Clinical Condition: Recurrent Lower Urinary Tract Infections in Women

Variant 1: “Uncomplicated” with no underlying risk factors.

<table>
<thead>
<tr>
<th>Radiologic Procedure</th>
<th>Rating</th>
<th>Comments</th>
<th>RRL*</th>
</tr>
</thead>
<tbody>
<tr>
<td>CT abdomen and pelvis without and with IV contrast</td>
<td>2</td>
<td></td>
<td>☢☢☢☢</td>
</tr>
<tr>
<td>X-ray abdomen</td>
<td>2</td>
<td></td>
<td>☢☢</td>
</tr>
<tr>
<td>CT abdomen and pelvis without IV contrast</td>
<td>2</td>
<td></td>
<td>☢☢☢☢</td>
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<tr>
<td>CT abdomen and pelvis with IV contrast</td>
<td>2</td>
<td></td>
<td>☢☢☢☢</td>
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<tr>
<td>X-ray IV contrast enema</td>
<td>2</td>
<td></td>
<td>☢☢☢</td>
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<tr>
<td>X-ray cystography</td>
<td>2</td>
<td></td>
<td>☢☢☢</td>
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<tr>
<td>MRI pelvis without and with IV contrast</td>
<td>2</td>
<td>MRI may be indicated if urethral diverticulum is suspected.</td>
<td>O</td>
</tr>
<tr>
<td>MRI pelvis without IV contrast</td>
<td>2</td>
<td></td>
<td>O</td>
</tr>
<tr>
<td>US kidneys and bladder retroperitoneal</td>
<td>2</td>
<td></td>
<td>O</td>
</tr>
<tr>
<td>Voiding cystourethrography</td>
<td>2</td>
<td></td>
<td>☢☢</td>
</tr>
<tr>
<td>X-ray intravenous urography</td>
<td>1</td>
<td>This procedure has been supplanted by CT and MR urography.</td>
<td>☢☢☢</td>
</tr>
</tbody>
</table>

Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate

*Relative Radiation Level
**Clinical Condition:** Recurrent Lower Urinary Tract Infections in Women

**Variant 2:** “Complicated,” or patients who are nonresponders to conventional therapy, get frequent reinfections or relapses, and have known underlying risk factors. (See Appendix 1.)

<table>
<thead>
<tr>
<th>Radiologic Procedure</th>
<th>Rating</th>
<th>Comments</th>
<th>RRL*</th>
</tr>
</thead>
<tbody>
<tr>
<td>CT abdomen and pelvis without and with IV contrast</td>
<td>7</td>
<td>CT urography protocol is preferred. If enterovesical fistulas are suspected, consider enteric and/or rectal contrast.</td>
<td>☢☢☢☢</td>
</tr>
</tbody>
</table>
RECURRENT LOWER URINARY TRACT INFECTIONS IN WOMEN

Expert Panel on Urologic Imaging: Elizabeth Lazarus, MD1; Brian C. Allen, MD2; M. Donald Blaufox, MD, PhD3; Fergus V. Coakley, MD4; Barak Friedman, MD5; Pat F. Fulgham, MD6; Stanley Goldfarb, MD7; Matthew S. Hartman, MD8; Matthew T. Heller, MD9; Keyanoosh Hosseinzadeh, MD10; Aytekin Oto, MD11; Christopher Porter, MD12; V. Anik Sahni, MD13; Gary S. Sudakoff, MD14; Sadhna Verma, MD15; Erick M. Remer, MD16; Steven C. Eberhardt, MD17

Summary of Literature Review

Introduction/Background

Urinary tract infections (UTI) are among the most common bacterial infections in women in the United States. The overall lifetime risk of UTI for women is greater than 50% [1]. Subpopulations at increased risk of UTI include pregnant women, the elderly, patients with spinal cord injuries or catheters, patients with diabetes, multiple sclerosis, human immunodeficiency syndrome, and patients with underlying urological abnormalities. In the nonobstructed, nonpregnant woman, uncomplicated UTIs are usually treated empirically, and respond to appropriate antimicrobial therapy [1,2]. An uncomplicated UTI is classified as a UTI without structural or functional abnormalities of the urinary tract and without relevant comorbidities. Complicated UTIs are those occurring in patients with underlying structural or medical problems [3,4].

Recurrent lower UTIs are usually defined as at least 3 episodes of infection within the preceding 12 months [3]. Recurrent UTIs involve reinfection from a source outside of the urinary tract or from bacterial persistence [1,5]. Antibiotic prophylaxis is the most effective way to reduce recurrent UTIs [3]. 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 spermaticides) [3,6]. A clean-catch or catheterized specimen for culture typically reveals >100,000 organisms per milliliter of urine. The typical infecting organism is *Escherichia coli* [6]. The route of infection is ascending from the perianal area and vagina via the urethra and into the bladder. UTIs, particularly if severe, may result in gross hematuria. Postmenopausal women are at increased risk for recurrent UTI in the presence of urinary incontinence, cystocele, or high postvoid residuals of urine [7]. Women who have 3 or more symptomatic infections over a 12-month period may benefit from prophylaxis [3,4,6]. Imaging is of low yield in patients without underlying risk factors (Appendix 1) and with lower UTIs as defined above that do not exceed 2 episodes per year on average, and that respond promptly to appropriate therapy [5,6,8,9].

Recurrent and chronic infections with the same organism are termed “relapses” or “persistent” infections. If infection develops more than 2 weeks after a symptomatic cure, or if it is caused by a second pathogen, it is termed a “reinfection” [6]. 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 relapses or reinfections, imaging is indicated to detect a treatable condition and monitor its progress.

Overview of Imaging Modalities

*Radiography, Intravenous Urography, and Voiding Cystourethrography*

Radiography of the abdomen has long been an important examination for detecting calculi, intramural bladder wall calcification, gas in the wall or lumen of the urinary bladder, and/or foreign bodies that may be the etiology of a UTI. Use of digital tomosynthesis of the abdomen results in improved detection of urinary stones in general over digital radiography, with only a slight increase in effective dose [10]. Historically, intravenous urography (IVU) was the imaging study of choice to evaluate the urinary tract. However, computed tomography (CT) and magnetic resonance (MR) urography have supplanted the use of IVU at most institutions [11]. IVU optimally...
includes thin-section nephrotomography, which may show renal scarring to indicate prior episodes of pyelonephritis. The weaknesses of IVU include the lack of parenchymal detail, the inability to characterize filling defects, and the inability to visualize adjacent soft-tissue organs [11-13]. When a bladder diverticulum is at or near a ureteral orifice, voiding cystourethrography should be considered to evaluate the possibility of vesicoureteral reflux [14]. Double-balloon urethrography is useful for demonstration of urethral diverticula. Although this procedure can be technically difficult and may be uncomfortable for the patient, it demonstrates a high level of agreement with MR imaging (MRI) for diagnosis [15]. Cystoscopy is the best method to evaluate bladder-wall pathology suspected on imaging studies. In patients with recurrent UTIs, investigators have found that 9 of 118 (8%) patients had abnormalities on cystoscopy [16].

Ultrasound, Computed Tomography, and Magnetic Resonance Imaging

CT and MR urography have supplanted the use of IVU at most institutions [11]. Complications of suspected pyelonephritis are best evaluated by CT. CT without and with intravenous contrast has been described as the “examination of choice” in evaluating complicated UTIs for detecting underlying structural problems or complications [11,17]. The benefits of CT 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 [18]. Ultrasound (US) does not use ionizing radiation, an advantage over CT. US can efficiently measure postvoid residuals within the bladder and detect some bladder diverticula. However, it is less accurate in the detection of pyelonephritis, renal abscess, and urinary tract calculi when compared with other imaging modalities, including CT and MRI [18,19]. MRI provides improved soft-tissue contrast resolution and sensitivity for contrast enhancement. It does not use ionizing radiation and therefore is favored in patient populations such as pregnant women, children, and patients who require repeated imaging examinations.

Discussion of Imaging Modalities by Variant

**Variant 1: “Uncomplicated” with no underlying risk factors**

Most women with recurrent symptomatic UTI have normal urinary tracts. Lawrentschuk et al [16] showed that women with no risk factors for UTI had a negative predictive value of 93% for normal cystoscopy. Recurrent uncomplicated UTIs do not routinely require cystoscopy or imaging [5,16].

**Variant 2: “Complicated,” or patients who are nonresponders to conventional therapy, get frequent reinfections or relapses, and have known underlying risk factors**

Complicated causes of UTI can be evaluated by history and physical examination. Host factors that classify a UTI as complicated include anatomic abnormalities such as cystocele, diverticulum, fistula, indwelling catheters, voiding dysfunction, urinary tract obstruction, and underlying conditions such as pregnancy, diabetes, and immunosuppression. In women suspected of having a recurrent complicated UTI, cystoscopy and imaging should be considered [5].

Other documented risk factors include prior urinary tract surgery or trauma, gross hematuria after infection resolution, urea-splitting bacteria on culture, prior abdominopelvic malignancy, prior urinary tract calculi, prior diverticulitis, symptoms of pneumaturia, fecaluria, or repeated pyelonephritis [5].

The following paragraphs discuss the various imaging examinations that may be useful in evaluating women with recurrent complicated UTIs.

**Radiography and Intravenous Urography**

When calcifications are seen in the bladder wall on radiography, 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 *Schistosoma* (uncommon in the United States, but very common in other parts of the world), tuberculosis, Cytokxan cystitis, or radiation cystitis [20]. For evaluation of the collecting system, IVU may detect the changes caused by reflux nephropathy, papillary necrosis, and subtle urothelial neoplasms, as well as other changes associated with infections such as pyelitis cystica and leukoplakia. 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. When a bladder diverticulum is at or near a ureteral orifice, voiding cystourethrography should be considered to evaluate the possibility of vesicoureteral reflux.
Computed Tomography
CT is the examination of choice in patients with known underlying risk factors, repeated episodes of reinfection, or persistent infection despite adequate therapy. Not only does CT have the ability to define the extent of the disease, but it also can identify complications such as renal and perirenal abscess, which may be associated with these infections [17,21,22]. CT has been found to be superior to US and equal to MRI in the sensitivity and reliability for the detection of acute pyelonephritis [18,19]. Lim and Ng [23] have recently shown good correlation between the clinical severity of acute pyelonephritis with severity of the findings on CT in 130 patients. 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. Reduced-radiation protocols for CT are being developed, which result in similar detection of renal stones while reducing patient radiation exposure [24]. CT urography can identify abnormalities of the collecting systems [11]. IVU and CT urography are also useful for detecting or excluding congenital anomalies or obstruction of the urinary tract.

Enterovesical fistulae are usually caused by diverticulitis (cancer is the second most common cause) and are almost all colovesical in nature. Clinical suspicion is frequently raised by the presence of UTI with pneumaturia and/or fecaluria. CT is the primary imaging modality for suspected cases of enterovesical fistulae [25,26]. Kavanagh et al [25] found that CT revealed fistulas in 12 of 15 patients (80%). Cystoscopy was performed in 16 patients, with 87.5% positive for fistulas, and barium enema in 8 patients, with 50% positive for fistulas. The authors concluded that CT is the optimum imaging modality for diagnosis, as it can also identify the underlying etiology.

Using a logistic regression model, Stojadinovic et al [18] showed that in patients with renal suppurrative infection, the risk of incorrect diagnosis is about 14.5 times higher when performing US alone and about 37 times less when using CT. Recent studies show promise in the emerging role of contrast-enhanced US (CEUS) for the initial diagnosis and follow-up of patients with complicated acute pyelonephritis [27-29] in order to avoid the radiation inherent in CT scans. Using CT as a reference standard, Mitterberger et al [29] demonstrated a sensitivity of 98% and a specificity of 100% for CEUS in the diagnosis of acute pyelonephritis in 100 patients.

Magnetic Resonance Imaging
MRI has been shown to be useful in the diagnosis and follow-up of UTI and acute pyelonephritis [11,19,30]. MRI is effective at diagnosing pelvic-organ prolapse. The resultant cystoceles and urinary incontinence associated with pelvic-organ prolapse are significant risk factors for recurrent UTIs in postmenopausal women [7,31,32]. MRI best assesses the structure and complexity of urethral diverticula, allowing for accurate diagnosis and improved surgical planning [33]. Given the excellent soft-tissue contrast on MRI, this modality is equally sensitive to CT for evaluating vesicovaginal and enterovesicular fistulae [34,35].

MRI is less sensitive than CT for detecting urinary tract calculi. In a study of 149 patients, MR urography demonstrated 69% sensitivity for detecting calculi versus 100% for CT [36]. However, MR urography has been shown to have increased sensitivity to perirenal fluid and ureteric dilatation in comparison with CT in the setting of acute obstruction [37]. Multiplanar reconstruction images in the coronal and sagittal planes are commonly included in MR urography images to improve visualization of urinary tract abnormalities [11,38]. MRI may be of greatest value in documenting active upper-tract infection versus scar formation to determine whether therapy has been effective in the high-risk patient. Pregnant women and patients who require multiple imaging examinations may be best served by MRI in order to minimize exposure to ionizing radiation [11,38].

A history of recurrent UTI is seen in 30%–50% of patients with urethral diverticula. Diverticula of the urethra can be evaluated with high sensitivity and specificity by double-balloon urethrography, voiding CT urography, and MRI [39-41]. MRI best assesses the structure and complexity of urethral diverticula, allowing for accurate diagnosis and improved surgical planning. In at least one report, MRI altered the surgical management in 15% of patients [33]. Double-balloon urethrography can be technically difficult and may be uncomfortable for the patient.

Patients with suspected bladder diverticula may be imaged with cystography, US, or CT [12]. Bladder diverticula are unusual in women and are associated with a neurogenic or postoperative bladder; they are rarely congenital. MRI has also been shown to be accurate in the diagnosis of colovesical fistula. The multiplanar imaging capability, lack of radiation, and high soft-tissue resolution inherent to MRI also makes this modality suitable for imaging suspected fistulae, particularly when repeat imaging and radiation doses are of issue [34,35]. IVU, US, and upper gastrointestinal/small-bowel follow-through have very low yields, making them even less cost-effective [42,43].

ACR Appropriateness Criteria®
5
Recurrent Lower UTIs in Women
Ultrasound

US has a limited role in the workup of complicated recurrent UTIs. Hydronephrosis can be demonstrated, as an indication of obstruction, but may not yield a specific etiology [44-46]. Sonography has a role in bladder evaluation for diverticula [12] and postvoid residual volume determination [47], either of which may be of interest in this clinical setting. Sonography is generally less sensitive to calculi determination with CT [48-50].

Summary of Recommendations

- Women with recurrent UTIs should have one or more additional risk factors to justify urologic or radiologic investigation.
- The basis for radiologic or urologic investigation of women with recurrent UTI is to detect abnormalities that could result in future morbidity.
- CT is a mainstream investigational modality for evaluating UTIs, especially in patients with underlying or known risk factors, episodes of reinfection, or infection resistant to conventional therapy. A host of complicating conditions can be detected relatively efficiently and reliably with this modality.
- MRI is useful in evaluation of disease of the urethra as well as for diagnosing organ prolapse and fistula.
- Cystography and urethrography still have roles in assessing abnormalities of the bladder and the urethra.
- US can be used ad hoc in the evaluation of complicated UTIs but can provide only limited information and often not a specific diagnosis.

Summary of Evidence

Of the 50 references cited in the ACR Appropriateness Criteria® Recurrent Lower Urinary Tract Infections in Women document, all of them are categorized as diagnostic references including 2 well-designed studies, 3 good quality studies, and 9 quality studies that may have design limitations. There are 36 references that may not be useful as primary evidence.


While there are references that report on studies with design limitations, 5 well-designed or good quality study provides good evidence.

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, both because of 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 to 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.
Relative Radiation Level Designations

<table>
<thead>
<tr>
<th>Relative Radiation Level*</th>
<th>Adult Effective Dose Estimate Range</th>
<th>Pediatric Effective Dose Estimate Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>☀</td>
<td>0 mSv</td>
<td>0 mSv</td>
</tr>
<tr>
<td>☀☢</td>
<td>&lt;0.1 mSv</td>
<td>&lt;0.03 mSv</td>
</tr>
<tr>
<td>☀☢☢</td>
<td>0.1-1 mSv</td>
<td>0.03-0.3 mSv</td>
</tr>
<tr>
<td>☀☢☢☢</td>
<td>1-10 mSv</td>
<td>0.3-3 mSv</td>
</tr>
<tr>
<td>☀☢☢☢☢</td>
<td>10-30 mSv</td>
<td>3-10 mSv</td>
</tr>
<tr>
<td>☀☢☢☢☢☢</td>
<td>30-100 mSv</td>
<td>10-30 mSv</td>
</tr>
</tbody>
</table>

*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”.

Supporting Documents

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

References


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.
## Appendix 1. Risk Factors

<table>
<thead>
<tr>
<th>Risk Factors, Signs, and Symptoms</th>
<th>Underlying Condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Flank pain</td>
<td>Obstruction and/or calculi</td>
</tr>
<tr>
<td>2. Infection with urea-splitting organism</td>
<td>Congenital abnormalities, sequelae of obstruction or infection, calculi (struvite)</td>
</tr>
<tr>
<td>3. Previous UTI or pyelonephritis</td>
<td>Congenital abnormalities and/or reflux</td>
</tr>
<tr>
<td>4. Fever (&gt;38.5° C)</td>
<td>Infection and/or obstruction</td>
</tr>
<tr>
<td>5. History of calculi or obstruction</td>
<td>Congenital abnormalities, calculi, sequelae of obstruction or infection</td>
</tr>
<tr>
<td>6. Obstructive symptoms</td>
<td>Congenital abnormalities, calculi, sequelae of obstruction or infection</td>
</tr>
<tr>
<td>7. Elevated serum creatinine</td>
<td>Obstructive versus renal parenchymal disease</td>
</tr>
<tr>
<td>8. Asymptomatic bacteriuria</td>
<td>Calculi or foreign body</td>
</tr>
<tr>
<td>9. Severe diabetes mellitus</td>
<td>Renal/papillary abnormalities</td>
</tr>
<tr>
<td>10. Childhood UTI</td>
<td>Congenital abnormalities and/or reflux</td>
</tr>
<tr>
<td>11. Analgesic abuse</td>
<td>Renal/papillary abnormalities</td>
</tr>
<tr>
<td>12. Neurogenic bladder dysfunction</td>
<td>Stasis, bladder diverticula, reflux, calculi</td>
</tr>
<tr>
<td>13. History of genitourinary surgery</td>
<td>Congenital and/or postsurgical abnormalities</td>
</tr>
<tr>
<td>14. Suspected bladder diverticula</td>
<td>Bladder diverticula</td>
</tr>
<tr>
<td>15. Suspected urethral diverticula</td>
<td>Urethral diverticula</td>
</tr>
<tr>
<td>16. Suspected enterovesical fistula</td>
<td>Enterovesical fistula</td>
</tr>
<tr>
<td>17. Urinary incontinence</td>
<td>Infection, stasis (B)</td>
</tr>
<tr>
<td>18. Pelvic floor dysfunction</td>
<td>Cystocele, stasis</td>
</tr>
<tr>
<td>19. Postvoid residuals</td>
<td>Stasis</td>
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