ARTICLE

Impact of a More Restrictive Approach to Urinary Tract Imaging After Febrile Urinary Tract Infection

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Objectives: To determine the impact of using an algorithm requiring selective rather than routine urinary tract imaging following a first febrile urinary tract infection (UTI) on imaging use, detection of vesicoureteral reflux (VUR), prophylactic antibiotic use, and UTI recurrence within 6 months.

Design: Retrospective review comparing outcomes during periods before algorithm use (September 1, 2006, to August 31, 2007) and after algorithm use (September 1, 2008, to August 31, 2009). The new algorithm, which adapted recommendations from the United Kingdom's National Institute for Health and Clinical Excellence 2007 guidelines, was implemented in 2008. The algorithm calls for renal ultrasonography in most cases and restricts voiding cystourethrography for use in patients with certain risk factors.

Setting: County health system.

Participants: Children younger than 2 years with a first febrile UTI.

Intervention: Selective algorithm for urinary tract imaging.

Main Outcome Measures: Urinary tract imaging use, detection of VUR, prophylactic antibiotic use, and UTI recurrence within 6 months.

Results: After introduction of the new algorithm, voiding cystourethrography and prophylactic antibiotic use decreased markedly. Rates of UTI recurrence within 6 months and detection of grades 4 and 5 VUR did not change, but detection of grades 1 to 3 VUR decreased substantially. Patients in the prealgorithm group with grades 1 to 3 VUR who would have been missed with selective screening underwent no interventions other than successive urinary tract imaging and prophylactic antibiotic use.

Conclusions: By restricting urinary tract imaging after an initial febrile UTI, rates of voiding cystourethrography and prophylactic antibiotic use decreased substantially without increasing the risk of UTI recurrence within 6 months and without an apparent decrease in detection of high-grade VUR. Clinicians can be more judicious in their use of urinary tract imaging.

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Given the high prevalence of vesicoureteral reflux (VUR) and other genitourinary abnormalities in infants and children with febrile urinary tract infection (UTI), the 1999 American Academy of Pediatrics UTI practice parameter[1] recommends renal ultrasonography (US) and voiding cystourethrography (VCUG) in all children with a first-time febrile UTI. The guideline further recommends daily antibiotic prophylaxis after UTI treatment until imaging studies are completed and the results are normal. However, recent studies and reviews have questioned the need for routine imaging, especially VCUG,[2-10] and the use of antibiotic prophylaxis remains controversial.[11-14]

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In 2007, the United Kingdom's National Institute for Health and Clinical Excellence (NICE)[15] published new guidelines for the management of UTI in children, which recommend more selective use of renal US and VCUG based on age and other risk factors. In May 2008, our group adapted the NICE guidelines for use in our medical system (**Figure**). The objective of this study was to assess the impact of the new guidelines on imaging use (renal US and VCUG), detection of VUR,

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Imaging After UTI or Pyelonephritis

Study	Responds well to Rx by 48 h Not atypical or recurrent UTI	Atypical UTI	History of prior UTI
Age ≤6 mo			
US acutely	No	Yes	Yes
US within 6 wk	Yes	No	No
VCUG	Only if US is abnormal, atypical UTI, or history of prior UTI		
Age >6 mo but <3 y			
US acutely	No	Yes	No
US within 6 wk	No	No	Yes
VCUG	Only if US is abnormal, poor urine flow, non–*Escherichia coli* infection, or family history of reflux		
Age ≥3 y			
US acutely	No	Yes	No
US within 6 wk	No	No	Yes
VCUG	Only if US is abnormal		

Atypical UTI	Abnormal US	Antibotic Prophylaxis
Sepsis or bacteremia	Dilation of kidney(s) or ureter(s)	While prophylaxis is generally no longer considered indicated for low-level reflux, it may be useful for high-level reflux, recurrent UTI, or significant urologic anomalies. Contact nephrology or urology for patients with grade 3 reflux or higher or US showing anomalies to discuss whether prophylaxis and/or specialty referral is warranted.
Poor urine flow	Renal size discrepancy >5 mm in longitudinal direction	
Abdominal or pelvic mass	Anomalous, cystic, or single kidney	
Elevated creatinine level		
Failure to respond within 48 h		
Infection with non–*Escherichia coli* organism		

Figure. Santa Clara Valley Medical Center guidelines for imaging after urinary tract infection (UTI) or pyelonephritis based on the United Kingdom's National Institute for Health and Clinical Excellence (NICE)[15] 2007 guidelines. US indicates ultrasonography; VCUG, voiding cystourethrography.

prophylactic antibiotic use, and UTI recurrence within 6 months. We focused on children younger than 2 years, who represent the upper age limit cutoff for the American Academy of Pediatrics' UTI practice parameter.

METHODS

ALGORITHM DEVELOPMENT AND IMPLEMENTATION

A multidisciplinary group at our institution in radiology, primary care pediatrics, pediatric nephrology, pediatric urology, and pediatric critical care and hospital medicine developed an algorithm by adapting the NICE[15] guidelines. The algorithm calls for renal US in most cases and more selective use of VCUG based on the following risk factors according to the NICE guidelines: bacteremia with the UTI, inadequate clinical response of the UTI to antibiotic treatment within 48 hours, non–*Escherichia coli* pathogen, poor urine flow, elevated serum creatinine level, palpable abdominal or pelvic mass, or abnormal renal US findings. Routine prophylactic antibiotic use was discouraged.

The concepts supporting the algorithm were introduced to departmental faculty and pediatric house staff during a grand rounds presentation on UTI, and the algorithm was presented during a subsequent departmental faculty meeting. Copies were e-mailed to each individual faculty member, and sheets displaying the algorithm were posted in all clinics and on the pediatric ward. In addition, radiologists were asked to remind health care practitioners of the guidelines when VCUG was ordered. The pediatric faculty members were asked but not required to follow the guidelines.

SETTING

Santa Clara Valley Medical Center is the county hospital and clinic system for San Jose, California, and surrounding communities. The pediatric department includes more than 100 physicians providing primary care (to >40 000 children), urgent care, and comprehensive subspecialty pediatric services at 6 clinics throughout Santa Clara County. The tertiary hospital includes a nursery and neonatal intensive care unit with approximately 5000 births per year, an emergency department, and a pediatric ward and pediatric intensive care unit. Urine cultures obtained anywhere within our system are sent to a central laboratory at the hospital. The institutional review board at Santa Clara Valley Medical Center approved this investigation.

DATA COLLECTION

Two periods were defined, September 1, 2006, to August 31, 2007 (before algorithm use), and September 1, 2008, to August 31, 2009 (after algorithm use), which allowed for a 4-month "run in" period after the introduction of the algorithm. The microbiology database was queried to identify children younger than 2 years with UTI during the specified periods. Urinary tract infection was defined by urine cultures containing at least 50 000 colony-forming units (CFU) per milliliter of a pathogenic organism for specimens obtained by urethral catheterization and at least 100 000 CFU/mL for specimens obtained by bag or clean catch. Medical records (electronic and paper) were then reviewed for each patient, and the presence or history of fever (≥38°C) was confirmed. Urinary tract infection recurrence was defined as a second UTI within 6 months of the first one. The blood culture was considered positive if it contained the same pathogenic organism that caused the UTI.

Individuals were excluded for the following reasons: (1) he or she had a prior UTI, (2) the health care practitioner did not consider the urine culture results to represent UTI (ie, multiple organisms were present), (3) he or she had known genitourinary abnormalities at the time of UTI diagnosis, (4) he or she had an underlying neuromuscular disease or chronic condition predisposing to UTI, (5) he or she had a nosocomial infection (eg, from a Foley catheter), or (6) the patient's only encounter with the county system was in the emergency department (no follow-up data were available on these patients).

STATISTICAL ANALYSIS

All calculations were performed using commercially available software (STATA 7.0; StataCorp LP, College Station, Texas). Proportions were compared using χ^2 analysis, and continuous variables were compared using the *t* test. Adherence to the guidelines was defined by the sum of the number of imaging tests that were ordered and obtained plus the number of imaging tests that were not ordered and not obtained divided by the total number of patients.

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RESULTS

For the prealgorithm period, 132 patients with positive urine cultures were identified. Ninety-eight patients were included in the analysis, and 34 patients were excluded (11 had preexisting conditions that predisposed to UTI, 10 had only 1 encounter in the county system, 5 had previous UTI, 4 were not considered to have UTI, and 4 had UTI that was nosocomial). For the postalgorithm period, 132 patients with positive urine cultures were identified. One hundred three patients were included in the analysis, and 29 patients were excluded (10 had previous UTI, 7 had preexisting conditions that predisposed to UTI, 6 had only 1 encounter in the county system, 3 were not considered to have UTI, and 3 had UTI that was nosocomial).

Clinical characteristics were similar between groups (**Table 1**), although there were significantly more positive blood cultures in the postalgorithm group. Ultrasonography, VCUG, and prophylactic antibiotic use decreased substantially in the postalgorithm period (**Table 2**) without an increase in UTI recurrence within 6 months. If patients with multiple organisms in the index UTI are excluded from the analysis, there is still no difference in rates of UTI recurrence within 6 months between groups (6.9% in the prealgorithm group vs 9.0% in the postalgorithm group, $P=.64$).

Similar numbers of cases of high-grade VUR were detected in the prealgorithm period (2 patients with grade 4 VUR) and the postalgorithm period (2 patients with grade 4 VUR and 1 patient with grade 5 VUR), but no cases of low-grade VUR (grades 1-3) were detected initially in the postalgorithm period compared with 19 cases in the prealgorithm period. The overall sensitivity of US for detecting any abnormality in patients with VUR was low: only 9 of 24 US findings (37.5%) were abnormal. The one patient with grade 5 VUR had abnormal US findings, and 2 of 4 patients with grade 4 VUR had abnormal US findings.

During the prealgorithm period, practitioners adhered strictly to the American Academy of Pediatrics[1] guidelines: 97 of 98 children (99.0%) underwent renal US and VCUG. After implementation of the new algorithm, adherence was fair (79.6% for renal US and 92.2% for VCUG) (**Table 3**). Renal US and VCUG tended to be underordered in children 6 months or younger, while renal US was overordered in children older than 6 months.

Only 1 patient who should have undergone VCUG following the first UTI because of bacteremia had UTI recurrence within 6 months. This UTI prompted performance of VCUG, which demonstrated grade 3 VUR of the right ureter. The patient's family opted against prophylactic antibiotic use, and during the next 2 years the patient had 3 urine cultures obtained during febrile illnesses but no documented UTI. Follow-up VCUG was scheduled.

Eight patients in the postalgorithm group had UTI recurrence within 6 months, and all were febrile UTI. Five of 8 underwent US with the initial UTI (3 with normal

Table 1. Characteristics of Patients With Febrile Urinary Tract Infection (UTI)

Variable	Prealgorithm Group (n=98)	Postalgorithm Group (n=103)	*P* Value
Clinical characteristic			
Age, mean (SD), mo	7 (6)	7 (6)	.94
Male sex, %	42.9	40.0	.66
Hospitalized, %	21.4	22.3	.88
Resistant organism, %	64.3	64.1	.98
Blood culture obtained, %	52.0	48.5	.62
Positive blood culture, No./Total No. (%)	1/51 (2.0)	6/50 (12.0)	.05
Primary UTI organism, No. (%)			
Escherichia coli	90 (91.8)	96 (93.2)	.30
Klebsiella species	4 (4.1)	4 (3.9)	
Proteus mirabilis	2 (2.0)	1 (1.0)	
Enterobacter cloacae	1 (1.0)	0	
Enterococcus faecalis	1 (1.0)	1 (1.0)	
Citrobacter koseri	0	1 (1.0)	
UTI with >1 organism, No. (%)	10 (10.2)	14 (13.6)	.46

Table 2. Outcomes of Patients With First-Time Febrile Urinary Tract Infection (UTI) During the Prealgorithm and Postalgorithm Periods

Outcome	Prealgorithm Group (n=98)	Postalgorithm Group (n=103)	Risk Ratio (95% CI)[a]
First UTI, No. (%)			
VCUG	97 (99.0)	13 (12.6)	0.13 (0.08-0.21)
Renal US	97 (99.0)	69 (67.0)	0.68 (0.59-0.78)
Recurrent UTI (within 6 mo of first), No. (%)	7 (7.1)	8 (7.8)	1.08 (0.41-2.89)
VUR identified, No. (%)			
Grade 4-5	2 (2.0)	3 (2.9)	1.43 (0.24-8.36)
Grade 1-3	19 (19.4)	0[b]	. . .
Prophylactic antibiotic use, No. (%)			
Until VCUG	69 (70.4)	2 (1.9)	0.03 (0.01-0.11)
Indefinitely	26 (26.5)	3 (2.9)	0.11 (0.03-0.35)
None	3 (3.1)	98 (95.1)	31.1 (10.2-94.8)
Subsequent urine cultures per patient, No. (95% CI)	0.3 (0.2-0.5)	0.4 (0.3-0.6)	. . .

Abbreviations: Ellipsis, not applicable; US, ultrasonography; VCUG, voiding cystourethrography; VUR, vesicoureteral reflux.
[a] Defined as the risk in the postalgorithm period divided by the risk in the prealgorithm period.
[b] One patient had grade 3 VUR identified on VCUG after a recurrent UTI.

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findings, 1 with mild prominence of the right renal pelvis and normal VCUG results, and 1 with fullness of the left renal pelvis and VCUG demonstrating grade 4 VUR on the left), and the remaining 3 had normal US findings after the UTI recurrence.

Because renal US and VCUG results were available for all but 1 patient in the prealgorithm group, patients in this group were analyzed to assess how the algorithm would have performed. Eleven of 21 patients would not have had their VUR initially detected; all 11 had grades 1 to 3 VUR (**Table 4**). Follow-up data were available on 8 of these patients; other than prophylactic antibiotic use, none had any interventions other than successive imaging. An additional 8 VCUGs and 9 US procedures were performed on these patients, and all VCUGs demonstrated resolution or near resolution of VUR.

COMMENT

To our knowledge, this is the first study to assess the effect of a more selective approach to imaging after a first febrile UTI in children. We demonstrated that VCUG use in particular can be reduced substantially without affecting the risk of UTI recurrence within 6 months and without compromising detection of high-grade VUR. We also experienced a large reduction in prophylactic antibiotic use.

Table 3. Compliance With New Algorithm Guidelines in Ordering of Renal Ultrasonography (US) and Voiding Cystourethrography (VCUG)

Variable	Age ≤6 mo (n=51)	Age >6 mo but <2 y (n=52)
Renal US		
Indicated, obtained	46	7[a]
Indicated, not obtained	5	0
Not indicated, obtained	. . .	16
Not indicated, not obtained	. . .	29
Adherence, No./Total No. (%)	46/51 (90.2)	36/52 (69.2)
VCUG		
Indicated, obtained	7[b]	4[c]
Indicated, not obtained	6[d]	0
Not indicated, obtained	2	0
Not indicated, not obtained	36	48
Adherence, No./Total No. (%)	43/51 (84.3)	52/52 (100.0)

[a] Five non–*Escherichia coli*, 1 prolonged fever, and 1 possible prenatal pelviectasis.
[b] Four abnormal US findings, 1 bacteremia, and 2 non–*E coli*.
[c] All non–*E coli*.
[d] One non–*E coli* and 5 bacteremia.

Because low-grade VUR in infants and young children with UTI is common, any algorithm like ours or the NICE[15] guidelines that significantly restricts the use of VCUG will by design diagnose fewer instances of low-grade VUR. Long-term renal prognosis for patients with low-grade VUR is outstanding, so we agree with the United Kingdom's NICE 2007 guidelines that it is clinically unnecessary to diagnose this condition.

Forgoing unnecessary VCUG has many benefits. Voiding cystourethrography is invasive, painful, and expensive and carries irradiation risk. The effective irradiation dose of 0.1 to 0.9 mSv[16,17] is 2 to 3 times the amount from a radiograph of the pelvis[18] and may carry a lifetime risk of fatal cancer induction of 1 case in 10 000 patients.[19] Nondiagnosis of low-grade VUR also avoids unnecessary successive imaging with further VCUG, often performed to document expected resolution or stability of VUR. The traumatic nature of VCUG has prompted several studies assessing its emotional impact[20-22] and investigating approaches for sedation[23,24] and hypnosis[25] to make the procedure less upsetting. In addition, VCUG may cause UTI, especially in children with VUR.[26] Although actual reimbursement rates vary, total charges for VCUG at our institution approach $2000. Given the estimated 1.1 million office visits per year for US children with UTI,[27] the potential cost savings incurred by moving from routine to selective screening are significant.

Nondiagnosis of low-grade VUR also reduces prophylactic antibiotic use, which is controversial. When we introduced our new algorithm in May 2008, most recent evidence suggested that prophylactic antibiotic use did not decrease the risk of recurrent UTI or renal scarring but increased the risk of resistant infection,[11-14] and we discouraged routine use for low-grade VUR. Since then, a large randomized trial[28] was published that demonstrated a small reduction in the risk of recurrent UTI among patients who received trimethoprim sulfate-sulfamethoxazole prophylaxis compared with those who received placebo. However, a substantial increase was noted in the development of antimicrobial resistance in the treatment group, no difference in hospitalization rates or subsequent renal scarring was observed between groups, and 16 patients would need to be treated with antibiotics for 1 year to prevent 1 patient from developing UTI. Exposure to prolonged antibiotic therapy is not benign. Aside from the many known immediate adverse effects of antibiotics, multiple research groups suggest an association between antibiotic exposure in early childhood and subsequent development of atopy and asthma that is stronger with successive doses of antibiotics.[29-31]

Table 4. Theoretical Performance of Algorithm for Detection of Vesicoureteral Reflux (VUR) in the Prealgorithm Period

	No. (%)			
	VUR Would Have Been Detected			
VUR Grade	Abnormal Ultrasonography Findings	Non–*Escherichia coli*	Positive Blood Culture	VUR Would Have Been Missed
1 (n=2)	1 (50.0)	0	0	1 (50.0)
2 (n=10)	2 (20.0)	0	1 (10.0)	7 (70.0)
3 (n=7)	3 (42.9)	1 (14.3)	0	3 (42.9)
4 (n=2)	1 (50.0)	1 (50.0)	0	0

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It is possible that decreased detection of low-grade VUR leads to net overall benefit to patients and to the health care system. Avoided are the initial painful, costly, and irradiation-exposing VCUG procedure and potentially harmful treatments, such as prophylactic antibiotic use.

In our algorithm, renal US is recommended for all infants 6 months or younger and for atypical or recurrent infection in children older than 6 months. Our study confirms prior investigations demonstrating that the sensitivity of US for detection of VUR is poor.[10] Ultrasonography may be beneficial for detecting anatomic abnormalities that would require corrective surgery, although many of these abnormalities are now diagnosed using prenatal US.[32] The value of routine US at this time is uncertain, but its low-risk profile makes it less controversial than VCUG.

This study has several limitations. First, because of its retrospective nature, we did not have comprehensive follow-up data on all patients. Patients may have had UTI diagnosed elsewhere and may have had imaging studies performed at another location. In addition, we only assessed UTI recurrence within 6 months. Therefore, our rate within 6 months of 7% to 8% may underrepresent the actual rate, and the rates may be different at 12 months. However, our 6-month rates are similar to rates demonstrated by Kaplan-Meier curves in other publications.[13,28] Furthermore, any underreporting bias that may have occurred should not have differed between the prealgorithm and postalgorithm groups.

Second, we allowed for multiple organisms in our definition of UTI, which may have led to inclusion of some false-positive urine cultures. In our initial medical record review, we found that practitioners generally treated polymicrobial urine culture as true UTI, and we were most interested in including all cultures that were treated as UTI. Patients were excluded if it was evident from medical record review that the practitioner did not believe the culture represented a true UTI. When patients with multiple organisms are excluded from the analysis, there is still no difference in UTI rates between groups.

Third, although institutional adherence to American Academy of Pediatrics[1] guidelines in the prealgorithm period was almost 100%, adherence to our algorithm was only fair, and several patients who should have undergone VCUG did not have it performed. The American Academy of Pediatrics guidelines are simpler: renal US and VCUG are recommended for every patient with a first-time febrile UTI. Our algorithm may have given practitioners the impression that diagnosing all VUR is unimportant, so they may not have been as vigilant in ordering VCUG in situations where the study would have been recommended using the algorithm. However, we were reassured that patients in the postalgorithm group had more subsequent urine cultures performed than patients in the prealgorithm group, indicating that practitioners were vigilant about checking for recurrent UTI. Practitioners within our institution continue to receive periodic reminders about the guidelines, and adherence is monitored. However, underdetection of high-grade VUR did not seem to occur, despite suboptimal adherence.

Finally, the NICE 2007 guidelines[15] recommended dimercaptosuccinic acid (DMSA) imaging in atypical cases, which we removed from our protocol for several reasons. First, although selectively ordered by pediatric nephrology or urology, DMSA imaging has never been requested by general pediatricians at our institution (for whom the guidelines were designed), even before implementation of the new guidelines. Second, similar to VCUG, DMSA imaging is not benign: it may require sedation to avoid excessive movement during the study, and it involves irradiation. Third, although DMSA imaging is effective in documenting renal scarring, it is less clear that documentation of renal scarring positively affects clinical management. Nevertheless, patients at our institution who have abnormal imaging or frequent UTI are generally referred to pediatric urology or nephrology, at which point DMSA imaging may be obtained for further evaluation.

In conclusion, a restrictive approach to urinary tract imaging after febrile UTI leads to improved resource use and to minimization of potentially harmful procedures and interventions, without affecting UTI recurrence within 6 months. Until conclusive studies demonstrate that detection of low-grade VUR leads to interventions for which benefits outweigh risks, VCUG should be performed only in high-risk patients after a first-time febrile UTI. Ongoing investigation of algorithms that safely allow even less imaging are warranted.

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