# American College of Radiology ACR Appropriateness Criteria® Post-Treatment Surveillance of Bladder Cancer

# <u>Variant 1:</u> Nonmuscle invasive bladder cancer with no symptoms or risk factors. Post-treatment surveillance.

Procedure	Appropriateness Category	Relative Radiation Level
US pelvis (bladder)	Usually Not Appropriate	0
Radiography chest	Usually Not Appropriate	€
Radiography intravenous urography	Usually Not Appropriate	<b>₩</b>
MRI abdomen and pelvis without and with IV contrast	Usually Not Appropriate	0
MRI abdomen and pelvis without IV contrast	Usually Not Appropriate	0
MRU without and with IV contrast	Usually Not Appropriate	0
CT abdomen and pelvis with IV contrast	Usually Not Appropriate	<b>₩</b>
CT abdomen and pelvis without IV contrast	Usually Not Appropriate	<b>₩</b>
CT chest with IV contrast	Usually Not Appropriate	<b>₩</b>
CT chest without and with IV contrast	Usually Not Appropriate	<b>⊕⊕</b>
CT chest without IV contrast	Usually Not Appropriate	<b>₩</b>
CT abdomen and pelvis without and with IV contrast	Usually Not Appropriate	≎≎≎
CTU without and with IV contrast	Usually Not Appropriate	<b>∞</b> •••
FDG-PET/CT skull base to mid-thigh	Usually Not Appropriate	<b>₩₩</b>

<u>Variant 2:</u>
Nonmuscle invasive bladder cancer with symptoms or risk factors. Post-treatment surveillance.

Procedure	Appropriateness Category	Relative Radiation Level
MRU without and with IV contrast	Usually Appropriate	0
CTU without and with IV contrast	Usually Appropriate	❖❖❖❖
Radiography chest	May Be Appropriate	<b>☆</b>
MRI abdomen and pelvis without and with IV contrast	May Be Appropriate	0
CT abdomen and pelvis with IV contrast	May Be Appropriate	❖❖❖
US pelvis (bladder)	Usually Not Appropriate	0
Radiography intravenous urography	Usually Not Appropriate	<b>���</b>
MRI abdomen and pelvis without IV contrast	Usually Not Appropriate	0
CT abdomen and pelvis without IV contrast	Usually Not Appropriate	❖❖❖
CT chest with IV contrast	Usually Not Appropriate	<b>♦</b>
CT chest without and with IV contrast	Usually Not Appropriate	<b>♦</b>
CT chest without IV contrast	Usually Not Appropriate	<b>♦</b>
CT abdomen and pelvis without and with IV contrast	Usually Not Appropriate	<b>₩₩₩</b>
FDG-PET/CT skull base to mid-thigh	Usually Not Appropriate	❖❖❖❖

**Variant 3:** Muscle-invasive bladder cancer with or without cystectomy. Post-treatment surveillance.

Procedure	Appropriateness Category	Relative Radiation Level
Radiography chest	Usually Appropriate	<b>②</b>
Fluoroscopy abdomen loopogram	Usually Appropriate	<b>€€</b>
MRI abdomen and pelvis without and with IV contrast	Usually Appropriate	0
MRU without and with IV contrast	Usually Appropriate	0
CT abdomen and pelvis with IV contrast	Usually Appropriate	<b>♥♥</b>
CTU without and with IV contrast	Usually Appropriate	<b>₹₹</b>
MRI abdomen and pelvis without IV contrast	May Be Appropriate (Disagreement)	0
CT chest with IV contrast	May Be Appropriate	<b>♦♦</b>
CT chest without IV contrast	May Be Appropriate	<b>♦♦</b>
CT abdomen and pelvis without and with IV contrast	May Be Appropriate (Disagreement)	❖❖❖❖
FDG-PET/CT skull base to mid-thigh	May Be Appropriate	❖❖❖❖
US pelvis (bladder)	Usually Not Appropriate	0
Radiography intravenous urography	Usually Not Appropriate	**
CT abdomen and pelvis without IV contrast	Usually Not Appropriate	**
CT chest without and with IV contrast	Usually Not Appropriate	<b>⊕⊕</b>

#### POST-TREATMENT SURVEILLANCE OF BLADDER CANCER

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## **Summary of Literature Review**

## Introduction/Background

Urothelial carcinoma (UC), previously known as transitional cell carcinoma, accounts for >90% of all urinary bladder cancers in the United States. In the genitourinary tract, UC is the second most common cancer and cause of cancer death [1]. The American Cancer Society estimated that there will be 81,400 new cases of bladder cancer and 17,980 deaths related to bladder cancer in 2020 [1]. Bladder cancer staging is based on the American Joint Committee on Cancer Tumor, Node, Metastasis system, and T-stage (depth of invasion) is used to differentiate patients into 2 groups: nonmuscle invasive bladder cancer (NMIBC) and muscle-invasive bladder cancer (MIBC) [2]. NMIBC accounts for 75% of bladder cancers and consists of a heterogeneous group of tumors that includes superficial papillary tumors (Ta), carcinoma in situ (Tis), and tumors invading the lamina propria (T1), all with different rates of recurrence and progression [2]. MIBC consists of tumors that invade the muscularis propria (T2) and beyond, and these tumors have a significantly higher rate of recurrence and progression after treatment. The 5-year survival rate for all stages of UC of the urinary bladder combined is 78% [1]. For NMIBC stages 0 and I, the 5-year survival rates are 95% and 75%, respectively; 5-year survival rates drop to 70%, 35%, and 5% for MIBC at stages II, III, and IV, respectively [1].

This manuscript relates to surveillance imaging following treatment for bladder cancer. For pretreatment staging considerations, see the ACR Appropriateness Criteria® topic on "Pretreatment Staging of Muscle-Invasive Bladder Cancer" [3]. The goals of surveillance imaging after the treatment of UC of the urinary bladder are to detect new or previously undetected urothelial tumors (both in the upper [collecting system and ureters] and lower [bladder and urethra] urinary tract), to identify metastatic disease, and to evaluate for complications of therapy.

The American Urological Association and Society of Urologic Oncology (AUA/SUO) Joint Guidelines recommends stratifying patients with NMIBC into low-, intermediate-, or high-risk categories for disease recurrence and progression based on the following risk factors [4]:

- 1. *Tumor size*: Tumors measuring ≥3 cm are associated with decreased time to first recurrence and time to progression compared with tumors measuring <3 cm [5-7].
- 2. *Tumor multifocality*: Multiple tumors are identified in >40% of cases and are associated with higher rates of recurrence and decreased time to first recurrence [5,6,8].
- 3. *Tumor grade*: The World Health Organization (WHO)/International Society of Urological Pathology (ISUP) 2004 grading system is used to classify tumor grade (I–III). Patients with higher-grade tumors have decreased recurrence-free intervals and increased rates of progression [5,6,8].
- 4. *Tumor stage*: Most UCs of the bladder are superficial (75%), although NMIBC consists of a heterogeneous group including Ta (70%), T1 (20%), and Tis (10%) lesions. Overall, most superficial tumors remain superficial, with only a minority progressing to MIBC; however, patients with Tis and T1 tumors have a high rate of recurrence and an increased rate of progression to MIBC compared with Ta tumors [5,7].

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- 5. *Lymphovascular invasion*: Studies have demonstrated an increased risk of lymph node metastases, recurrence, and decreased survival with the presence of lymphovascular invasion [9,10].
- 6. Prostatic urethral invasion: Involvement of the prostatic urethra increases risk of urethral recurrence [11].
- 7. *Variant histology*: Patients with variant histology (squamous, glandular, micropapillary, nested, plasmacytoid, neuroendocrine, sarcomatoid) have a higher incidence of locally advanced disease and poor outcomes [12-14].
- 8. Poor response to Bacillus Calmette-Guérin therapy: Patients with persistent or recurrent disease following intravesical Bacillus Calmette-Guérin therapy for NMIBC are at increased risk for disease progression [15,16].

The AUA/SUO and National Comprehensive Cancer Network (NCCN) guidelines differ slightly in imaging recommendations following treatment for NMIBC. The NCCN guidelines recommend upper-tract surveillance imaging for patients at low or intermediate risk, as clinically indicated, and scheduled upper-tract imaging every 1 to 2 years for patients at high risk [17]. The AUA/SUO guidelines recommend upper-tract surveillance imaging patients at both intermediate and high risk at 1 to 2 year intervals [4]. For the purposes of this manuscript, NMIBC has been divided into 2 categories: NMIBC without symptoms or risk factors (low-risk patients) and NMIBC with symptoms or risk factors (intermediate- and high-risk patients). Local practice patterns (NCCN versus AUA/SUO) should determine whether upper-tract surveillance should be considered in patients with intermediate risk and no symptoms.

## **Special Imaging Considerations**

# Cystoscopic and Virtual Cystoscopic Surveillance

Patients with NMIBC undergo routine surveillance cystoscopy to assess for recurrence and progression to MIBC. As cystoscopy is a relatively invasive procedure, there was previous interest in developing virtual cystoscopic or cystographic techniques using CT or MRI, particularly for problem solving and for cases in which conventional cystoscopy is difficult, such as for the evaluation of narrow-necked diverticula. CT cystography, following the instillation of air, saline, or water-soluble contrast into the urinary bladder via a Foley catheter, and MRI evaluation of the urinary bladder with virtual cystoscopy (3-D fly through) and cystography (T2-weighted turbo spin-echo imaging) are not commonly performed and do not eliminate the need for conventional cystoscopy.

#### CTU

CT urography (CTU) is an imaging study that is tailored to improve visualization of both the upper and lower urinary tracts. There is variability in the specific parameters, but it usually involves unenhanced images followed by intravenous (IV) contrast-enhanced images, including nephrographic and excretory phases acquired at least 5 minutes after contrast injection. Alternatively, a split-bolus technique uses an initial loading dose of IV contrast and then obtains a combined nephrographic-excretory phase after a second IV contrast dose; some sites include arterial phase. CTU should use thin-slice acquisition. Reconstruction methods commonly include 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. CT abdomen and pelvis without and with IV contrast is defined as any protocol not specifically tailored for evaluation of the upper and lower urinary tracts and without both the precontrast and excretory phases.

## **MRU**

MR urography (MRU) is also tailored to improve imaging of the urinary system. Unenhanced MRU relies upon heavily T2-weighted imaging of the intrinsic high signal intensity from urine for evaluation of the urinary tract. IV contrast is administered to provide additional information regarding obstruction, urothelial thickening, focal lesions, and stones. A contrast-enhanced T1-weighted series should include 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. MRI abdomen and pelvis without and with IV contrast is defined as any protocol not specifically tailored for evaluation of the upper and lower urinary tracts, without both the precontrast and excretory phases, and without heavily T2-weighted images of the urinary tract.

## **Discussion of Procedures by Variant**

# Variant 1: Nonmuscle invasive bladder cancer with no symptoms or risk factors. Post-treatment surveillance.

In patients with NMIBC without symptoms or risk factors, metastatic disease is uncommon, thus screening for distant metastatic disease is not recommended. Bladder recurrence is common following treatment for NMIBC. In a study of 190 patients with low-grade Ta disease, bladder cancer recurrence was identified in 43.2% (82 of 190)

of patients; however, progression to MIBC was seen in only 2 patients [18]. The incidence of upper-tract UC (UTUC) in this patient population is 0.6% to 0.9% [19,20]. Routine surveillance of the upper urinary tract in asymptomatic, low-risk patients is not recommended. Urine cytological analysis and cystoscopy are performed routinely in the setting of NMIBC and are felt to be sufficiently accurate for the diagnosis of bladder cancer recurrent in this patient population [4,21,22].

## **CT Abdomen and Pelvis**

In patients with NMIBC without risk factors or symptoms, screening for distant metastatic disease with cross-sectional imaging (CT abdomen and pelvis without or with IV contrast) is not supported.

#### CT Chest

Chest CT is generally not appropriate for patients with NMIBC without symptoms or risk factors.

#### CTU

CTU is a primary imaging test for comprehensive evaluation of the genitourinary tract that can be used to identify metastatic disease and metachronous UC. In the setting of NMIBC without symptoms or risk factors, metastatic disease is uncommon; thus, screening for distant metastatic disease is not supported.

Although bladder recurrence is common, CT is not supported to screen for bladder recurrence, and it is generally felt that urine cytological evaluation and cystoscopy are sufficiently accurate for the diagnosis of bladder recurrence in this patient population.

The incidence of UTUC in this patient population is 0.6% to 0.9% [19,20]. In addition, in a study of 935 patients with history of NMIBC, only 29% (15 of 51) of UTUCs were diagnosed on routine imaging while the remaining UTUCs were diagnosed once patients became symptomatic, for an overall imaging efficacy of 0.49% (15 UTUC out of 3,074 CT examinations) [23]. Routine surveillance of the upper urinary tract in asymptomatic, low-risk patients is not supported.

# FDG-PET/CT Skull Base to Mid-Thigh

Imaging with PET using the tracer fluorine-18-2-fluoro-2-deoxy-D-glucose (FDG)/CT is generally not appropriate for patients with NMIBC without symptoms or risk factors. The risk of metastatic disease is extremely low. FDG is excreted by the kidneys, and activity obscures evaluation of the upper and lower urinary tract for recurrent disease.

## **MRI Abdomen and Pelvis**

In patients with NMIBC without risk factors or symptoms, screening for distant metastatic disease with cross-sectional imaging is not supported.

There has been increasing interest in using MRI for local staging of bladder cancer in the pretreatment setting [24-28]. However, progression to MIBC in this patient population is rare. MRI has been used to evaluate the urinary bladder following transurethral resection of bladder tumor (TURBT). In a study including 47 patients with recurrent bladder cancer, MRI demonstrated a sensitivity of 67% and 73% and a specificity of 81% and 62% for 2 readers, respectively, and false-negatives included low-grade Ta lesions [29]. In another study, diffusion-weighted imaging (DWI) had a sensitivity of 100% and specificity of 81.8% for recurrent tumor in 11 patients [30].

Despite these results, there is limited data for using MRI as a screening test in patients with previously treated bladder cancer. At this time, it is generally felt that urine cytological evaluation and conventional cystoscopy are sufficiently accurate for the diagnosis of bladder recurrence in this patient population.

## **MRU**

MRU can be used as a primary imaging test for comprehensive evaluation of the genitourinary tract that can be used to identify metastatic disease and metachronous UC. Currently, evaluation for metastatic disease and routine surveillance of the upper urinary tract in asymptomatic, low-risk patients is not supported. Although MRU has been shown to have a sensitivity of 63% and specificity of 91% in a small study of 35 patients with suspected UTUC, the incidence of UTUC in this patient population is only between 0.6% and 0.9% [19,20,31].

# **Radiography Chest**

Chest radiography is generally not appropriate for patients with NMIBC without symptoms or risk factors.

## Radiography Intravenous Urography

CTU and, to a lesser extent, MRU have replaced IV urography (IVU) for the evaluation of the upper urinary tract. IVU does not have a current role in surveillance of NMIBC.

## **US Pelvis (Bladder)**

Because cystoscopy is relatively invasive and time consuming, there is interest in noninvasive and effective imaging modalities to identify recurrent bladder cancer. In a small prospective study, transabdominal ultrasound (US) was found to have a sensitivity of 78.5% and specificity of 100% for the diagnosis of recurrent UC of the urinary bladder, with cystoscopy as the reference standard [32]. In this study, US accurately diagnosed bladder cancer in 78.6% (11 of 14) of patients, missing 2 tumors <3 mm and 1 lesion located in a diverticulum. In another study, the combination of grayscale US, multiplanar reconstruction, and 3-D virtual US had a sensitivity of 96.4% and specificity of 88.8% compared with conventional cystoscopy [33]. Despite these results, it is generally understood that US has limited ability to identify MIBC in clinical practice and is sparingly used. As cystoscopy allows identification of recurrent neoplasm, concurrent biopsy, and local staging, US has not replaced the need for conventional cystoscopic surveillance for patients with NMIBC.

## Variant 2: Nonmuscle invasive bladder cancer with symptoms or risk factors. Post-treatment surveillance.

Patients with NMIBC and risk factors require frequent surveillance for recurrent bladder cancer, which is generally done with conventional cystoscopy. In patients at intermediate risk with a history of TURBT and intravesical chemotherapy, recurrent bladder cancer is identified in up to 57% (413 of 724) of patients [8]. In patients at high risk, 59.6% (2,694 of 4,521) of patients develop multiple recurrences within 2 years of initial treatment [34]. In addition, progression to MIBC is seen in 8.6% to 15% of patients with high-risk disease [35-37].

#### **CT Abdomen and Pelvis**

NMIBC is a heterogeneous group of tumors, and although distant metastatic disease is uncommon in this patient population, cross-sectional imaging may be used to assess for metastatic disease in patients with symptoms or risk factors. There is no relevant literature regarding the use of CT abdomen and pelvis without or with IV contrast for the evaluation of metastatic bladder cancer; however, in the absence of contraindications, IV contrast is generally indicated to improve sensitivity for the identification of metastatic disease. CT abdomen and pelvis without and with IV contrast (excluding CTU) adds little information over CT abdomen and pelvis with IV contrast and does not offer a complete examination of the urinary tract. CTU, however, is a comprehensive examination and can be used to assess for metastatic disease and metachronous upper-tract UC (see below).

## **CT Chest**

Chest CT without or with IV contrast is generally not appropriate for patients with NMIBC with symptoms or risk factors, unless an abnormality is identified with chest radiography.

#### CTU

CTU is a primary imaging test for comprehensive evaluation of the genitourinary tract that can be used to identify metastatic disease and metachronous UC in patients with NMIBC who have symptoms or risk factors. Although CTU has not replaced cystoscopy, CT performs well in identifying recurrent bladder cancer following TURBT. In a study of CTU in 121 patients at risk for urothelial recurrence after TURBT (with symptoms or positive urine cytology), 59 bladder recurrences were identified in 38 patients. The authors found that overall accuracy was better in the urinary bladder during the nephrographic phase compared with the pyelographic/excretory phase (91.7% [354 of 386] versus 83.2% [321 of 386], P = .038) [38]. In another study of patients with a history of UC, CTU had a sensitivity of 77.8% (63 of 81) and specificity of 77.9% (60 of 77) for the detection of bladder cancer [39].

CTU for the evaluation of the upper urinary tract is effective in patients with symptoms, particularly in the setting of a negative cystoscopy. In a study of CTU in 121 patients at risk for urothelial recurrence after TURBT (with symptoms or positive urine cytology), 19 upper-tract recurrences were identified in 13 patients. In this study, accuracy for upper-tract recurrence was better in the nephrographic phase compared with the pyelographic phase (86.7% [260 of 300] versus 80.0% [240 of 300], P = .028) [38].

## FDG-PET/CT Skull Base to Mid-Thigh

FDG-PET/CT is generally not appropriate for patients with NMIBC. The risk of metastatic disease is extremely low, FDG is excreted by the kidneys, and activity obscures evaluation of the upper and lower urinary tract for recurrent disease.

## **MRI Abdomen and Pelvis**

Although distant metastatic disease is uncommon in this patient population, cross-sectional imaging may be used to assess for metastatic disease in patients with symptoms or risk factors. There is no relevant literature regarding the use of MRI abdomen and pelvis without IV contrast in the evaluation of metastatic UC. Given the improved

soft-tissue contrast of MRI compared with CT, MRI of the abdomen and pelvis without IV contrast may be acceptable for the identification of metastatic disease; however, MRI without and with IV contrast is preferred to improve sensitivity. MRU, however, is a comprehensive examination and can be used to assess for metastatic disease and metachronous upper-tract UC (see below).

There has been increasing interest in using MRI for local staging of bladder cancer in the pretreatment setting. Several meta-analyses of MRI for local staging of bladder cancer have been performed. For the differentiation of NMIBC from MIBC, sensitivity ranges from 97% to 92% and specificity ranges from 79% to 88% [24-26]. Vesical Imaging-Reporting and Data System (VI-RADS) using multiparametric MRI with T2-weighted imaging, DWI and dynamic contrast-enhanced imaging has been developed to identify MIBC and standardize reporting. A multireader validation study of VI-RADS for the identification of MIBC demonstrated an intraclass correlation coefficient of 0.85 among 5 readers with a pooled area under the curve of 0.90 [27]. A larger study of 340 patients (255 with NMIBC and 85 with MIBC) concluded that VI-RADS had an accuracy of 94% for identifying MIBC among 2 readers [28].

For evaluation of the urinary bladder following TURBT, Rosenkrantz et al [29] evaluated 47 patients with recurrent bladder cancer and demonstrated a sensitivity of 67% and 73% and specificity of 81% and 62% for 2 readers, respectively. In this study, false-positives were seen in patients who underwent Bacillus Calmette-Guérin therapy, and false-negatives included low-grade Ta lesions. Wang et al [30] found that DWI had a sensitivity of 100% and specificity of 81.8% for recurrent tumor in 11 patients, and the authors found that DWI outperformed dynamic contrast-enhanced imaging in the differentiation of tumor from postoperative inflammation or fibrosis.

Despite these results, there are limited data for use of MRI as a screening test in patients with previously treated bladder cancer. At this time, it is generally felt that urine cytological evaluation and conventional cystoscopy are sufficiently accurate for the diagnosis of bladder recurrence in this patient population.

#### **MRU**

MRU offers a comprehensive evaluation of the genitourinary tract and can be used to evaluate for metastatic disease and metachronous UTUC following treatment of NMIBC. In a study of 91 examinations in 88 patients with suspected UTUC, MRU had a sensitivity of 72.4% to 86.2% and specificity of 97.9% to 99.5% for 2 readers, respectively [40].

## **Radiography Chest**

Metastatic disease in patients with NMIBC is uncommon; however, chest radiography may be appropriate in patients with NMIBC with symptoms or risk factors.

## Radiography Intravenous Urography

CTU and, to a lesser extent, MRU have replaced IVU for the evaluation of the upper urinary tract. IVU does not have a current role in surveillance of NMIBC.

#### **US Pelvis (Bladder)**

In a small prospective study, transabdominal US was found to have a sensitivity of 78.6% and specificity of 100% for the diagnosis of recurrent UC of the urinary bladder, with cystoscopy as the reference standard [32]. In this study, US accurately diagnosed bladder cancer in 78.6% (11 of 14) of patients, missing 2 tumors <3 mm and 1 lesion located in a diverticulum. In another study, the combination of grayscale US, multiplanar reconstruction, and 3-D virtual US had a sensitivity of 96.4% and specificity of 88.8% compared with conventional cystoscopy [33]. Despite these results, US has limited ability to identify MIBC or nodal metastatic disease. As cystoscopy allows identification of recurrent neoplasm, concurrent biopsy, and local staging, US has not replaced the need for cystoscopic surveillance for patients with NMIBC.

# Variant 3: Muscle-invasive bladder cancer with or without cystectomy. Post-treatment surveillance.

Following radical cystectomy for MIBC, 5-year recurrence-free survival is approximately 58%; risk factors for recurrence include advanced tumor stage, lymph node involvement, lymphovascular invasion, high tumor grade, and positive surgical margins [10,41-43]. Recurrences can be described as pelvic relapse; surgical bed recurrence; internal and external iliac and obturator lymph node involvement or distant metastatic disease; and osseous, pulmonary, hepatic, extrapelvic lymphadenopathy, peritoneal, and brain metastases. Most recurrences occur within the first 2 years following cystectomy, and most recurrences are distant metastatic disease [44]. Pelvic relapse is seen in 34% of patients, and the 2-year risk of local failure exceeds 30% [45].

In a study of 1,110 patients following radical cystectomy, recurrences were identified in 29.2% (324 of 1,110) of patients, and 61.7% (200 of 324) of recurrences were single-site recurrences with 43 local (22 cystectomy bed and 21 pelvic lymph node) and 138 distant (36 lung, 19 liver, 52 bone, 17 extrapelvic lymph node, 7 peritoneal, 4 brain, and 3 other) [46]. In a smaller study of 343 patients, 46% (158) of patients developed recurrence; 30% (104) were distant, 6% (21) were distant and local, and 10% (33) were only local. Eighty-four percent of recurrences were identified within 2 years. Following cystectomy, patients are also at risk of developing UTUC, which is found in up to 3.7% of patients [47,48]. As recurrence can involve the entire urinary tract, the urethra also needs to be screened, often with urethral wash cytology, although urethral recurrence may occasionally be identified on cross-sectional imaging. The risk of urethral recurrence is 2.7% to 3.8%, and risk factors include prostatic involvement of the MIBC [47-49].

## **CT Abdomen and Pelvis**

As described earlier, recurrences can be described as pelvic relapse; surgical bed recurrence; internal and external iliac and obturator lymph node involvement or distant metastatic disease; and osseous, pulmonary, hepatic, extrapelvic lymphadenopathy, peritoneal, and brain metastases.

There is no relevant literature regarding the use of CT abdomen and pelvis without or with IV contrast for the evaluation of metastatic bladder cancer; however, in the absence of contraindications, IV contrast is generally indicated to improve sensitivity for the identification of metastatic disease. CT of the abdomen and pelvis without and with IV contrast (excluding CTU) adds little over CT abdomen and pelvis with IV contrast and does not offer a complete examination of the urinary tract.

#### **CT Chest**

All patients with MIBC require imaging of the thorax. In the setting of bladder cancer, there is a lack of data comparing the utility of chest radiography and chest CT. Chest radiography is an effective screening examination and should be performed at regular intervals. Any abnormality identified at radiography should be followed up with a CT examination for improved characterization. There is no relevant literature regarding the use of CT chest without or with and without IV contrast in the evaluation of bladder cancer metastases to the thorax; however, CT chest is often performed as a component of the imaging follow-up of patients with MIBC.

#### CTU

CTU is a primary imaging test for comprehensive evaluation of the genitourinary tract and can be used to identify distant metastatic disease and metachronous UTUC in this patient population. In one study, accuracy of CTU for UTUC was better in the nephrographic phase compared with the pyelographic phase for upper-tract recurrences (86.7% [260 of 300] versus 80.0% [240 of 300], P = .028), although the 2 phases are complementary [38].

## FDG-PET/CT Skull Base to Mid-Thigh

FDG-PET/CT in the setting of MIBC is typically used to resolve equivocal findings identified on other imaging tests, but there is increasing evidence that FDG-PET/CT alters patient management and has prognostic value compared with other staging examinations.

Kibel et al [50] evaluated FDG-PET/CT prior to cystectomy for MIBC and found that FDG-PET/CT had a sensitivity of 70% (7 of 10) and specificity of 94% (30 of 32) for metastatic disease. However, occult metastatic disease was found in 7 of 42 patients with FDG-PET/CT compared with CT alone. In another study of 44 patients with MIBC, FDG-PET/CT demonstrated a sensitivity of 57% for pelvic lymph node involvement compared with 33% for CT, and FDG-PET/CT identified all bone lesions that were detected by scintigraphy [51]. A more recent study demonstrated a sensitivity of 62% to 79% for nodal metastases based on standardized uptake values [52]. A meta-analysis for nodal metastatic disease demonstrated a pooled sensitivity of 57% and specificity of 92% [53]. Given FDG activity in excreted urine, pelvic staging may be difficult. One group of authors found that with diuretics and oral hydration there was improved assessment of locally recurrent disease [54].

In a study that included 41 patients with suspected recurrent bladder cancer after primary treatment that underwent FDG-PET/CT, authors found that FDG-PET/CT had a sensitivity of 87% and specificity of 94% for recurrent/metastatic bladder cancer following treatment [55]. In this study, metastatic disease was found in abdominal and pelvic lymph nodes, including suprarenal lymph nodes; pulmonary and osseous metastatic disease was also identified. Perhaps more importantly, the results of the FDG-PET/CT changed the treatment decision in 40% of patients and had prognostic value in determining overall survival and progression-free survival. In another study of the National Oncologic PET Registry, authors found that FDG-PET/CT changed management in approximately 35% of patients and had a large impact on chemotherapy monitoring [56]. In addition, there is

increasing evidence that FDG-PET/CT can be used to assess for treatment response after neoadjuvant or induction chemotherapy [57-59].

Although not widely available, there is increasing interest in <sup>11</sup>C-choline-PET. In a study of 27 patients with either MIBC or recurrent NMIBC that failed TURBT and intravesical therapy, the presence of residual bladder cancer was detected in 84% (21 of 25) of patients with CT and 96% (24 of 25) of patients with <sup>11</sup>C-choline PET, and lymph node involvement was identified correctly in 50% (4 of 8) of patients with CT and 62% (5 of 8) of patients with PET [60].

# Fluoroscopy Abdomen Loopogram

Abdominal radiography can be useful in the early postoperative setting to evaluate for ureteral stent location and to evaluate patients with abdominal distention and postoperative ileus. A fluoroscopic loopogram, in which water-soluble contrast is instilled into an ileal conduit in a retrograde fashion, can be used to evaluate for leak in the early postoperative period and to confirm patent ureteral anastomoses in the setting of hydronephrosis and declining renal function following urinary diversion. Abdominal radiography and fluoroscopic examinations are not useful for detection of tumor recurrence.

#### **MRI Abdomen and Pelvis**

MRI performs well for identifying metastatic disease within the abdomen and pelvis; however, nodal disease is largely based on size criteria. A recent meta-analysis evaluating nodal metastatic disease in the setting of bladder or prostate cancer demonstrated a pooled per-patient sensitivity of 56% and specificity of 94% [61]. There is no relevant literature regarding the use of MRI of the abdomen and pelvis without IV contrast in the evaluation of metastatic UC. Given the improved soft-tissue contrast of MRI compared with CT, MRI of the abdomen and pelvis without IV contrast may be acceptable for the identification of metastatic disease; however, MRI without and with IV contrast is preferred to improve sensitivity.

Although MRI can be used for local staging of bladder cancer, the presence of inflammation and fibrosis affects the accuracy of MRI following neoadjuvant chemoradiation, when accuracy drops to only 30% [62]. However, DWI may help distinguish inflammation and fibrosis from tumor; in a small study of 20 patients who underwent low-dose neoadjuvant chemoradiation, MRI had an accuracy rate of 44% in determining pathologic response for T2-weighted imaging alone, 33% for dynamic contrast-enhanced imaging, and 80% for DWI [63].

## **MRU**

MRU is a primary imaging test for the comprehensive evaluation of the genitourinary tract and can be used to assess for metastatic disease and metachronous UTUC. In a study of 91 examinations in 88 patients with suspected UTUC, MRU had a sensitivity of 72.4% to 86.2% and specificity of 97.9% to 99.5% for UTUC for 2 readers, respectively [40].

# **Radiography Chest**

All patients with MIBC require imaging of the thorax. Chest radiographs are an effective screening examination and should be performed at regular intervals. Any abnormality identified on radiography should be followed with a CT examination for improved characterization.

# Radiography Intravenous Urography

CTU and, to a lesser extent, MRU have replaced IVU for the evaluation of the upper urinary tract. In a study of 128 patients at high risk for UTUC, in whom 46 patients were diagnosed with UTUC, excretory urography had a perpatient sensitivity of 80.4% (37 of 46) and a specificity of 81.0% (47 of 58), whereas CTU had a sensitivity of 93.5% (43 of 46) and a specificity of 94.8% (55 of 58) [64]. IVU is not recommended for detection of tumor recurrence. However, IVU could be used to assess for ureteral anastomotic patency if reflux cannot be demonstrated on a loopogram.

## **US Pelvis (Bladder)**

Following cystectomy, the acoustic window is limited, and US is of little clinical use for the identification of local recurrence or nodal metastatic disease. Given the high incidence of recurrent disease (up to 46% of patients) following cystectomy for MIBC, surveillance imaging with CT or MRI is recommended [43]. US may be useful to assess the kidneys for hydronephrosis in the setting of declining renal function, regardless of whether the urinary bladder has been resected or not.

## **Summary of Recommendations**

- Variant 1: Imaging is usually not appropriate for post-treatment surveillance of patients with NMIBC without symptoms or risk factors.
- Variant 2: MRU without and with IV contrast or CTU without and with IV contrast is usually appropriate for post-treatment surveillance of patients with NMIBC with symptoms or risk factors. These procedures are equivalent alternatives (ie, only one procedure will be ordered to provide the clinical information to effectively manage the patient's care).
- Variant 3: MRI abdomen and pelvis without and with IV contrast, MRU without and with IV contrast, CT abdomen and pelvis with IV contrast, or CTU without and with IV contrast are usually appropriate equivalent alternatives for post-treatment surveillance of patients with MIBC with or without cystectomy (ie, only one procedure will be ordered to provide the clinical information to effectively manage the patient's care). Radiography chest or fluoroscopy abdomen loopogram is also usually appropriate as complementary to the abovementioned procedures. The panel did not agree on recommending MRI abdomen and pelvis without IV contrast or CT abdomen and pelvis without and with IV contrast for post-treatment surveillance of patients with MIBC with or without cystectomy. There is insufficient medical literature to conclude whether or not these patients would benefit from MRI or CT for post-treatment surveillance of patients with MIBC with or without cystectomy. Imaging with these procedures in this patient population is controversial but may be appropriate.

# **Supporting Documents**

The evidence table, literature search, and appendix for this topic are available at <a href="https://acsearch.acr.org/list">https://acsearch.acr.org/list</a>. 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 <a href="https://www.acr.org/ac.">www.acr.org/ac.</a>

## **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.

## **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 below). Additional information regarding radiation dose assessment for imaging examinations can be found in the ACR Appropriateness Criteria. Radiation Dose Assessment Introduction document [65].

Relative Radiation Level Designations			
Relative Radiation Level*	Adult Effective Dose Estimate Range	Pediatric Effective Dose Estimate Range	
0	0 mSv	0 mSv	
€	<0.1 mSv	<0.03 mSv	
<b>⊕⊕</b>	0.1-1 mSv	0.03-0.3 mSv	
<b>⊕⊕</b>	1-10 mSv	0.3-3 mSv	
❖❖❖❖	10-30 mSv	3-10 mSv	
❖❖❖❖❖	30-100 mSv	10-30 mSv	

<sup>\*</sup>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."

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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.