

Radiological Investigations of Urinary Tract Infection in Children: Update on the Clinical Practice Guidelines

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INTRODUCTION

The urinary tract commences from the renal pelvis and terminates at the urethra. Essentially the tract is subdivided into the upper tract (renal pelvis and the ureters) and the lower tract (bladder and the urethra). This lengthy anatomic enclosure is uniquely made to be sterile. Its sterility is partly maintained by these mechanisms: effective urinary drainage and complete bladder emptying. Thus, urine stasis within the tract will potentially disrupt this sterility by creating an environment conducive for microbes to thrive. Furthermore, any congenital or acquired anomaly which causes obstruction to urine flow or promotes retro-grade urine flow will encourage stasis with subsequent microbial multiplication and involvement of the upper tract.

Apart from urinalysis and urine culture, the investigation of Urinary Tract Infection (UTI) in children also involves imaging studies which can be highly informative, particularly when the clinician and the radiologist work in synergy. The imaging studies consist of Ultrasound (US), plain abdominal radiograph, Intravenous Urogram (IVU), Micturating Cystourethrogram (MCUG), radio isotope imaging, Computerized Tomography (CT) scan and Magnetic Resonance Imaging (MRI). The core imaging modalities proposed after a UTI episode are ultrasonography,

micturating cystourethrography, and technetium 99 Dimercaptosuccinic Acid (DMSA) scan. The main reason for imaging is to detect obstructive malformations, Vesico-Ureteric Reflux (VUR), and renal parenchymal damage; however, there is no consensus as to the nature of the malformations, severity of reflux, or degree of renal parenchymal damage that warrants detection. Whereas an intensive approach was recommended by some authorities, there has been a proliferation of guidelines that have proposed different diagnostic algorithms, with the hope of minimizing invasive procedures while maintaining an acceptable sensitivity and specificity for the detection of abnormalities.

This book chapter seeks to discuss the update on the major clinical practice guidelines.

SOME CURRENT RADIOLOGICAL INVESTIGATIONS: ADVANTAGES AND DISADVANTAGES

Given the invasiveness and radiation risks associated with majority of the radiological investigations, the extent to which childhood UTI should be investigated has remained controversial. Moreover, an evidence base to establish an improved outcome is lacking.

In order to appreciate the basis for the current guidelines, it is important to consider briefly the risk-benefit profile of these radiological investigations. The radiation exposure associated with some of them is shown in (Table 1). Their advantages and disadvantages are as follows:

Table 1: Radiation exposure associated with some of the radiological investigations.

Procedure	Radiation dose (mSv)	Background radiation (equivalent)	Chest X- ray (equivalents)
Abdominal X-ray	1.0	161 days	50
IVU	2.5	403 days	125
DMSA scan	1.0	161 days	50
CT abdomen/pelvis	10	1613 days	500
Ultrasound scan	0	0 days	0
MR scan	0	0 days	0
MCUG	1.5 (boys)/0.9 (girl)	242/145 days	75/45

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Ultrasound (US)

Advantages

- Non-invasive, radiation-free, easily accessible and affordable
- Useful in kidney length measurements
- Excellent for detecting nephrolithiasis/urolithiasis and renal masses
- Useful in the diagnosis of acute pyelonephritis
- May detect changes secondary to vesico ureteric reflux (VUR) -> grade 2

Disadvantages

- Operator-dependent with considerable inter-observer variability
- Low sensitivity in detecting renal parenchymal scars
- May miss renal calculi if there is significant obesity

Plain abdominal Radiograph

Advantages

- Useful for detecting calculi (especially radio-opaque ones) and calcification
- Can also detect sacral agenesis

Disadvantages

- Significant radiation risk
- Poor detection of non-radio-opaque calculi

Intravenous urogram (IVU)

Advantages

- Easy to perform without any specialist equipment
- Useful in clearly defining the renal anatomy and structure (especially the pelvis and calyces)
- Useful in identifying the site of urinary tract obstruction such as congenital vesico-ureteric junction (VUJ) or pelvis-ureteric junction (PUJ) obstruction
- Can also identify the site of obstruction due to renal calculi

Disadvantages

- Risk of radiation exposure
- Requires pre-procedure precaution such as ensuring normal renal excretory function

Micturating cystourethrogram (MCUG)

Advantages

- Gold standard test to confirm posterior urethral valves (PUV)
- Excellent for detecting and grading VUR

Disadvantages

- Painful procedure as it requires bladder catheterization

- Exposure to comparatively high radiation dose
- Associated with 2-3% risk of UTI; thus it may require antibiotic prophylaxis before and after the procedure especially in neonates and patients with VUR

DMSA (99Tcm dimercaptosuccinic acid) scan

Advantages

- Gold standard test for detecting renal cortical scars
- Can help to identify ectopic kidneys
- Can provide information about differential renal function
- Procedure does not generally require sedation

Disadvantages

- Scan finding of acute parenchymal inflammation post-UTI (pyelonephritis) may be confused with that of cortical scarring
- Similarly, scan finding in congenital dysplastic kidneys may be identical to that of acquired renal cortical scarring (hence the term- 'renal defects' preferred to 'renal scars')

MRI (Magnetic Resonance Imaging)

Advantages

- No radiation burden
- Used for the assessment of renal parenchyma and function (MR renography) or the urinary drainage systems (MR urography)
- MR urography can give detailed 3-dimensional images of the urinary tract for the evaluation of complex congenital urological anomalies

Disadvantages

- Sedation often required
- Contrast-associated nephrotoxicity in late stages (stages 4 & 5) of chronic kidney disease (CKD)

CT Scanning

Advantages

- Very reliable for imaging renal parenchyma; its availability makes it the modality of choice for assessing renal masses
- Also provides additional information to US in acute pyelonephritis
- Clearly identifies renal calculi

Disadvantages

- Exposure to significant radiation dose
- The problem of motion artifact and thus the need for sedation (circumvented by modern rapid image acquisition)

RADIOLOGICAL INVESTIGATIONS: THE CLINICAL PRACTICE GUIDELINES

Before the age of 11 years, about 3% of female children and 1% of their male counterparts experience a symptomatic UTI; 50% of them have a recurrence within a year. Notably, the highest incidence of UTI in children is in the first year of life, and about 50% of them with a UTI have a structural abnormality of their urinary tract. This underscores the importance of imaging studies in the investigation of these children: a consideration which has been reflected in the various clinical practice guidelines.

American Academy of Pediatrics (AAP) Guidelines

In 1999, the American Academy of Pediatrics (AAP) published a clinical practice guideline on the diagnosis, treatment, and evaluation of initial urinary tract infections (UTIs) in febrile infants and young children along. Urinary tract imaging was recommended in a febrile infant or young child between the ages of 2 months and 2 years with a first documented UTI. The imaging studies typically consist of renal and bladder ultrasound (RBUS) and MCUG. The evidence supporting the use of MCUG for older children is however less convincing. Imaging is indicated if patients have known anatomic abnormalities, present with unusual uropathogens such as *Proteus* or mycobacterium tuberculosis, fail to improve with appropriate antimicrobial therapy within 48 hours, or have an unclear source of infection (atypical UTI). MCUG should be performed as soon as a child is infection-free and bladder irritability has resolved, since delaying the imaging study may be associated with loss to follow-up.

In 2011, AAP released a revision of its 1999 clinical practice guideline on UTIs in febrile infants and young children aged 2 months to 2 years. The new clinical practice guideline has several important updates based on evidence generated over the past decade. Specifically, RBUS is still recommended, but the most significant change in the current guideline is that routine MCUG is no longer recommended after the first UTI. The rationale for this paradigm shift is partly due to the radiation, cost, and considerable discomfort associated with this test. In addition, there has been a deviation from traditional protocols which use age alone to determine investigations after an episode of UTI to protocols which identify children for investigation who are at the most risk of renal parenchymal damage. Therefore in the revised AAP guideline, although MCUG should not be performed routinely after the first febrile UTI, it is indicated if RBUS reveals hydronephrosis, scarring, or other findings that suggest high-grade VUR or obstructive uropathy, and in other atypical or complex clinical circumstances. Further evaluation should be conducted if there is a recurrence of febrile UTI. Evaluation with MCUG identifies and helps to determine the severity of

VUR (grades 1 through 5). Despite the drawbacks earlier mentioned, the investigation has been recommended because results influence treatment decisions; infants and young children with VUR receive a long course of daily antibiotic prophylaxis, and those with high-grade VUR (grades 4 & 5) are candidates for surgical intervention

National Institute of Clinical Excellence (NICE) Guidelines

NICE guidelines-published in 2007- have remarkably changed clinical practice with respect to the diagnosis, clinical management and subsequent radiological investigation of the child with a UTI.

Current NICE guidelines recommend that different radiological investigations are performed according to:

- Whether there is good response to treatment within 48 hours
- Whether there is evidence of atypical UTI (seriously ill child; poor urine flow; abdominal or bladder mass; raised plasma creatinine level; septicaemia; non-response to treatment within 48 hours; non-E.coli UTI)
- Whether there is evidence of recurrent UTI (> 2 upper UTI; 1 upper and > 1 lower UTI; > 3 lower UTI)
- The age of the child

Thus, according to severity of UTI and age, NICE recommended guidelines are summarized in (Table 2, Table 3 and Table 4).

Table 2: Radiological investigations following UTI in infants under 6 months of age.

	Good response within 48 hours	Atypical UTI	Recurrent UTI
US at time of acute infection	No	Yes †	Yes
US within 6 weeks	Yes*	No	No
DMSA at 4-6 months	No	Yes	Yes
MCUG	No	Yes	Yes

*If abnormal consider MCUG once infection-free

†US at 6 weeks if non-E coli UTI, but responding well

Reproduced from: Pediatric Nephrology. In: Rees L, Brogan PA, Bockenhauer D, Webb NJA (Editors). Oxford Specialist Handbooks in Pediatrics, 2nd edition. Oxford University Press. 2012.

Table 3: Radiological investigations following UTI in children of 6 months to 3 years.

	Good response within 48 hours	Atypical UTI	Recurrent UTI
US at time of acute infection	No	Yes [†]	No
US within 6 weeks	No	No	Yes
DMSA at 4-6 months	No	Yes	Yes
MCUG	No	No [*]	No [*]

*MCUG if dilatation on US, poor urine flow, non E. coli UTI, family history of VUR

†US at 6 weeks if non E.coli UTI, but responding well

Reproduced from: Pediatric Nephrology. In: Rees L, Brogan PA, Bockenhauer D, Webb NJA (Editors). Oxford Specialist Handbooks in Pediatrics, 2nd edition. Oxford University Press. 2012.

Table 4: Radiological investigations following UTI in children over 3 years of age.

	Good response within 48 hours	Atypical UTI	Recurrent UTI
US at time of acute infection	No	Yes ^{††}	No
US within 6 weeks	No	No	Yes
DMSA at 4-6 months	No	No	Yes
MCUG	No	No	No

*US with full bladder (measure pre- and post-micturition volume)

†US at 6 weeks if non-E coli UTI, but responding well

Reproduced from: Pediatric Nephrology. In: Rees L, Brogan PA, Bockenhauer D, Webb NJA (Editors). Oxford Specialist Handbooks in Pediatrics, 2nd edition. Oxford University Press. 2012.

Key points on the radiological investigations recommended in the NICE protocol:

- The initial US will detect severe structural abnormalities and urinary obstruction, bladder wall thickness and emptying, as well as renal defects
- The DMSA scan is considered the gold standard investigation to identify renal parenchymal damage; should however be delayed until 4-6 months after the acute pyelonephritis in order to allow for resolution as well as avoid a false positive result from renal parenchymal inflammation
- The MCUG is considered the gold standard investigation for the diagnosis of urethral abnormalities and VUR

Follow-up guidelines proposed by NICE

a. For children with no further UTIs:

- Normal US requires no further follow-up
- US indicating unilateral defects requires yearly blood pressure checks for life

- US indicating bilateral defects requires yearly blood pressure checks, regular renal function tests and US assessment of renal growth
- b. For children with recurrent UTIs, radiological investigations are needed to determine the presence of new scars or continuing VUR:
 - Repeat US for renal size, presence of ureteric dilatation and bladder emptying
 - Ureteric dilatation and incomplete bladder emptying if present, DMSA scan and MCUG are required to establish any increase in renal defects with VUR

Other three clinical practice guidelines will be considered briefly, and a summary of the imaging recommendations from the five guidelines is displayed in (Table 5).

Italian Society of Pediatric Nephrologists (ISPN) Guideline

Published in 2011, the ISPN clinical practice guideline recommends US following first UTI; if positive and/or child has risk factors, MCUG is indicated. Late DMSA scan is indicated if US is positive and/or VUR is present

The Royal Children's Hospital of Melbourne (RCH) Guideline

This guideline was proposed in 2006 and also recommends US following UTI episode in infants; if US is positive and/or if boys < 6 months, MCUG is advocated.

Top down approach (TDA)

This is the only guideline which does not recommend initial US; it adopts a more 'aggressive' approach. Published in 2007, it suggests MCUG and late DMSA scan if there is evidence of positive acute DMSA scan.

Table 5: A Summary of the Imaging Recommendations from the 5 Clinical Practice Guidelines.

Guidelines	US	MCUG	Late DMSA scan
RCH	Yes	If boys < 6 months and/or positive US	No
NICE < 6 months	Yes	If positive US and/or atypical UTI ^a	If atypical UTI ^a
≥ 6 months	If atypical UTI ^a	If children with risk factors ^b	If atypical UTI ^a
TDA	No	If positive acute DMSA	If positive acute DMSA
AAP	Yes	If positive US	No
ISPN	Yes	If positive US/ or children with risk factors ^c	If positive US and/or VUR

^aSeriously ill, poor urine flow, abdominal or bladder mass raised creatinine, septicaemia, failure to respond to correct antibiotic treatment within 48 hours, or infection with non-E. coli organisms

^bDilatation on US, poor urine flow, non-E. coli infection or family history of VUR

^cAbnormal prenatal US of the urinary tract, family history of VUR, septicaemia, renal failure, age < 6 months in a male infant, likely non-compliance of the family, abnormal bladder emptying, no clinical response to correct antibiotic treatment within 72 hours, or non- E. coli infection

Reproduced from: La Scola C, De Mutiis C, Hewitt IK, et al. Different Guidelines for Imaging after first Urinary Tract Infection in febrile infants: Yield, Cost and Radiation. *Pediatrics*. 2013; 131: e665-e67.

CONCLUSION

Despite these proposed guidelines, there is no consensus regarding the optimal protocol for investigating a first febrile UTI. The reasons for this absence of consensus include the following: uncertainty about the long-term clinical significance of VUR and UTI-related renal scarring, the shift from recognizing renal damage as being due to UTI-related renal scarring to being more commonly congenital in nature, and the doubts cast on the efficacy of antibiotic prophylaxis after a febrile UTI by some recent studies. A recent study has actually established that there is no ideal diagnostic protocol following a first febrile UTI. For instance, it was reported that for the detection of VUR and renal scarring, the TDA showed the highest sensitivity but also the highest economic and radiation costs; NICE and AAP had the highest specificities for VUR; and ISPN had the highest specificity for scars. In addition, NICE would have been the least costly and AAP would have resulted in the least radiation exposure. Therefore, an ‘aggressive’ protocol may have a high sensitivity for detecting VUR and renal scarring but carries high financial and radiation costs with questionable benefit. Nonetheless, the management of every patient is individualized; and the clinician should apply the appropriate protocol that will best meet the peculiar circumstances and needs of the patient being investigated.

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