

**American College of Radiology
ACR Appropriateness Criteria®**

Clinical Condition: Recurrent Lower Urinary Tract Infections in Women

Variant 1: With no underlying risk factors.

Radiologic Procedure	Rating	Comments	<u>RRL*</u>
CT abdomen and pelvis without and with contrast	2		High
X-ray abdomen	2		Med
CT abdomen and pelvis without contrast	2		High
X-ray contrast enema	2		Med
X-ray cystography	2		Med
MRI pelvis without and with contrast	2	MRI may be indicated if urethral diverticulum is suspected.	None
US kidneys and bladder retroperitoneal	2		None
US pelvis (bladder)	2		None
NUC Tc-99m sulfur colloid cystography	2		Min
X-ray voiding cystourethrography	2		Low
X-ray intravenous urography	2	Not cost-effective in this group.	Med
US pelvis (urethra)	1		None
Rating Scale: 1=Least appropriate, 9=Most appropriate			*Relative Radiation Level

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Clinical Condition:**Recurrent Lower Urinary Tract Infections in Women****Variant 2:**

Patients, who are nonresponders to conventional therapy, get frequent reinfections, and have known underlying risk factors.

Radiologic Procedure	Rating	Comments	<u>RRL*</u>
CT abdomen and pelvis without and with contrast	7		High
MRI pelvis without and with contrast	6	For suspected diverticulum or prolapse. See comments regarding contrast in text under "Anticipated Exceptions."	None
X-ray voiding cystourethrography	6	For reflux, bladder or urethral fistula, or prolapse.	Low
US pelvis (urethra)	5		None
X-ray intravenous urography	4	May be used in young women, but will not detect abscesses or small stones. May demonstrate scarring, stones, congenital anomalies.	Med
US kidneys and bladder retroperitoneal	3		None
X-ray abdomen	2		Med
CT abdomen and pelvis without contrast	2		High
X-ray contrast enema	2	May be useful for vesicoenteric fistula.	Med
X-ray cystography	2	May be useful for vesicoenteric fistula.	Med
US pelvis (bladder)	2	Also to evaluate for postvoid residual.	None
NUC Tc-99m sulfur colloid cystography	2		Min
Rating Scale: 1=Least appropriate, 9=Most appropriate			*Relative Radiation Level

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RECURRENT LOWER URINARY TRACT INFECTIONS IN WOMEN

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Summary of Literature Review

It is estimated that 20%-35% of all females have at least one urinary tract infection (UTI) at some time in their lives [1]. Most occur in healthy, sexually active women with a normal urinary tract and normal renal function [2]. These infections are usually limited to the lower urinary tract, are not recurrent, and respond to appropriate antimicrobial therapy [3]. Lower UTIs are confined to the bladder and occasionally the urethra and result in irritative voiding symptoms such as frequency, dysuria, urgency, and hematuria in severe cases. There is usually no associated flank pain, fever, or other systemic symptoms.

Recurrent lower UTIs are usually defined as two or more episodes of such infection occurring in the preceding 12 months [4]. In most cases, such infections are the result of sexual habits and hygiene (eg, women who are sexually active, especially those using diaphragms and/or spermicides) [4,5]. In fact, such lower UTIs are commonly referred to as “honeymoon cystitis.” A clean-catch or catheterized specimen for culture typically reveals greater than 100,000 organisms per milliliter of urine. The typical infecting organism is *Escherichia coli*. The route of infection is ascending from the perianal area and vagina via the urethra and into the bladder. It is not at all uncommon for such infections to be severe enough to result in gross hematuria. However, in uncomplicated lower UTIs, there is complete clearing of bacteriuria and hematuria with appropriate antimicrobial therapy. In some cases, single-dose antimicrobial therapy after intercourse or at the onset of irritative voiding symptoms is adequate to control frequent recurrences of cystitis. In patients

without underlying risk factors (Appendix 1) and with lower UTIs as defined above that do not exceed two episodes per year on average, and that respond promptly to appropriate therapy, imaging is usually not cost-effective.

Uncomplicated recurrent lower UTIs in women must be differentiated from “reinfection,” which may indicate causes such as a vesicovaginal or vesicoenteric fistula or a paravesical abscess with fistula to the bladder [3,6-9]. Furthermore, “bacterial persistence” is defined as an infection with the same organism, typically from a site within the urinary tract, after the bacteriuria has resolved for at least several days and antimicrobial therapy has ceased. Causes of bacterial persistence include calculi, foreign bodies, urethral or bladder diverticula, infected urachal cyst, and postoperative changes such as a remaining ureteral stump that retains urine and results in stasis. In such patients with frequent recurrences and reinfections with the same bacteria, imaging is indicated to detect a treatable condition and monitor its progress.

Imaging Options

In support of the premise that imaging has little efficacy in uncomplicated lower UTIs in women, Fair et al [10] reported a series of 164 women with recurring UTIs who had intravenous urography (IVU). Of the IVUs, 88% were completely normal, and there were no cases with abnormalities in which the findings altered the medical or surgical management. Engel et al [11] studied 153 women with IVU and cystoscopy and found that 89% were entirely normal. None of the abnormalities discovered in the remaining 11% were judged to be related to recurrent infections or influenced subsequent therapy. Fairchild et al [12] studied 78 women with recurrent UTIs and found 6% with “major structural urologic abnormalities requiring further therapy.” All women with such abnormalities had risk factors (to be defined subsequently). Fowler and Pulaski [13] described studies in 104 of 126 patients, urographic (n=75) and cystoscopic (n=74)—after exclusion of 22 patients from the study for a variety of reasons—mean age 40 years (range 16-72 years), at a military hospital (Walter Reed Army Medical Center). They found what they believed were incidental findings in 12%, including duplications (four), small renal calculi (two), calyceal diverticulum (two) and renal cell carcinoma (one). Possibly related to past or current infections were findings in 5%—renal cortical scarring (three), scarred atrophic kidney (one), ureteritis cystica (one). DeLange and Jones [14] reported on 201 young women with recurrent UTIs, of whom 121 had uncomplicated lower UTIs. The IVUs for all of the latter either were normal or showed insignificant abnormalities. They also concluded that a risk factor should be present to justify an imaging study.

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Therefore, imaging studies should be reserved for women who do not respond promptly to appropriate antimicrobial therapy, those who suffer frequent reinfections (or bacterial persistence), and those with known risk factors. Other documented risk factors include: childhood UTIs, flank pain, fever more than 38.5° C, history of urinary calculi or urinary tract obstruction, obstructive voiding symptoms (straining to urinate, feeling of incomplete bladder emptying, etc), infection with a urea-splitting organism, abnormal renal function studies, neurogenic bladder dysfunction, history of genitourinary surgery, asymptomatic bacteriuria, diabetes mellitus or other immunocompromised states, and analgesic abuse [10-14]. It should be remembered in all cases of UTI that it is often difficult to distinguish between infections associated with pathology in the upper from those in the lower urinary tract. As an example, in a series of 293 patients, the most common presenting symptom in women with reflux nephropathy was lower UTI (72% of cases) [15]. The following paragraphs discuss the various imaging examinations that may be useful in evaluating women with recurrent UTIs who fall outside the category of uncomplicated.

Radiography

Radiographs of the abdomen has long been an important examination for detecting calculi, bladder wall calcifications, gas in the wall or lumen of the urinary bladder, and/or foreign bodies that may be the etiology of a UTI [3]. When calcifications are seen in the bladder wall, it is often possible to make a correct clinical diagnosis if these findings are viewed in the context of the clinical history, physical examination, appropriate laboratory studies, and further imaging of the remainder of the urinary tract. Bladder wall calcification is typically due to prior infection with schistosomiasis (uncommon in the United States, but very common in other parts of the world), tuberculosis, Cytoxan cystitis, or radiation cystitis [16].

Intravenous Urography

IVU remains an inexpensive and effective modality for evaluating the urinary tract. The study optimally includes thin-section nephrotomography, which may show renal scarring to indicate prior episodes of pyelonephritis. Although ill-defined renal margins may suggest a perirenal inflammatory process, complications of suspected pyelonephritis are best evaluated by computed tomography (CT). However, for evaluation of the collecting system, IVU is virtually unexcelled and may correctly detect the changes caused by chronic atrophic pyelonephritis, papillary necrosis, and subtle urothelial neoplasms, as well as other changes associated with infections such as pyelitis cystica and leukoplakia. IVU is also useful for detecting or excluding congenital anomalies or obstruction of the urinary tract. The bladder phase of the IVU can usually identify contour abnormalities suggestive of inflammation or neoplasm.

Further, the ability of the bladder to empty on voiding can be reasonably assessed. Cystoscopy is the best method to evaluate bladder wall pathology suspected on imaging studies.

For many other indications, CT of the abdomen and pelvis without and with contrast and including high resolution imaging during the excretory phase (so-called CT urography) has superseded IVU when imaging is required to evaluate the urinary tract [17-19].

Computed Tomography

Although abdominal radiography is considered the most cost-effective imaging modality for detecting opaque calculi associated with recurrent UTI, it may prove inadequate in some cases (eg, poor definition due to moderate overlying bowel). In such instances, unenhanced helical CT may be used. In many locations, the cost of this examination has been reduced so that it is competitive with that of an IVU. Its benefits include increased accuracy in detecting calculi (contrast resolution and lack of overlying bowel and bone), increased speed of examination, and increased abdominal detail, allowing, in some cases, an alternate diagnosis to explain patients' signs, symptoms, and laboratory findings. As a result, unenhanced CT has been used predominantly for the emergency patient with "renal colic" and/or hematuria. It has also been used to define the severity and extent of upper-tract calculi, which are sometimes associated with recurrent UTIs.

Additionally, CT without and with intravenous contrast has been very helpful and has been described as the "examination of choice" in evaluating complicated UTIs (eg, abscess) [20-23]. More recently, CT has become accepted as the modality of choice for the diagnosis and follow-up of urinary tract infections. This is especially true in patients with known underlying risk factors, repeated episodes of reinfection, or persistent infection despite adequate therapy. CT can not only define the extent of disease but also identify complications such as renal and perirenal abscess which may be associated with these infections [6,24].

Ultrasound

Some investigators [25] have advocated the use of renal and pelvic ultrasound (US) combined with radiographs as a replacement for IVU. They conclude that young women with recurrent UTIs should have this combination of exams (ie, US and radiographs) as the investigation of choice because it is cost-effective, "noninvasive, inexpensive, and acceptable to the patient." Others [26,27] have supported the continued use of IVU by citing the level of experience required to perform accurate US as well as the dependence of this examination on operator skills.

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Diverticula

Patients with suspected bladder diverticula may be imaged with IVU, cystography, or US. When a bladder diverticulum is at or near a ureteral orifice, voiding cystourethrography should be considered to evaluate the possibility of vesicoureteral reflux [28]. Although used commonly in children to reduce the dose of radiation, nuclear cystography has not been used widely in adults.

Bladder diverticula are unusual in women and are associated with neurogenic bladder, or postoperative bladder, or rarely are congenital. Diverticula of the urethra can be evaluated by voiding cystourethrography (VCUG) or retrograde urethrography [29]. Some have also advocated US and magnetic resonance imaging (MRI) for detection. Endovaginal and transperineal sonography has been suggested as a “noninvasive screening technique for female urethral diverticula.” It is said to better demonstrate the “spatial relationship of the diverticula to the urethra” [30]. MRI is accurate but expensive and should be reserved for those patients in whom there is strong clinical suspicion of a diverticulum and when the findings of more conventional modalities are equivocal [31].

When performing cystography and urethrography for evaluating the lower urinary tract, the use of digital radiography has been shown to decrease radiation dose by approximately 90% while maintaining diagnostic accuracy. This is particularly important in reducing the gonadal radiation dose during the examination of young women [32].

Enterovesical Fistulae

Enterovesical fistulae are usually caused by diverticulitis (cancer is the second most common cause). Clinical suspicion is frequently raised by the presence of UTI with pneumaturia and/or fecaluria. The diagnosis and localization usually require more than one examination. In one large series, cystoscopy and barium enema were used in 75% of the patients but were positive in only 36% and 34% of the patients, respectively. IVU was performed in 55% of the patients but was only 12.5% diagnostic; cystography was used 36% of the time and was 44% diagnostic; CT scan was used in 23% of patients and was 60% diagnostic. Colonoscopy, US, upper gastrointestinal/small bowel follow-through, sigmoidoscopy, MRI, and nuclear imaging have very low yields, making them even less cost-effective. The authors concluded that CT, cystoscopy, and oral charcoal are the most effective modalities for diagnosing the presence of a fistula [33]. Yet, after analysis of another large series, the authors concluded that a combination of cystoscopy, cystography, and barium enema “resulted in diagnosis of all patients” [34].

When UTI accompanies neuropathic bladder, cystography or US may demonstrate the morphologic changes of the bladder wall [35], and VCUG or

transrectal sonographic voiding cystourethrography may document neuromuscular dysfunction of the bladder and/or associated sphincters [36].

Summary

Women with recurrent UTIs should have one or more additional risk factors to justify urologic or radiologic investigation. In such cases, cystoscopy is often the most rewarding examination for achieving a cost-effective diagnosis. More recently CT has been added as a mainstream investigational modality for the evaluation of urinary tract infections, especially in patients with underlying or known risk factors, episodes of reinfection or infection resistant to conventional therapy. Abnormalities of the bladder and the urethra have traditionally been demonstrated with cystography and urethrography, respectively, with MRI now playing a more central role in evaluation of the urethra as well as for diagnosing bladder prolapse. For the detection of fistulae, contrast enema and CT scan have also been shown to be diagnostic and may supplement cystoscopy and cystography. Nuclear scintigraphy has a limited role to play in the evaluation of the patient with recurrent lower UTIs.

Anticipated Exceptions

Exceptions to the above guidelines occur when there is clinical confusion regarding the source of recurrent UTI or when risk factors (enumerated above and in Appendix 1) are present. In such cases, appropriate imaging as previously described is indicated.

Nephrogenic systemic fibrosis (NSF), also known as nephrogenic fibrosing dermopathy) was first identified in 1997 and has recently generated substantial concern among radiologists, referring doctors and lay people. Until the last few years, gadolinium-based MR contrast agents were widely believed to be almost universally well tolerated, extremely safe and non-nephrotoxic, even when used in patients with impaired renal function. All available experience suggests that these agents remain generally very safe, but recently some patients with renal failure who have been exposed to gadolinium contrast agents (the percentage is unclear) have developed NSF [37-39], a syndrome that can be fatal. Further studies are necessary to determine what the exact relationships are between gadolinium-containing contrast agents, their specific components and stoichiometry, patient renal function and NSF. Current theory links the development of NSF to the administration of relatively high doses (eg, >0.2mM/kg) and to agents in which the gadolinium is least strongly chelated. The FDA has recently issued a “black box” warning concerning these contrast agents (http://www.fda.gov/cder/drug/InfoSheets/HCP/gcca_200_705HCP.pdf).

This warning recommends that, until further information is available, gadolinium contrast agents should not be administered to patients with either acute or significant

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chronic kidney disease (estimated GFR <30 mL/min/1.73m²), recent liver or kidney transplant or hepato-renal syndrome, unless a risk-benefit assessment suggests that the benefit of administration in the particular patient clearly outweighs the potential risk(s) [38].

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

Relative Radiation Level Designations	
Relative Radiation Level	Effective Dose Estimate Range
None	0
Minimal	< 0.1 mSv
Low	0.1-1 mSv
Medium	1-10 mSv
High	10-100 mSv

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Appendix 1. Risk Factors

Risk Factors, Signs, and Symptoms	Underlying Condition
1. Hematuria	Infection, calculi
2. Flank pain	Obstruction and/or calculi
3. Infection with urea-splitting organism	Congenital abnormalities, sequelae of obstruction or infection, calculi (struvite)
4. Previous UTI or pyelonephritis	Congenital abnormalities and/or reflux
5. Fever (>38.5 °C)	Infection and/or obstruction
6. History of calculi or obstruction	Congenital abnormalities, calculi, sequelae of obstruction or infection
7. Obstructive symptoms	Congenital abnormalities, calculi, sequelae of obstruction or infection
8. Elevated serum creatinine	Obstructive vs. renal parenchymal disease
9. Asymptomatic bacteriuria	Calculi or foreign body
10. Severe diabetes mellitus	Renal/papillary abnormalities
11. Childhood UTI	Congenital abnormalities and/or reflux
12. Analgesic abuse	Renal/papillary abnormalities
13. Neurogenic bladder dysfunction	Stasis, bladder diverticula, reflux, calculi
14. History of genitourinary surgery	Congenital and/or postsurgical abnormalities
15. Suspected bladder diverticula	Bladder diverticula
16. Suspected urethral diverticula	Urethral diverticula
17. Suspected enterovesical fistula	Enterovesical fistula

An 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 exams 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.