



# Critical appraisal of the top-down approach for vesicoureteral reflux

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Vesicoureteral reflux (VUR) has been linked to recurrent urinary tract infections (UTIs), renal scarring, hypertension, renal insufficiency and end-stage kidney disease. Different imaging strategies have been proposed to approach children presenting with UTI to sort out patients with significant VUR while minimizing patient morbidity, radiation exposure and financial burden. None of these imaging strategies is universally accepted. The “top-down approach” (TDA) aims at restricting the number of voiding cystourethrograms (VCUGs) and its associated morbidity while identifying patients with clinically-significant reflux. In this approach, children presenting with febrile UTIs are acutely investigated with dimercapto-succinic acid (DMSA) renal scans to identify patients with renal parenchymal inflammation. Those with evidence of renal affection are offered VCUG and late DMSA scan to identify VUR and permanent renal scarring, respectively. Although TDA could identify clinically-significant VUR with high sensitivity, it is not without limitations. The approach segregates patients based on the presence of DMSA cortical lesions omitting the morbidity and the economic burden of UTI. Additionally, some of DMSA lesions are attributed to congenital dysplasia and unrelated to UTI. Ionizing radiation exposure, financial costs, limited availability of DMSA scans in the acute setting, variability in interpreting the results and low yield of actionable findings on DMSA scans are some other limitations. In this review, we tried to address the drawbacks of the TDA and reinforce the value of patient-centered approach for VUR.

**Keywords:** Cost-benefit analysis; Ionizing radiation; Technetium Tc 99m dimercaptosuccinic acid; Urinary tract infections; Vesicoureteral reflux

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## INTRODUCTION

Undoubtedly, not all patients with vesicoureteral reflux (VUR) are identical. Some patients have no sequelae from VUR while others suffer recurrent urinary tract infections (UTIs) and a minority may develop renal scars. This leads us to the fact that VUR is a multidimensional disease with more hues than we can see on a voiding cystourethrogram (VCUG). Patient gender, reflux grade, laterality, bowel and

bladder dysfunction, perineal hygiene, clinical presentation (antenatally diagnosed vs. symptomatic UTI) and circumcision status are some of the factors that significantly alter the natural history of the disease and the individual risk for UTI, parenchymal scarring and renal insufficiency [1-5]. These individual and reflux characteristics should be always considered in the equation when treating a child with VUR. Treatment plan should be guided by the risk of future UTIs or renal scarring rather than merely the presence or absence

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of reflux.

Traditionally, it was mistakenly believed that every reflux should be identified and promptly treated to prevent UTI and minimize the risk of renal damage. As our understanding of the interplay of VUR, UTI and renal scarring evolved over the past few decades, this traditional approach has been gradually replaced by a more individualized approach for VUR. Patients at low-risk of renal damage and recurrent UTIs can be now managed expectantly, while antibiotic prophylaxis and surgical correction should be offered to the high-risk population [36]. This paradigm shift in the management of VUR was paralleled by a similar shift of the imaging algorithms. Identifying the population at-risk of recurrent infections and renal damage, rather than simply detecting VUR, is now the primary goal of modern radiologic workup for children presenting with UTI. Different imaging strategies have been proposed to identify patients with clinically-significant VUR while minimizing radiation exposure, invasive testing, patient discomfort, parental distress and financial burden for those who are less likely to suffer VUR consequences. Three imaging strategies are commonly in use: the National Institute for Health and Care Excellence (NICE) [7], the bottom-up (the American Academy of Pediatrics guidelines) [8] and the top-down approach (TDA) [9] (Table 1). The ideal imaging strategy is the one that can define clinically significant anomalies that would alter management and eventually improve outcomes. None of these protocols is universally accepted.

## THE TOP-DOWN APPROACH

VCUG remains the gold standard tool to identify VUR. However, the test is usually a traumatic experience

to both patients and their families due to the need for catheterization. Additionally, it carries a risk of introducing infection into the urinary tract [10]. More importantly, it identifies a population with clinically-insignificant VUR that may never come to clinical attention leading to potential overtreatment. Therefore, the "top-down" approach was advocated to overcome the aforementioned flaws of VCUG. The approach was based on the assumption that VUR becomes clinically significant only if it results in renal injury. In this approach, children presenting with febrile UTI (FUTI) are acutely investigated with a 99mTc-labeled dimercapto-succinic acid (DMSA) scan at the outset to diagnose renal parenchymal involvement. Patients who demonstrate photon defects representative of parenchymal inflammation are later investigated with a VCUG to assess for reflux and a late DMSA (6–12 months) to evaluate for permanent scarring [11].

Hansson et al. [12] retrospectively reviewed 303 with initial UTI who were investigated with VCUG and DMSA within 3 months after UTI. In this study, abnormal DMSA scans were strongly associated with high-grade VUR ( $p \leq 0.001$ ). Although 7 patients had dilating VUR despite normal initial DMSA, none of them had recurrent UTI. Five of them had spontaneous VUR resolution, while reflux was down-graded to grade I in 2 of them. Herz et al. [13] prospectively evaluated 121 children presenting with FUTI with renal/bladder ultrasound, VCUG, acute and delayed DMSA scans. Overall, 6% had abnormal renal ultrasounds, 64% had VUR and 73% were diagnosed with pyelonephritis on initial DMSA scans. Of 88 patients with abnormal acute DMSA scan, 44 (50%) had dilating VUR. In this study, abnormal initial DMSA scan could predict clinically significant reflux (odds ratio, 35.4). Among 32 patients (26.5%) who developed subsequent UTI, 85% had

**Table 1.** Imaging guideline for children with FUTI

Guideline	Age	Imaging recommendation	Reference
AAP 1999	2–24 Months	Prompt RBUS and either VCUG or radionuclide scan after the first UTI	[34]
AAP 2011	2–24 Months	RBUS during the first 2 days of FUTI. VCUG if RBUS demonstrates hydronephrosis, scarring, high grade VUR, obstructive uropathy or after the 2nd FUTI. DMSA: not routinely recommended.	[8]
NICE 2007		RBUS: <6 months or atypical UTI. VCUG if positive ultrasound or atypical UTI DMSA (4–6 months): atypical UTI	[7]
TDA 2007		Acute DMSA to identify patients with renal parenchymal affection. VCUG and late DMSA (6–12 months) for patients with abnormalities on acute DMSA scan.	[11]

FUTI, febrile urinary tract infection; AAP, American Academy of Pediatrics; RBUS, renal bladder ultrasound; VCUG, voiding cysto-urethrogram; DMSA, dimercapto-succinic acid renal scan; NICE, National Institute of Health and Care Excellence; UTI, urinary tract infection; TDA, top-down approach; VUR, vesicoureteral reflux.

an abnormal initial scan. In another study of 523 children  $\leq 2$  years presenting with FUT1, 178 (34%) had VUR and 397 (75.9%) had abnormal acute DMSA. Among 151 patients with dilating VUR, 149 (98.7%) had abnormal acute-phase renal scans yielding a sensitivity of 96.15% and a positive predictive value (PPV) of 34%. Overall, 46 patients (8.8%) had scars on delayed DMSA scans [14]. It can be gleaned from these studies and some others that DMSA can be used as an effective screening tool to identify patients who are likely to have dilating VUR and UTI recurrence.

However, the results of these studies should be interpreted with caution. Although 51%–73% of patients would depict evidence of parenchymal affection on acute-phase DMSA scans after a single UTI, only 9.5%–11.9% would develop renal scars on late DMSA scans [2,15,16]. Moreover, the association between renal scarring on one end and the development of hypertension, renal insufficiency and end-stage renal disease on the other was based on outdated studies conducted several decades ago. These studies used intravenous urography which is certainly less sensitive than  $^{99m}\text{Tc}$ -labeled DMSA scans for identification of renal scars and has definitely identified only patients with extensive renal damage [17]. Conversely, most of the developed renal scars detected on today's renal scans are small, especially with timely institution of antimicrobial therapy [16]. The long-term implications of small scars detected by DMSA renal scans are not well studied.

Furthermore, the etiology and significance of scars noted on DMSA scans as well as their relation to the absence or presence of VUR are contentious. On their review of 303 children presenting after their initial UTI, Hansson et al. [12] reported that 46% of their patients with signs of parenchymal affection on DMSA had no demonstrable reflux on VCUG. Some patients may manifest parenchymal defects on DMSA scans without experiencing a previous UTI. These defects may be attributed to congenital dysplasia rather than renal damage from infection or

reflux. Discrimination between congenital and acquired parenchymal defects cannot be solely made based on DMSA findings. History of prior UTI and the presence or absence of cortical lesions on previous scans is critical to distinguish between both [18]. Failure of DMSA to differentiate parenchymal defects caused by congenital dysplasia and acquired renal scars may eventually lead to overtreatment in a subset of patients with static congenital renal lesions who are unlikely to encounter subsequent UTIs and/or parenchymal damage. Moreover, some reports have depicted resolution of some of the cortical lesions observed on DMSA scans with further follow-up [19,20].

Although TDA could detect clinically-significant VUR with a sensitivity of 85%–96% [13,14,21,22], the low specificity and modest PPV of TDA does not justify the prohibitive cost and the unnecessary ionizing radiation exposure to all children after febrile UTIs should the TDA be universally adopted. Bearing in mind that 85% of children with symptomatic or febrile UTI will never experience UTI recurrence [23], only 15% would benefit from further testing and possible treatment. Interestingly, a significant number of patients with significant VUR would be missed if the TDA was used. In the study of Herz et al. [13], 16 of 78 patients (20.5%) with VUR had normal acute-phase DMSA scan. Of them, 14 (78.5%) had grade III VUR. The authors, however, argue that the majority of this cohort remained asymptomatic off antibiotic prophylaxis and their reflux eventually resolved. Surgical intervention was required in 1 patient who received Deflux injection. Hansson et al. [12], found that 24% (7 of 29) of patients with dilating VUR had normal DMSA scans. Among 108 patients with UTI enrolled in another study, 13% of renal units with grades 1–3 and 50% of those with grade 4–5 VUR had normal DMSA scans [24]. Table 2 demonstrates the correlation between acute DMSA findings and the presence or absence of VUR. Finally, most of the studies advocating the TDA did not address the long-term implications of DMSA lesions on renal

**Table 2.** The correlation between acute DMSA scan findings and the presence or absence of VUR

Study	Normal DMSA				Abnormal DMSA			
	Total	No VUR	VUR 1–2	VUR 3–5	Total	No VUR	VUR 1–2	VUR 3–5
Hoberman [15] 2003	119/309 (39)	N/A	N/A	N/A	190/309 (61)	N/A	N/A	N/A
Hansson [12] 2004	147 (49)	120 (81.6)	20 (13.6)	7 (4.8)	156/303 (51)	103 (66)	24 (15.4)	29 (18.6)
Preda [43] 2007	141/290 (49)	133 (94.3)	7 (5)	1 (0.7)	149/290 (51)	105 (70.5)	18 (12.1)	26 (17.4)
La Scola [22] 2013	144/304 (47.4)	128 (89)	15 (8.3)	4 (2.8)	160/304 (52.6)	113 (70.6)	25 (15.6)	22 (13.8)
Sheu [44] 2013	191/473 (40.4)	162 (84.8)	25 (13.1)	4 (2.1)	282/473 (59.6)	158 (56)	33 (11.7)	91 (32.3)
Zhang [14] 2014	126 (24.1)	112 (88.9)	12 (9.5)	2 (1.6)	397/523 (75.9)	233 (58.7)	15 (3.8)	149 (37.5)

Values are presented as number (%).

DMSA, dimercapto-succinic acid; N/A, not available; VUR, vesicoureteral reflux.

health or management algorithm. In a study by Merguerian et al. [25], DMSA findings failed to alter the treatment plan in 96.5% with abnormal scans.

## PREVENTION OF UTI RECURRENCE IS THE ULTIMATE GOAL OF VUR MANAGEMENT

UTI is a serious common health problem with serious health consequences and a significant financial burden. It has been estimated that 2.6%–3.4% of children in the United States develop UTI annually. Of them, 2%–3% require hospitalization with costs exceeding US \$180 million every year, not mention the cost of diagnostic studies, outpatient care, emergency room visits and the indirect cost of parental work absenteeism [26]. Therefore, the morbidity of UTI and the associated financial burden should never be overlooked when treating children with UTI and/or VUR. In addition, early treatment of UTI would minimize the risk of renal scarring substantially [16,27,28].

Therefore, treating patients with recurrent UTIs and/or VUR based solely on the presence or absence of renal scars is one of the major drawbacks of the TDA. Children with recurrent FUTIs with/without VUR should not only be treated for fear of hypertension, chronic renal insufficiency or end-stage kidney disease, but also to prevent the morbidity of a serious acute illness that may be complicated with sepsis, liable to recurrence and associated with significant economic burden [29]. Children with VUR approached in the TDA are stratified according to the presence of renal scars, regardless of their risk of UTI recurrence. However, reduction of the acute morbidity of pyelonephritis is as equally important as prevention of renal scarring. In a prospective observational study by Snodgrass et al. [30] in which 565 consecutive children were referred for UTI and/or VUR, all patients underwent DMSA scans 3 or more months after FUTI. Interestingly, 43% of patients with grade IV or V reflux had no identifiable renal scarring. Similarly, among 40.9% of patients with recurrent FUTIs, 76% had normal DMSA scans. Should the TDA be implemented, this patient cohort would be labeled as low-risk despite UTI recurrence and the resulting morbidity.

As previously mentioned, focal DMSA defects may be the result of congenital dysplasia, rather UTI or VUR [18,31]. Even with recurrent FUTI, the overall risk of renal scarring is low [30,32]. Therefore, treatment algorithm should be centered on the prevention of UTI-related morbidity. Clinicians and care givers should work side by side to expeditiously diagnose and properly treat UTI. Further, the underlying risk factors should be proactively addressed to

prevent UTI recurrence, rather than simply awaiting for the development of renal scars.

## WHAT IS THE BEST INITIAL IMAGING STUDY AFTER THE FIRST FUTI: ULTRASOUND, VCUG OR DMSA?

Although ultrasonography is widely-available, noninvasive testing without risk of radiation exposure that can effectively detect upper tract dilatation, it has limited sensitivity for detection of VUR and parenchymal scarring. Up to 60% of reflux and 50% of renal scars detected on DMSA are missed by sonography [18]. In a prospective study by Hoberman et al. [15], ultrasound was normal in 85% of patients with grade III and 40% of those with grade IV VUR presenting after the first FUTI. Overall, initial treatment was not altered in any of the 12% with abnormal ultrasounds based on sonographic findings. The authors concluded that the probability that ultrasound would reveal clinically important findings that would modify management is less than 1% [15]. In another study, 24% of patients with a normal ultrasound after the first FUTI had a dilating VUR [33]. Similarly, Bush et al. [34] reported poor sensitivity (34%) and limited positive predictive value (47%) of renal ultrasound to identify renal damage after FUTIs. Of 512 patients with normal renal bladder ultrasound (RBUS) enrolled in their study, 19% had renal abnormalities on DMSA. VUR was identified in 76% of them [34]. In agreement with the previous studies, ultrasound was found to be less sensitive and specific than DMSA-single-photon emission computed tomography (CT), gadolinium-enhanced magnetic resonance imaging and spiral CT for diagnosing pyelonephritis in an animal study using histopathologic examination as the standard of reference [35].

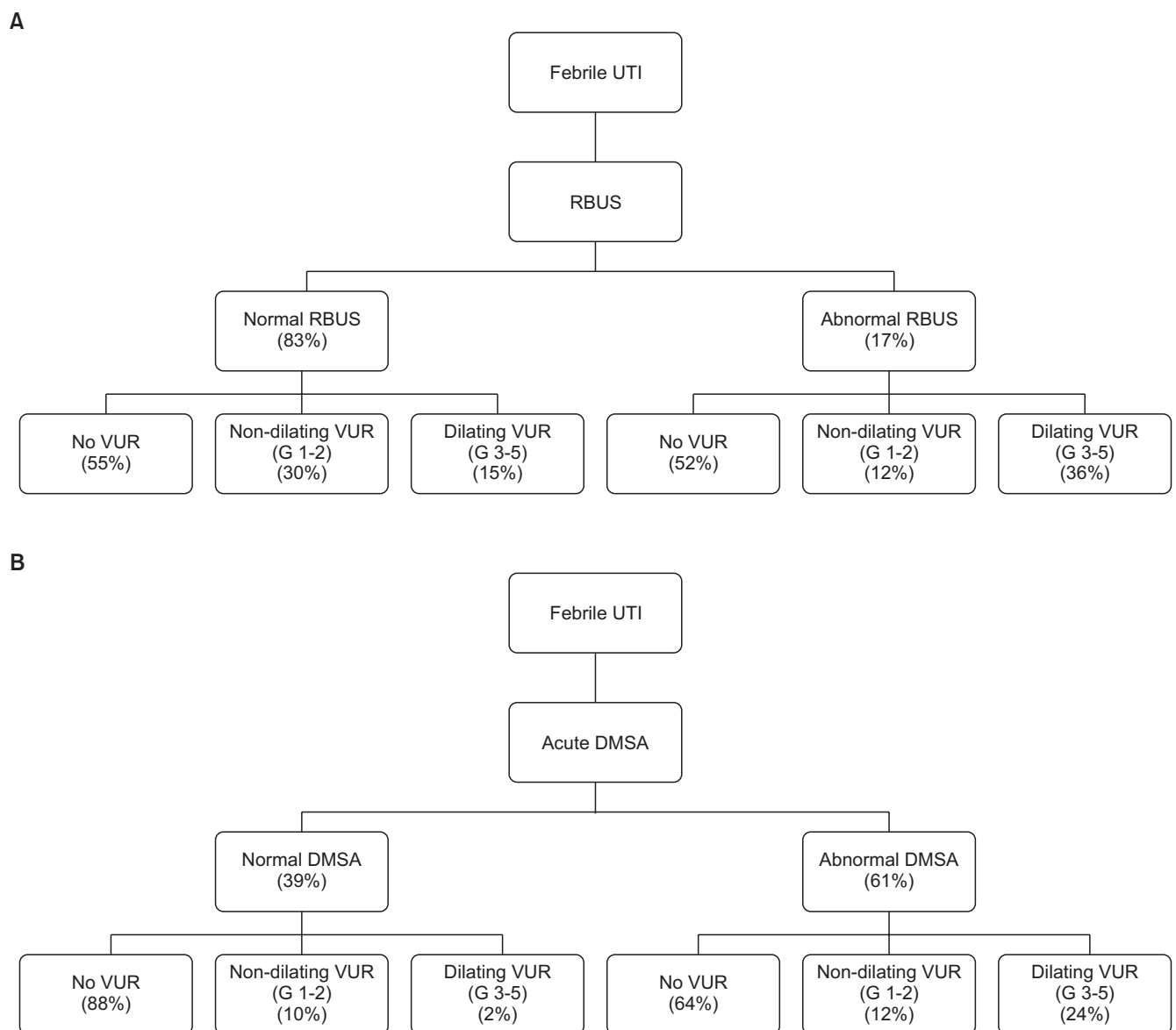
More recent studies have reported improved diagnostic capacity of ultrasound in identifying renal involvement in children following acute UTI. Using a combination of gray-scale ultrasound and amplitude-coded color Doppler, ultrasound could reliably diagnose renal affection secondary to UTI with a sensitivity of 92.1% using DMSA as the reference standard in a study by Brader et al. [9]. Similarly, renal scars were diagnosed using Doppler ultrasound with a sensitivity of 70% in a study by Mohammadjafari et al. [36]. Conversely, the utility of Doppler ultrasound in detecting renal scarring in children following UTI was debated in a study by Narchi including 23 patients [37].

Despite the fact that ultrasound has limited sensitivity in detecting VUR or renal scars, the seriousness of urinary tract abnormalities detected on RBUS (obstructive uropathy,

hydronephrosis, pyonephrosis, hydroureter, duplication anomalies, renal scars, asymmetric renal size, bladder wall thickening, ... etc.) and the absence of physical harm justify routine ultrasound during acute pyelonephritis [8]. Although DMSA is unquestionably the most sensitive imaging study for detection of renal scars, most of the aforementioned studies comparing RBUS to DMSA did not address the clinical significance of VUR or the rate of UTI recurrence in patients with DMSA abnormalities. Additionally, the low prevalence of scintigraphic abnormalities that would affect treatment decision speaks against the routine use of DMSA when evaluating children with UTI. Furthermore, most of clinically-important scintigraphic abnormalities are readily

identified on RBUS. In a 1999 retrospective review of 386 patients with VUR, Merguerian et al. [25] assessed the utility of ultrasound in detecting renal scars diagnosed on DMSA scans. Despite the poor correlation between ultrasound and DMSA in patients with focal scarring, ultrasound correlated well with DMSA scan in all patients with diffuse scarring. DMSA results altered the treatment plan in only 3.5% of patients. All of them had gross abnormalities on ultrasound [25]. These results question the value of DMSA findings in clinical decision-making. Fig. 1 illustrates the prevalence of VUR in children presenting with FUTI based on ultrasound and DMSA findings.

Radiologic evaluation of children with UTI should be



**Fig. 1.** (A) The prevalence of vesicoureteral reflux (VUR) based on ultrasound findings in children presenting with febrile urinary tract infection (UTI) [13,15,22,33,34,45]. (B) The prevalence of VUR based on acute dimercapto-succinic acid (DMSA) findings in children presenting with febrile UTI [12-14,22,43,44]. RBUS, renal bladder ultrasound.

rationally tailored based on the anticipated frequency of radiographic abnormalities, their clinical relevance and impact on decision-making. Historically, prompt RBUS and VCUG were routinely offered to infants after the first FUTI according to the 1999 American Academy of Pediatrics (AAP) guidelines [38]. Given the low-risk of UTI recurrence and the uncertainty about the value of antibiotic prophylaxis, the 2011 guidelines revisions reserved VCUGs for patients with ultrasound abnormalities, atypical clinical course or UTI recurrence [8]. These revisions have limited unnecessary testing in approximately 85% of patients who would never experience a second UTI [33]. Alike, performing DMSA scans routinely after the first FUTI would unnecessarily expose 90% of patients who would not develop renal scars to ionizing radiation during a lengthy costly test without substantial clinical benefit.

In summary, DMSA can accurately detect renal parenchymal affection. Only 60% of children presenting with FUTI would, however, demonstrate evidence of renal inflammation on acute DMSA. Of them, 64% will have normal VCUGs and 12% will have low-grade VUR (Fig. 1B). Moreover, DMSA findings are unlikely to alter treatment decision in many clinical scenarios. For instance, children diagnosed with VUR who remain UTI-free and exhibit interval renal growth on follow-up renal ultrasounds can be safely observed even in the setting of DMSA defects. In contrast, those who suffer breakthrough UTIs should be aggressively treated with risk factor modification, antibiotic prophylaxis, endoscopic injection or ureteral reimplantation.

On the other hand, although the yield of actionable findings on RBUS after the first FUTI is low (1%–2%) [15], patients with sonographic abnormalities usually have serious pathology and may benefit from immediate intervention or further imaging. Ultrasound undeniably has limited sensitivity in diagnosing VUR, particularly low-grade. Nevertheless, high-grade VUR is relatively uncommon after the first FUTI. After the first febrile UTI, 15% would have dilating VUR, 5% would have grade IV and only 1% would have grade V VUR [8,15]. Additionally, patients with high-grade VUR are more likely to demonstrate abnormal ultrasound findings that would warrant VCUG. More importantly, the low risk of renal damage after the first UTI [39] coupled with the wide availability and safety of ultrasound would justify routine ultrasound evaluation after the first UTI. VCUG can be reserved for patients with abnormal ultrasound findings or UTI recurrence without substantial harm, particularly with lack of strong evidence supporting the routine use of antibiotic prophylaxis [1].

## ACUTE VERSUS DELAYED SCANS

The question whether to use acute or late DMSA scans to sort out patients for VCUG was deliberately answered by previous studies. In a study by Herz et al. [13], acute phase DMSA scans correctly predicted clinically-significant reflux with a sensitivity of 95.7% and a specificity of 71.9% compared to 27.5% and 76.9% respectively on late scans. Subsequently, relying on delayed DMSA scans to sort out patients for VCUG will result in missing a significant portion of patients with VUR. Further, treatment would be delayed for at least 6 months with risk of UTI recurrence. Not surprisingly, relying on acute phase DMSA scans to sort out patients for VCUG would expose a large number of children unnecessarily to VCUG and late DMSA scans. Overall, only 10% would develop renal scarring after the first episode of pyelonephritis and 85% will never encounter a second episode [2,15,16].

Patients in the TDA approach are ideally investigated with acute DMSA scan within 1 week of the symptom onset. Those who depict evidence of parenchymal affection on acute scans are addressed with management of the underlying bowel and bladder dysfunction. VCUG is performed within 1 month of acute illness in patients with DMSA abnormalities to diagnose VUR. Late DMSA scans are obtained at 6–12 months to diagnose permanent renal scars. Some authors adopted a modified approach. This approach entails an acute RBUS and delayed DMSA after FUTI, reserving VCUG for patients with abnormal DMSA, RBUS and/or recurrent FUTI [34]. Patients diagnosed with VUR should be managed according the risk-stratified approach.

## RADIATION EXPOSURE

Significant exposure to ionizing radiation is another sensible criticism for the TDA. Hazards of radiation exposure including gonadal damage and secondary malignant neoplasms have been well identified, particularly in the pediatric population. These hazards should be taken particularly into account in children who would require repeated radiologic evaluation. DMSA carries a 5–10 fold higher radiation dose than pulsed fluoroscopy, which is now the standard for VCUG exams in most centers [13,40]. In their comparison of five imaging guidelines for children presenting with UTI, La Scola et al. [22] found that the TDA conferred the highest radiation exposure (624 mSv) while the AAP guidelines resulted in the least radiation exposure (42 mSv). Of note, a reliable comparison cannot

be made between the diffuse radiation exposure in DMSA scans and the localized exposure in VCUG. In addition, renal scans entail radiation exposure to the renal parenchyma which is relatively radio-resistant compared to the radio-sensitive gonads during VCUG. Gonadal dosimetry is lower for continuous fluoroscopic cystography (effective dose, 0.45 mSv) when compared with DMSA renal scans (effective dose, 1.8 mSv; ovary, 85 mrad; testis 45 mrad) [18].

## ECONOMIC BURDEN

In a study comparing 5 different guidelines for urinary tract imaging in 304 children after their first FUTI, the TDA had the highest sensitivity for detection of all VUR grade 76% vs. 27% and 29% when employing the AAP and NICE guidelines, respectively. However, the TDA had a limited specificity of only 54% relative to 90% and 91% for the AAP and NICE guidelines, respectively. Similarly, the TDA had the highest sensitivity (85%) for the detection of grades III–IV reflux with a low specificity of 50%. In comparison, both NICE and AAP had lower sensitivities of 50% and 38% and higher specificity of 90% and 88%, respectively. The TDA conferred the highest radiation exposure (15 times higher than AAP) and the highest financial burden (€172/patient compared to €88 and €94/patient for NICE and AAP, respectively) [22].

In their review of the TDA, Pohl and Belman [18] estimated the cost needed for the diagnosis of one case of VUR as US \$2,630–3,033 when the TDA is used and US \$3,368–8,420 when using the bottom-up approach. Though, the real question should be "what is the cost of detecting clinically-significant reflux that could incite recurrent infections or cause potential renal damage?" or "what is the cost of radiologic workup needed to prevent one UTI?" Assuming a 10% prevalence of renal cortical abnormalities on DMSA after the first FUTI and that 14 patients need to be treated to prevent one febrile/symptomatic UTI while on trimethoprim-sulfamethoxazole prophylaxis, Tasian [41] assumed that 275 children would need to undergo DMSA and VCUG to prevent one UTI recurrence if only children with VUR were treated with antibiotic prophylaxis.

## OTHER LIMITATIONS

The availability of the DMSA scans and inconsistency in interpretation of its results are among the limitation for this approach. Among patients enrolled in the Randomized Intervention for Children with Vesicoureteral Reflux trial, 17% of DMSA scans were considered not interpretable

[42]. Besides, the radio-active isotope needed for the scan is not always readily available. In addition, the test is time-consuming and requires an intravenous access which may not be favored by some families. Many centers require sedation for renal scans particularly for young patients. Additionally, the approach may not be universally applicable due to resource allocation concerns. The ability to perform an urgent DMSA scan during the acute phase may not be achievable in the real clinical world, given the limited availability of nuclear medicine renal scans.

## CONCLUSIONS

VUR is a heterogeneous disease. Patient's factors, reflux characteristics and bacterial genetics significantly determine the clinical course of the disease. Thus, treatment should be dynamic and stratified based on the risk of UTI recurrence, parenchymal scarring, renal insufficiency and end-stage kidney disease. Different imaging strategies have been proposed to screen children presenting with UTI and identify patients at risk for VUR sequelae. None of these strategies is optimal. Although the TDA approach can decrease the number of VCUGs and detect VUR with a sensitivity of more than 95%, the majority of patients would have low-grade reflux clinically-insignificant reflux. Moreover, patients are stratified based on the risk of renal scarring omitting UTI recurrence and the associated substantial patients' morbidity and enormous economic burden. Limited DMSA scan availability in the acute setting, radiation exposure, higher cost and delay in treatment initiation are some other critical limitation of the TDA. Finally, DMSA findings rarely, if ever, alter the management of patients with UTIs.

The combined efforts of health care providers and families should be directed towards early and reliable identification of UTI, early institution of effective treatment and addressing bowel and bladder dysfunction and other risk factors as a part of the risk-stratified approach for VUR. These measures would lower the risk of renal scarring and minimize the chances of UTI recurrence.

## CONFLICTS OF INTEREST

The authors have nothing to disclose.

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