities: superior contrast resolution and multiparametric assessment with MRI and metabolic assessment with PET. A pilot study with 22 FDG-PET/MRI examinations [42] found that FDG-PET/MRI had a higher accuracy than MRI alone for detecting bladder tumors (86% versus 77%), metastatic pelvic lymph nodes (95% versus 76%), and nonnodal pelvic malignancies (100% versus 91%). FDG-PET/MRI changed suspicion for bladder tumors in 36% of cases (50% increased, 50% decreased), for pelvic lymph nodes in 52% (36% increased, 64% decreased), and for nonnodal pelvis in 9% of cases (100% increased). Another recent study using FDG-PET/MRI [43] demonstrated a similar performance of FDG-PET/MRI (sensitivity 80%, specificity 56%) compared with CT (sensitivity 91%, specificity 43%) in detecting primary bladder tumors. However, evaluation of nodal status was limited, because of the lack of patients with true pathologic lymph nodes. Civelek et al [44] determined the clinical benefit of FDG-PET/MRI for surveillance and restaging of patients with locally advanced metastatic MIBC compared with conventional imaging methods. FDG-PET/MRI identified 82 metastatic malignant lesions involving lymph nodes, liver, lung, soft tissue, adrenal glands, prostate, and bone with a resultant advantage of 36% for lesion visibility in comparison with CT. They concluded that FDG-PET/MRI can detect metastatic lesions that would

not be identified on conventional CT, and this can allow for better treatment planning and improve disease monitoring during therapy.

MRI Abdomen and Pelvis Without and With IV Contrast. Although there is no relevant literature to support the use of MRI abdomen and pelvis without and with IV contrast (separate from MRU) in the evaluation of MIBC, it may be useful in some clinical situations. However, CTU and MRU are of greater usefulness because they allow for the comprehensive evaluation of the genitourinary tract, as well as the assessment of retroperitoneal and pelvic lymph nodes (see CTU and MRU sections).

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CTU and MRU are of greater usefulness because they allow for the comprehensive evaluation of the genitourinary tract, as well as the assessment of retroperitoneal and pelvic lymph nodes (see CTU and MRU sections).

MRI Abdomen Without IV Contrast. There is no relevant literature to support the use of MRI abdomen without IV contrast (separate from MRU) in the evaluation of MIBC.

CTU and MRU are of greater usefulness because they allow for the comprehensive evaluation of the genitourinary tract, as well as the assessment of retroperitoneal and pelvic lymph nodes (see CTU and MRU sections).

MRI Head Without and With IV Contrast. Bladder cancer rarely causes neurological complications directly, because it usually occurs due to local extension. According to a study on the metastatic pattern of MIBC, brain metastases occurred in only 5% of patients, making it the ninth most common site of metastasis [45]. As a result, asymptomatic patients are not suggested to undergo MRI of the head and should only be considered on an individual basis [46].

MRI Head Without IV Contrast. There is no relevant literature to support the use of MRI head without IV contrast in the evaluation of MIBC.

MRI Pelvis Without and With IV Contrast. For local staging of bladder cancer, MRI is considered the best imaging technique because of its superior soft tissue contrast resolution compared with CT [106]. MRI is particularly useful for detecting bladder cancer invasion of the detrusor muscle, perivesical tissues, and nearby organs [5,47,48]. Klein and Pollack [49] noted that MRI has a better sensitivity and specificity than CT for local staging, with the most significant advantage being its ability to distinguish between superficial and deep invasion of the bladder detrusor muscle. For deeply infiltrating tumors (stages T3b-T4b), they concluded that MRI is the most accurate staging technique, making CT unnecessary when MRI is available. Beyersdorff et al [21] concluded that MRI is superior to CT for assessing the depth of invasion in the bladder wall, although both techniques may have difficulty differentiating between tumor and inflammation from previous transurethral biopsy. However, recent studies suggest that adding DWI to conventional pelvic MRI may aid in distinguishing treatment response and detecting residual/recurrent disease [50].

Newer imaging sequences have been shown to enhance the accuracy of local staging for bladder cancer [12,107-110]. El-Assmy et al [107] found that DWI was more effective in staging organ-confined tumors \leq T2 disease compared with T2-weighted sequences. Similarly, Takeuchi et al [109] found that DWI provided additional information to T2-weighted images in evaluating T stage, leading to improved accuracy and specificity. In a study by Thoeny et al [12], a combination of DWI signal intensity and morphologic criteria at T2-weighted imaging was used to detect malignant lymph nodes in patients with bladder cancer and patients with prostate cancer. This approach resulted in sensitivity ranging from 61% to 94%, specificity ranging from 90% to 99%, and accuracy ranging from 83% to 96% on a per-patient basis. Razik et al [111] compared the diagnostic performance of stalk morphology on DWI to conventional MRI in predicting muscle invasion in bladder cancer, finding that absent or distorted stalk on DWI had the highest sensitivity (87.5%) and specificity (97.6%). Additionally, DWI was more accurate than T2-weighted imaging in staging both organ-confined and higher-stage tumors, with a reported sensitivity of 98.1% and a PPV of 100%.

The addition of gadolinium contrast agent on MRI has been found to improve the accuracy of local staging for bladder cancer. In a prospective study by Daneshmand et al [61], 122 patients were examined using contrast-enhanced MRI, which had an 88% sensitivity, a 48% specificity, and a 74% accuracy in distinguishing organ-confined from

non-organ-confined bladder cancer and a 41% sensitivity, a 92% specificity, and an 80% accuracy in detecting positive nodal disease. Moderate interobserver agreement was found for T and N staging, consistent with other studies [53,54]. Other studies demonstrated the sensitivity and specificity of MRI in distinguishing NMIBC from MIBC ranging from 78% to 98% and 82% to 100% and the sensitivity and specificity for distinguishing organ-confined from non-organ-confined bladder tumors ranging from 90% to 94% and 60% to 94%, respectively [51-54]. Multiparametric MRI, which combines dynamic contrast-enhanced imaging with DWI and T2-weighted imaging, is likely the most optimal MRI technique for local staging of bladder cancer [48,55].

The standardization of bladder cancer staging with multiparametric MRI is facilitated by the VI-RADS scoring system, which was introduced in 2018 [56]. The VI-RADS uses a 5-point scoring system to estimate the likelihood of detrusor muscle invasion, a poor prognosis indicator that requires radical surgery. Wang et al [57] assessed the ability of VI-RADS score to detect MIBC in a group of patients who had multiparametric MRI before surgery. They concluded that VI-RADS effectively predict the likelihood of detrusor muscle invasion in bladder cancer and should be considered for evaluation before surgery. Kufukihara et al [58] compared the diagnostic accuracy of VI-RADS scoring with cystoscopy and found that VI-RADS had superior performance in detecting detrusor muscle invasion, especially in tumors located at the bladder neck/trigone/dome/posterior and anterior wall, but inferior performance in detecting tumors located on the lateral wall or ureteral orifice. Makboul et al [59] evaluated the usefulness of multiparametric MRI in differentiating MIBC from NMIBC with the accuracy of the VI-RADS scoring system. They found that multiparametric MRI is a comprehensive and effective tool for determining muscle invasion in bladder cancer and that VI-RADS can accurately differentiate between MIBC and NMIBC. Hagen et al [60] assessed the clinical applicability of preoperative multiparametric MRI using the 5-point VI-RADS scoring system to stage bladder cancer and compared it to dual-phase CECT. Both CECT and multiparametric MRI correctly identified tumor stages as either MIBC or NMIBC, but T stages bordering the histopathologic limits of muscle invasiveness resulted in overestimation of muscle invasion in 43% of cases for the multiparametric MRI image data sets and underestimation of muscle invasion in up to 55.5% of cases for the CECT data.

In addition to its use in detecting muscle invasion, MRI has also been studied as a predictor of bladder cancer progression and prognosis. Yajima et al [41] conducted a study to evaluate the significance of the “inchworm sign” on DWI

for the recurrence and progression of T1 bladder cancer. The absence of an inchworm sign on DWI was found to be a significant prognostic factor for progression of T1 bladder cancer, suggesting that morphological evaluation of DWI signals may be a helpful addition to preoperative assessment of the bladder cancer's aggressiveness.

MRI has been found to be more accurate than CT in identifying and localizing lymph nodes in the pelvic region for patients with pelvic malignancies, especially for smaller lymph nodes ranging from 1 to 5 mm in size [11,12]. Although lymph node metastases are rare for patients with tumors <T3 stage, the incidence increases from 20% to 30% and from 50% to 60% for patients with deep muscle layer involvement (T2b) and extravesical invasion, respectively. Thoeny et al [12] conducted a study on both patients with bladder cancer and patients with prostate cancer, using a combination of DWI compared with morphologic criteria on T2-weighted imaging to detect groin malignant lymph nodes. The study showed sensitivity ranging from 61% to 94%, specificity ranging from 90% to 99%, and accuracy ranging from 83% to 96% for malignant lymph node detection on a per-patient basis, as well as sensitivity ranging from 55% to 87%, specificity ranging from 94% to 100%, and accuracy ranging from 88% to 96% for malignant lymph node detection on a per-pelvic side basis.

MRI Pelvis Without IV Contrast. There is little literature to support the use of MRI pelvis without IV contrast in the evaluation of MIBC. The addition of a gadolinium contrast agent on MRI has been found to improve the accuracy of local staging for bladder cancer. In a prospective study by Daneshmand et al [61], 122 patients were examined using contrast-enhanced MRI, which had an 88% sensitivity, a 48% specificity, and a 74% accuracy in distinguishing organ-confined from non-organ-confined bladder cancer and a 41% sensitivity, a 92% specificity, and an 80% accuracy in detecting positive nodal disease. Moderate interobserver agreement was found for T and N staging, consistent with other studies [53,54]. Other studies demonstrated the sensitivity and specificity of MRI in distinguishing NMIBC from MIBC ranging from 78% to 98% and 82% to 100% and the sensitivity and specificity for distinguishing organ-confined from non-organ-confined bladder tumors ranging from 90% to 94% and 60% to 94%, respectively [51-54]. Multiparametric MRI, which combines dynamic contrast-enhanced imaging with DWI and T2-weighted imaging, is likely the most optimal MRI technique for local staging of bladder cancer [48,55].

MRU Without and With IV Contrast. Abdominal MRI, specifically MRU, can be used to stage bladder cancer by evaluating nodal, synchronous upper tract or bladder,

and metastatic involvement along with dedicated pelvic imaging to assess local staging. MRU is a viable alternative for CTU in the evaluation of upper tract disease. The main benefit of MRU over CTU includes inherent higher contrast resolution [62]. In addition, when the entire upper tract is not visualized or degraded by motion artifact, MRU sequences can be repeated without fear of added radiation risk. Inherent higher contrast resolution of MRU is particularly beneficial for small tumor detection.

MRU Without IV Contrast. Noncontrast MRU using a heavily T2-weighted sequence can be an alternative for assessing the renal collecting systems and ureters [63]. MRU may be performed for nodal, synchronous upper tract or bladder, and metastatic staging. The main benefit of MRU over CTU includes inherent higher contrast resolution [62]. In addition, when the entire upper tract is not visualized or degraded by motion artifact, MRU sequences can be repeated multiple times without fear of added radiation risk. Inherent higher contrast resolution of MRU is particularly beneficial for small tumor detection.

Radiography Chest. It is recommended that all patients with MIBC undergo pulmonary evaluation [30]. A chest radiograph is a low-morbidity screening tool that has been shown to be effective [74]. Patients with MIBC who have abnormal chest radiograph findings or are at high risk should undergo chest CT, consistent with other guidelines [31,32].

Radiography Intravenous Urography. The use of CTU and MRU has largely replaced IVU for evaluating the upper urinary tract urothelium. Excretory urography has a reported sensitivity of 50% to 70% for detecting upper urinary tract lesions [37]. However, a study comparing the accuracy of CTU and excretory urography in detecting and locating upper urinary tract UC favored CTU, with per-patient sensitivity, specificity, and overall accuracy rates of 93.5%, 94.8%, and 94.2%, respectively. This contrasts with excretory urography, which had rates of 80.4%, 81.0%, and 80.8%, respectively [37].

US Kidneys and Bladder Retroperitoneal. There is no relevant literature to support the use of US kidneys and bladder retroperitoneal in the evaluation of MIBC.

US Pelvis (Bladder). Transabdominal grayscale US is not commonly used for staging bladder cancer because of its potential to overstage superficial tumors in 48% to 49% of cases and to underestimate invasive tumors in 5% to 11% of cases [35]. However, US can be a useful tool for evaluating hematuria. In a study of 1,007 patients with gross hematuria [65], US had a sensitivity of 63% and a specificity of 99% in detecting bladder cancer. Another study by Fang et al [66],

which included 214 new cases of bladder cancer with pathological correlation, reported an overall accuracy of 79% in local staging using transabdominal US, with 10% overstaging and 12% understaging. It is important to note that transabdominal US is limited in visualizing beyond the bladder wall and cannot reliably detect nodal enlargement [112]. Furthermore, transabdominal US is less accurate in detecting stage T3 and T4 disease compared with T1 and T2 disease [64].

Three-dimensional US rendering is a new diagnostic tool that shows potential in discriminating NMIBC from MIBC [68]. It allows for retrieval and manipulation of volume data in multiple planes, increasing objectivity and improving primary bladder tumor diagnosis rate (100% with 3-D US versus 88.9% with 2-D US) when identifying T3b disease [69]. However, the technique has limitations, including difficulty in visualizing the entire tumor, particularly in flat or plaque-like tumors, presence of coexistent calcification, a rigid abdominal wall, or central obesity [70]. Contrast-enhanced US has also been shown to better differentiate MIBC from NMIBC [71]. In a study of 34 patients who underwent both grayscale and contrast-enhanced US before TURBT [71], contrast-enhanced US performance was similar to the reference standard of TURBT in differentiating MIBC from NMIBC. Ge et al [72] also found that preoperative contrast-enhanced US is highly efficient in discriminating Ta to T1 or low-grade bladder cancer from stage T2 or high-grade bladder cancer. Contrast-enhanced US shows high sensitivity, specificity, and diagnostic accuracy, making it a promising method for distinguishing T staging and grading of bladder cancer. Li et al [73] demonstrated that the combined use of contrast-enhanced US and DWI-MRI is more accurate in diagnosing bladder cancer than either method alone, making it a feasible and effective diagnostic approach for bladder cancer.

Variant 3: Adult. Upper urinary tract urothelial cancer. Pretreatment staging

The goal of imaging is to stage a known upper UTUC. This includes evaluating for both local and distant spread of the cancer and assessing for synchronous sites of UC in the upper tracts and bladder. With the information from imaging, this will initiate the appropriate treatment plan sooner and can improve patient outcome by reducing length of illness. This will ideally help to reduce delaying the appropriate treatment and hasten the patient's recovery.

Bone Scan Whole Body. There are not many references available regarding the routine use of bone scans in UTUC separate from bladder cancer guidelines because of the lower frequency of occurrence of bone metastases in UTUC.

There is also conflicting evidence for the use of whole-body bone scan to evaluate for bone metastases in bladder cancer. The incidence of metastases in patients with bladder cancer increases with tumor stage at time of diagnosis, and this statement may extend to the UTUC population [74]. Additionally, bone scanning may be limited to patients with bone pain and/or elevated levels of serum alkaline phosphatase. Further evaluation with radiographs and/or MRI can be helpful, and, if necessary, guided-needle biopsy can be definitive.

CT Abdomen and Pelvis With IV Contrast. There is limited evidence to support the use of CT abdomen and pelvis with IV contrast (separate from CTU protocol) in the pretreatment staging of UTUC although abdominopelvic lymph node involvement and metastases could still be evaluated this way, although its sensitivity for urothelial lesions is limited, and CTU/MRU are preferred and more comprehensive. The European Association of Urology guidelines [31] recommendations specific to UTUC indicate that CTU is generally the most accurate and preferred modality for diagnosis and staging, both local and distant. This is supported by several studies concluding that CT, particularly CTU, is the most used imaging modality worldwide for the diagnosis and staging of urothelial malignancies [2], and CTU is the favored modality used for localizing, locoregional staging, and detecting distant metastases in UC [34]. The American Urology Association has recently published guidelines for UTUC separate to bladder cancer [19]. CTU is also essential to evaluate for synchronous UTUC or bladder UC. Approximately two-thirds of UTUCs present as high-grade invasive disease at the time of diagnosis, and multifocal disease has been reported in approximately 25% to 30% of UTUC [7,8]. A meta-analysis and systematic review of CTU for UTUC reported a pooled sensitivity of 96% (95% confidence interval [CI], 88%-100%) and a specificity of 99% (95% CI, 98%-100%) for identifying UC [113]. In a recent review by Mirmomen et al [35], CTU demonstrated a 91% diagnostic accuracy in detecting UCs, but it may miss very small or flat lesions that are more easily detected by direct visualization [23].

CT is commonly used to determine nodal involvement, but relying on size alone is not reliable because small nodes may be metastatic and large nodes may be reactive [83]. CT cannot detect microscopic tumor metastases in nonenlarged lymph nodes [5].

CT Abdomen and Pelvis Without and With IV Contrast. There is limited literature to support the use of CT abdomen and pelvis without and with IV contrast (separate from CTU protocol) in the pretreatment staging of UTUC. There is no relevant literature documenting additional

benefit of CT without and with IV contrast, relative to CT with IV contrast in this setting.

CTU and MRU are of greater usefulness because they allow for the comprehensive evaluation of the genitourinary tract, as well as the assessment of retroperitoneal and pelvic lymph nodes (see CTU and MRU sections).

CT Abdomen and Pelvis Without IV Contrast. There is limited literature to support the use of CT abdomen and pelvis without IV contrast (separate from CTU protocol) in the pretreatment staging of UTUC, although it may be an option in certain patient groups.

CT Abdomen With IV Contrast. There is limited literature to support the use of CT abdomen with IV contrast (separate from CTU protocol) in the pretreatment staging of UTUC. Imaging of the entire abdomen and pelvis would be indicated for a comprehensive assessment of the entire urothelial system and evaluation for metastases.

CTU and MRU are of greater usefulness because they allow for the comprehensive evaluation of the genitourinary tract, as well as the assessment of retroperitoneal and pelvic lymph nodes (see CTU and MRU sections).

CT Abdomen Without and With IV Contrast. There is limited literature to support the use of CT abdomen without and with IV contrast (separate from CTU protocol) in the pretreatment staging of UTUC. Imaging of the entire abdomen and pelvis would be indicated for a comprehensive assessment of the entire urothelial system and evaluation for metastases.

CTU and MRU are of greater usefulness because they allow for the comprehensive evaluation of the genitourinary tract, as well as the assessment of retroperitoneal and pelvic lymph nodes (see CTU and MRU sections).

CT Abdomen Without IV Contrast. There is limited literature to support the use of CT abdomen without IV contrast (separate from CTU protocol) in the pretreatment staging of UTUC.

CT Chest With IV Contrast. All patients with UTUC need pulmonary evaluation [31]. Patients with findings on chest radiographs and those thought to be at high risk should have chest CT, as is recommended in other guidelines [31,32]. Original research comparing the usefulness of chest radiographs with chest CT in this patient population is lacking.

CT Chest Without and With IV Contrast. There is no relevant literature to support the use of CT Chest without and with IV contrast in the pretreatment staging of UTUC.

CT Chest Without IV Contrast. All patients with UTUC need pulmonary evaluation [31]. Patients with

findings on chest radiographs and those thought to be at high risk should have chest CT, as is recommended in other guidelines [31,32]. Original research comparing the usefulness of chest radiographs with chest CT in this patient population is lacking. CT chest with IV contrast is preferred over CT chest without IV contrast when evaluating for metastatic disease and lymphadenopathy.

CT Pelvis With IV Contrast. There is no relevant literature to support the use of CT pelvis with IV contrast (separate from CTU protocol) in the pretreatment staging of UTUC. Imaging of the entire abdomen and pelvis would be indicated for a comprehensive assessment of the entire urothelial system and evaluation for metastases.

CTU and MRU are of greater usefulness because they allow for the comprehensive evaluation of the genitourinary tract, as well as the assessment of retroperitoneal and pelvic lymph nodes (see CTU and MRU sections).

CT Pelvis Without and With IV Contrast. There is no relevant literature to support the use of CT pelvis without and with IV contrast (separate from CTU protocol) in the pretreatment staging of UTUC. Imaging of the entire abdomen and pelvis would be indicated for a comprehensive assessment of the entire urothelial system and evaluation for metastases.

CTU and MRU are of greater usefulness because they allow for the comprehensive evaluation of the genitourinary tract, as well as the assessment of retroperitoneal and pelvic lymph nodes (see CTU and MRU sections).

CT Pelvis Without IV Contrast. There is no relevant literature to support the use of CT pelvis without IV contrast (separate from CTU protocol) in the pretreatment staging of UTUC. Imaging of the entire abdomen and pelvis would be indicated.

CTU Without and With IV Contrast. The European Association of Urology guidelines [31] recommendations specific to UTUC indicate that CTU is generally the most accurate and preferred modality for diagnosis and staging, both local and distant. This is supported by several studies concluding that CT, particularly CTU, is the most used imaging modality worldwide for the diagnosis and staging of urothelial malignancies [2], and CTU is the favored modality used for localizing, locoregional staging, and detecting distant metastases in UC [34]. The American Urology Association has recently published guidelines for UTUC separate to bladder cancer [19]. CTU is also essential to evaluate for synchronous UTUC or bladder UC. Approximately two-thirds of UTUCs present as high-grade invasive disease at the time of diagnosis, and multifocal disease has been reported in approximately 25% to 30% of UTUC [7,8]. A meta-analysis and systematic review

of CTU for UTUC reported a pooled sensitivity of 96% (95% CI, 88%-100%) and a specificity of 99% (95% CI, 98%-100%) for identifying UC [113]. In a recent review by Mirmomen et al [35], CTU demonstrated a 91% diagnostic accuracy in detecting UCs, but it may miss very small or flat lesions that are more easily detected by direct visualization [23]. In recent years, CTU has largely replaced IVU for evaluating the renal collecting systems and ureters [37,38]. The cross-sectional technique offers several advantages, such as the ability to visualize small masses, which may be obscured on excretory urography due to contrast material or bowel gas, identify focal wall thickening, and distinguish enhancing tumors from nonenhancing calculi or blood clots [5,37]. Additionally, CTU and MRU can evaluate nonfunctioning/obstructed kidneys that would not excrete the contrast medium required for excretory urography.

A retrospective review of 39 patients with histologically verified UTUC showed that CTU was 87.8% accurate in predicting TNM stage [114]. Several groups have attempted to further evaluate CT's ability to differentiate between T stages for local staging. In a blinded retrospective study of 158 patients who underwent unilateral nephroureterectomy over a 5-year time period, 69 fulfilled the inclusion criteria having had a split-bolus CTU study before surgery. The investigators reported that CT values before and after administration of iodine-based contrast agent could not distinguish between muscle-invasive (T2 or higher) and noninvasive (T1 or lower) urothelial tumors in the upper urinary tract [115]. Another study investigated the diagnostic benefit of tumor appearance and texture in CT images for upper UTUC staging in a retrospective blinded study reviewing CT images of 48 patients that had undergone nephroureterectomy and preoperative CT over a 2-year time period. They concluded that spiculated margins were associated with T2 or higher stages and that higher-stage tumors were subjectively more heterogeneous and showed greater entropy in histogram texture analysis [116].

A blinded retrospective review by Honda et al [117] of a group of 30 patients who had CTU before surgery looked at detailed criteria focusing on smooth or irregular margins to classify images into 6 patterns of T2 or lower stages and T3 or higher stages. A grading system for ureteral UCs focused on the presence of spiculation and masses along the ureter using axial nephrographic- and excretory-phase CECT images was developed. Spiculation was defined as thin strands of soft tissue extending from the tumor into the periureteric fat. The diagnostic sensitivity and specificity with respect to T3 or higher-stage tumors were 87.5% (14/16) and 92.9% (13/14), respectively. It is challenging to identify microscopic invasion of a tumor into surrounding tissue or inflammation in CT images.

Other research groups have attempted to search for factors that can predict stage or prognosis for treatment decisions before surgery. In a preoperative multivariate analysis, Ito et al [118] showed that a high hydronephrosis grade predicted the pathological T stage (T3 or higher). In their study, ipsilateral hydronephrosis was graded into 5 stages, and they concluded that a higher hydronephrosis grade (2-4: mild calyceal dilatation or higher grade) predicted non-organ-confined disease.

A retrospective study by Yu et al [119] looked at the correspondence of T staging on multidetector CTU and the pathologic stage of UTUC in 125 patients. The researchers concluded that 71 out of 85 low T stage (T1-T2) tumors were correctly detected by multidetector CTU, whereas 30 out of 40 advanced T stage (T3-T4) tumors were correctly diagnosed by multidetector CTU. Multidetector CTU led to understaging in 8% (10/125) of tumors and overstaging in 11.2% (14/125) of tumors. The overall accuracy of multidetector CTU in the diagnosis of low and advanced T stage tumors was 80.8% (101/125 patients). The sensitivity for advanced T stage tumors was 75% (30/40), the specificity was 83.5% (71/85), and the positive and negative predictive values were 68.1% (30/44) and 87.6% (71/81), respectively.

Distant metastases can also be evaluated for at the same time as local disease staging on CTU. Because of the rarity of metastatic UTUC, few studies have reported the predictors of metastatic patterns. The presence of enlarged lymph nodes can be suggestive of metastases [31]. Limited original research looking at nodal disease on CT specifically in UTUC separate from bladder UC is available. A study of 233 patients by Goodfellow et al [90] found the sensitivity and specificity of CT for pelvic lymph node involvement in bladder UC were 45% and 98%, respectively. Studies looking at the frequency of metastases in UTUC found, in a case series of 250 patients with UTUC, that 56 (22.4%) presented with stage IV disease. The most common metastatic sites were lung (39.6%), distant lymph nodes (39.2%), bone (19.6%), liver (18.0%), and adrenal gland (7.2%) [120]. The incidence of lymph node involvement does not seem to be related to the location of the UTUC. Some of the original data for pretreatment staging of renal cell carcinoma involving the pelvis and UTUC arising in the renal pelvis have been traditionally reported together, which makes separating the true sensitivity and specificity for UTUC in this region difficult to accurately evaluate. Focal liver masses or other solid organ findings on CTU may need further workup for metastases depending on their appearance. Peritoneal metastatic disease can also occur and can be readily assessed for with CT.

FDG-PET/CT Skull Base to Mid-Thigh. Conventional PET is limited for the local staging of UTUC because of high FDG activity in excreted urine. The current body of literature regarding the ability of FDG-PET to stage UTUC suggests it improves sensitivity for diagnosing nodal and metastatic disease, particularly when combined with CT.

FDG-PET/CT has an 82% sensitivity and an 84% specificity for the detection of lymph node metastases in patients with UTUC [121]. Presence of suspicious lymph nodes on FDG-PET/CT has also been associated with worse recurrence-free survival [121]. Additionally, higher FDG uptake in metastases was significantly and independently associated with poor chemosensitivity and worse survival outcomes [122].

A study of 233 patients by Goodfellow et al [90] found the sensitivity and specificity of CT for pelvic lymph node involvement was 45% and 98%, respectively. Using PET/CT, the sensitivity for pelvic lymph node involvement increased to 69% with a 3% reduction in specificity to 95%. In a prospective study of 25 patients by Nayak et al [91], in 9 patients who had positive lymph nodes for metastases on histopathology, CT and PET/CT scans had a sensitivity of 44% and 78%, respectively. Other authors have found the FDG-PET/CT sensitivity for the detection of nodal metastases to range between 47% and 56% and the specificity to range between 93% and 98%, with specificity often slightly lower than for CT [92].

A patient-based analysis of consecutive UTUC patients by Tanaka et al [123] showed that the sensitivity of PET/CT was significantly better than that of CT (85% versus 50%, $P = .0001$). The sensitivity, specificity, and accuracy of PET/CT tended to be superior to those of CT, but these values were not significantly different (95%, 91%, and 93% versus 82%, 85%, and 84%; $P = .25$, $.50$, and $.063$, respectively). The clinicians changed their assessments of disease extent and management plans in 18 (32%) and 11 (20%) patients, respectively, based on the PET/CT results [123].

FDG-PET/MRI Skull Base to Mid-Thigh. There is no relevant literature to support the use of FDG-PET/MRI in the pretreatment staging of UTUC.

MRI Abdomen and Pelvis Without and With IV Contrast. Although there is limited literature to support the use of MRI abdomen and pelvis without and with IV contrast (separate from MRU) in the pretreatment staging of UTUC, it may be useful in some clinical situations. However, CTU and MRU are of greater usefulness because they allow for the comprehensive evaluation of the genitourinary tract, as well as the assessment of

retroperitoneal and pelvic lymph nodes (see CTU and MRU sections).

MRI Abdomen and Pelvis Without IV Contrast. Although there is limited literature to support the use of MRI abdomen and pelvis without IV contrast (separate from MRU) in the pretreatment staging of UTUC, it may be useful in some clinical situations. However, CTU and MRU are of greater usefulness because they allow for the comprehensive evaluation of the genitourinary tract, as well as the assessment of retroperitoneal and pelvic lymph nodes (see CTU and MRU sections).

MRI Abdomen Without and With IV Contrast. There is limited literature to support the use of MRI Abdomen without and with IV contrast (separate from MRU) in the pretreatment staging of UTUC. Imaging of the entire abdomen and pelvis would be indicated for a comprehensive assessment of the entire urothelial system and evaluation for metastases.

CTU and MRU are of greater usefulness because they allow for the comprehensive evaluation of the genitourinary tract, as well as the assessment of retroperitoneal and pelvic lymph nodes (see CTU and MRU sections).

MRI Abdomen Without IV Contrast. There is limited literature to support the use of MRI Abdomen without IV contrast (separate from MRU) in the pretreatment staging of UTUC. Imaging of the entire abdomen and pelvis would be indicated for a comprehensive assessment of the entire urothelial system and evaluation for metastases.

CTU and MRU are of greater usefulness because they allow for the comprehensive evaluation of the genitourinary tract, as well as the assessment of retroperitoneal and pelvic lymph nodes (see CTU and MRU sections).

MRI Head Without and With IV Contrast. There is no relevant literature to support the routine use of MRI head without and with IV contrast in the pretreatment staging of UTUC. Metastatic involvement of the brain in UTUC is rare. Individual use in patients with neurologic symptoms could be considered.

MRI Head Without IV Contrast. There is no relevant literature to support the use of MRI head without IV contrast in the pretreatment staging of UTUC.

MRI Pelvis Without and With IV Contrast. There is no relevant literature to support the use of MRI pelvis without and with IV contrast (separate from MRU) in the pretreatment staging of UTUC.

MRI Pelvis Without IV Contrast. There is no relevant literature to support the use of MRI pelvis without IV

contrast (separate from MRU) in the pretreatment staging of UTUC.

MRU Without and With IV Contrast. MRU may be performed for nodal, synchronous upper tract or bladder, and metastatic staging. MRU is a viable alternative for CTU in the evaluation of UTUC.

The main benefit of MRU over CTU includes inherent higher contrast resolution [62]. When the entire upper tract is not visualized or degraded by motion artifact, MRU sequences can be repeated without fear of added radiation risk. Inherent higher contrast resolution of MRU is particularly beneficial for small tumor detection.

Takahashi et al [62] performed a retrospective review of 110 patients who had undergone MRU to identify patients with small (<2 cm) tumors. They concluded that gadolinium-enhanced 3-D spoiled gradient echo MRU helped detect 74% of small UCs. Nephrographic and excretory-phase images are essential for helping detect small UCs.

No direct comparison of MRU to CTU for UTUC exists; however, overall, MRU takes much longer to perform. Technical challenges for MRU also include the poorer detection of nonobstructing stones than by CT, which is critical when evaluating hematuria, and MRU is much more prone to motion and peristalsis artifacts with overall lower spatial resolution than CTU. A retrospective study of 91 MRU examinations by Takahashi et al [124] found a sensitivity of 69% and a specificity of 97% for upper tract malignancy.

Another retrospective review by Obuchi et al [125] of patients over a 5-year time period who had undergone MRI within 2 months of surgery showed that MRI T staging improved with gadolinium-enhanced fat-suppressed T1-weighted images in combination with morphologic changes and signal intensity changes.

For UTUC arising in the renal pelvis, assessment for any renal extension for T staging is important. A retrospective review of 40 patients with renal pelvic tumors and MRI showed that T2-weighted imaging plus DWI enabled a 98% detection rate. For discriminating tumors with macroscopic renal invasion from those with microscopic renal invasion or less, T2-weighted imaging plus DWI (93%) was significantly more accurate than T2-weighted imaging alone (75%) [126].

MRU Without IV Contrast. Noncontrast enhanced MRU can be used to assess the renal collecting systems and ureters using a heavily T2-weighted sequence [63]. MRU may be performed for nodal, synchronous bladder, and metastatic staging. The main benefit of MRU over CTU includes inherent higher contrast resolution [62]. In addition, when the entire upper tract is not visualized or degraded by motion artifact, MRU sequences can be

repeated multiple times without fear of added radiation risk. Inherent higher contrast resolution of MRU is particularly beneficial for small tumor detection.

Radiography Chest. All patients with UTUC need pulmonary evaluation [31]. The chest radiograph is an effective and low-morbidity screen [74]. Patients with UTUC who have abnormal chest radiograph findings or are at high risk should undergo chest CT, consistent with other guidelines [31,32].

Radiography Intravenous Urography. The widespread use of CTU and emerging use of MRU have essentially replaced IVU for evaluation of the urothelium in the renal collecting systems and ureters. Sensitivity of excretory urography to detect upper urinary tract lesions is reportedly 50% to 70% [37]. However, a study comparing the accuracy of detection and localization of upper urinary tract UC with CTU versus excretory urography favored CTU with per-patient sensitivity, specificity, and overall accuracy rates of 93.5%, 94.8%, and 94.2%, respectively, compared with 80.4%, 81.0%, and 80.8%, respectively, for excretory urography [37].

US Kidneys and Bladder Retroperitoneal. Limited literature is available to support the use of US kidney and bladder retroperitoneal in the evaluation of UTUC. Due to limited sensitivity, a negative US kidney and bladder retroperitoneal study should not be considered adequate, and further imaging studies would be required for pretreatment staging. Likewise, a positive US kidney and bladder retroperitoneal study would also need follow-up evaluation for more complete staging. A few small n-value reports evaluating the use of endoluminal US in local T staging of UTUC are available; however, this is not in widespread use clinically.

US Pelvis (Bladder). There is no relevant literature to support the use of US bladder retroperitoneal in the pretreatment staging of UTUC.

SUMMARY OF RECOMMENDATIONS

- **Variant 1:** MRI pelvis without and with IV contrast or MRU without and with IV contrast or CT abdomen and pelvis with IV contrast or CTU without and with IV contrast is usually appropriate for the pretreatment staging of NMIBC. These procedures are equivalent alternatives (eg, only one procedure will be ordered to provide the clinical information to effectively manage the patient's care).
- **Variant 2:** MRI abdomen and pelvis without and with IV contrast or MRI pelvis without and with IV contrast

or MRU without and with IV contrast or MRU without IV contrast or CT abdomen and pelvis with IV contrast or CTU without and with IV contrast or FDG-PET/CT skull base to mid-thigh is usually appropriate for pretreatment staging of muscle invasive bladder cancer. These procedures are equivalent alternatives (eg, only one procedure will be ordered to provide the clinical information to effectively manage the patient's care) and are complemented by radiography chest or CT chest with IV contrast (ie, more than one procedure is ordered as a set or simultaneously in which each procedure provides unique clinical information to effectively manage the patient's care). Although the panel did not agree on recommending CT abdomen and pelvis without and with IV contrast (separate from dedicated CTU protocol), its use may be appropriate. However, MRU and CTU are of greater utility because they allow for the comprehensive evaluation of the genitourinary tract and the assessment of retroperitoneal and pelvic lymph nodes.

- **Variant 3:** MRI abdomen and pelvis without and with IV contrast or MRU without and with IV contrast or CTU without and with IV contrast is usually appropriate for pretreatment staging of upper urinary tract urothelial cancer. These procedures are equivalent alternatives (eg, only one procedure will be ordered to provide the clinical information to effectively manage the patient's care) and are complemented by radiography chest or CT chest with IV contrast (ie, more than one procedure is ordered as a set or simultaneously in which each procedure provides unique clinical information to effectively manage the patient's care).

SUPPORTING DOCUMENTS

The evidence table, literature search, and appendix for this topic are available at <https://acsearch.acr.org/list>. The appendix includes the strength of evidence assessment and the final rating round tabulations for each recommendation.

For additional information on the Appropriateness Criteria methodology and other supporting documents go to www.acr.org/ac.

RELATIVE RADIATION LEVEL INFORMATION

Potential adverse health effects associated with radiation exposure are an important factor to consider when selecting the appropriate imaging procedure. Because there is a wide range of radiation exposures associated with different diagnostic procedures, a relative radiation level (RRL) indication has been included for each imaging examination. The RRLs

are based on effective dose, which is a radiation dose quantity that is used to estimate population total radiation risk associated with an imaging procedure. Patients in the pediatric age group are at inherently higher risk from exposure, because of both organ sensitivity and longer life expectancy (relevant to the long latency that appears to accompany radiation exposure). For these reasons, the RRL dose estimate ranges for pediatric examinations are lower as compared with those specified for adults (see [Table 2](#)). Additional information regarding radiation dose assessment for imaging examinations can be found in the ACR Appropriateness Criteria® Radiation Dose Assessment Introduction document [127].

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