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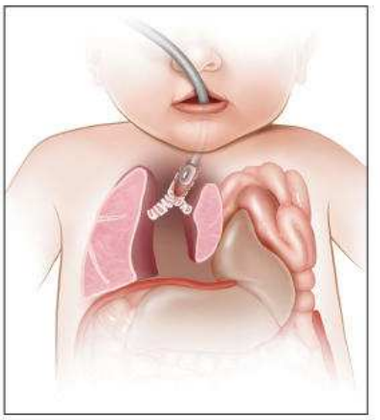

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Prediction of High-grade Vesicoureteral Reflux in Children Younger Than 2 Years Using Renal Sonography

A Preliminary Study

Sun Kyoung You, MD, Jong Chun Kim, PhD, Won Hong Park, MD, So Mi Lee, MD, Hyun-Hae Cho, MD

Objectives—To investigate the predictive value of renal sonography for vesicoureteral reflux (VUR) and the efficacy of renal sonography, technetium Tc 99m–labeled dimercaptosuccinic acid (DMSA) scanning, and a combination of the two for VUR screening in children younger than 2 years with a first episode of febrile urinary tract infection.

Methods—Thirty-eight patients younger than 2 years with a first febrile urinary tract infection were included in our study, which was conducted from April through October 2014. Each kidney was considered a separate renal unit. A retrospective review of clinical information and images (renal sonography, DMSA scanning, and voiding cystourethrography) was performed.

Results—Of the 14 renal units (18.4%) with VUR, 4 (28.5%) had high-grade VUR. Among single findings, dilatation of the renal collecting system, wall thickening of the renal collecting system, and DMSA scans significantly predicted VUR ($P = .038$, .027, and .01, respectively). Dilatation was the most common single finding (46 of 76 renal units). The sensitivity values for dilatation, wall thickening, and DMSA scans were 85.7%, 64.2%, and 50.0%, and the negative predictive values were 93.3%, 89.7%, and 87.9%.

Conclusions—The negative predictive values indicate that normal renal sonographic and DMSA findings can predict the absence of high-grade VUR. We propose that renal sonographic findings of wall thickening as well as dilatation of the renal collecting system should be considered predictive of high-grade VUR.

Key Words—pediatric ultrasound; renal sonography; technetium Tc 99m–labeled dimercaptosuccinic acid scanning; urinary tract infection; vesicoureteral reflux; voiding cystourethrography

Urinary tract infection (UTI) is one of the most common bacterial infections in febrile children in the first 2 years of life. It may be associated with renal abnormalities and long-term sequelae. Many guidelines for diagnosis and management of UTI have been developed.[1–3] The best diagnostic protocol to use for a first episode of febrile UTI has been debated.[3] The 2011 American Academy of Pediatrics (AAP) guidelines no longer recommend using routine voiding cystourethrography (VCUG) to screen for vesicoureteral reflux (VUR) in first episodes of febrile UTI in younger children in whom renal sonographic results are within normal limits.[1] In the 2011 AAP guidelines, abnormal renal sonographic results are defined as hydronephrosis, scarring, and other findings that would suggest either high-grade VUR or obstructive uropathy. However,

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Abbreviations

AAP, American Academy of Pediatrics; DMSA, dimercaptosuccinic acid; NPV, negative predictive value; PPV, positive predictive value; UTI, urinary tract infection; VCUG, voiding cystourethrography; VUR, vesicoureteral reflux

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"other findings" suggesting high-grade VUR are not defined. Previous studies have investigated the relationship of renal pelvic wall thickening with VUR and UTI.[4–6]

The most accurate diagnostic modality for VUR is VCUG. We hypothesized, however, that if renal pelvic wall thickening was considered an abnormal finding on renal sonography, it could have predictive value for VUR in younger patients with UTI. In this study, we investigated renal sonographic findings in cases of VUR confirmed by VCUG (the diagnostic reference standard). We also explored the efficacy of renal sonography, technetium Tc 99m–labeled dimercaptosuccinic acid (DMSA) scanning, and a combination of renal sonography and DSMA scanning to screen for VUR in children with a first episode of febrile UTI.

Materials and Methods

Patients

A retrospective review of clinical information and imaging findings (renal sonography, DMSA scans, and VCUG) was performed in records of 59 children with a diagnosis of UTI from April through October 2014 at the pediatric department of our institution. This study was approved by the Institutional Review Board. Of the 59 patients, we excluded 21, including 11 patients for whom no DMSA scans or VCUG procedures after renal sonography were available and 10 who were older than 2 years. Each kidney was considered a separate renal unit. Ultimately, 76 renal units in 38 patients who underwent all 3 imaging modalities by 2 years of age were included in our study.

Clinical Information

Febrile UTI was defined as a body temperature higher than 38.0°C and substantial bacteriuria (>105 colony-forming units/mL) on a urine culture. Urine samples were collected with a urine-collecting pad.

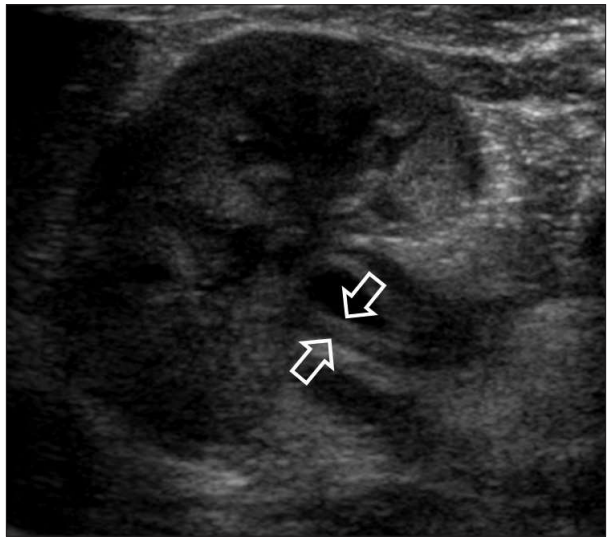
Imaging Protocol

All renal sonographic procedures were performed within 3 days of admission by a single pediatric radiologist (S.K.Y.) with 6 years of experience using an iU22 ultrasound system (Philips Healthcare, Bothell, WA) with a linear array probe (12–5 MHz) and a curved array probe (8–5 MHz). Patients underwent DMSA scanning during the first week of admission (mean interval ± SD between sonography and DMSA, 2.7 ± 1.9 days; range, 1–10 days). After confirmation of a negative urine culture result, patients underwent VCUG (mean interval between sonography and VCUG, 6.7 ± 4.1 days; range, 0–20 days).

Renal sonographic findings suggesting VUR were grouped into 3 categories: (1) dilatation of the renal collecting system, including hydronephrosis and hydroureteronephrosis; (2) wall thickening of the renal collecting system (Figure 1), defined as increased thickness of the wall of the renal collecting system[6,7]; measurements of the wall thickness of the renal pelvis were obtained from a transverse scan in the prone position, and renal pelvic wall thickness of greater than 0.8 mm was considered abnormal according to a previous study[7]; and (3) renal parenchymal changes, including renomegaly, a focal bulging contour of an involved site, increased cortical echogenicity, and loss of corticomedullary differentiation.[7–10] The finding of 1 or more areas of decreased uptake on a DMSA scan was considered abnormal. Vesicoureteral reflux was diagnosed on the basis of VCUG and graded from I to V according to the International Reflux Study grading system.[11] Patients were divided into 2 groups: VUR and non-VUR. Grades III to V were further defined as high-grade VUR, and grades I and II were defined as low-grade VUR.

To assess the diagnostic utility of abnormalities detected by renal sonography and DMSA scans, "single," "or," and "and" strategies were compared. With the "single" strategy, a positive result was a single abnormality found on either renal sonography or DMSA scanning. With the "or" strategy, a positive result was an abnormality found on either renal sonography or on the combination of renal

Figure 1. Transverse sonogram of the left kidney of a 2-month-old boy in the prone position, obtained with a linear array probe, showing dilatation of the renal pelvis and echogenic renal pelvic wall thickening (arrows). Voiding cystourethrography revealed grade V VUR on the left side (not shown).



sonography and DMSA scanning. With the "and" strategy, a positive result was an abnormality found on both renal sonography and DMSA scanning.

Statistical Analysis

For statistical analysis, we used SPSS version 21.0 software for Windows (IBM Corporation, Armonk, NY). The χ^2 test, Fisher exact probability test, and Mann-Whitney *U* test were used to compare results between the VUR and non-VUR groups. $P < .05$ was considered statistically significant. The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and odds ratio with 95% confidence interval for prediction of VUR were calculated. Data are expressed as mean ± standard deviation.

Results

The mean age at the time of admission was 5.0 ± 3.1 months (range, 1–15 months). Twenty-eight patients (73.7%) were male, and 10 (26.3%) were female (male-to-female ratio, 3.1:1). Thirty-seven (97.4%) patients were younger than 1 year; 1 patient was 15 months old. There were no significant differences in age and sex distributions between the VUR and non-VUR groups.

Table 1. Voiding Cystourethrographic Findings in 76 Renal Units

VUR Grade	Renal Units	%
Non-VUR	62	81.6
I	6	7.9
II	4	5.3
III	1	1.3
IV	0	0
V	3	3.9
Total	76	100

Of the 38 patients in the study, VUR was detected in 9 patients (14 of 76 renal units [18.4%]). Reflux was present in both kidneys in 5 of the 38 patients (13.0%). Of the 14 renal units with VUR, 4 (28.5%) were of high grade (Table 1). The sensitivity, specificity, PPV, NPV, and odds ratios for prediction of VUR by renal sonography and DMSA scanning are shown in Table 2.

Using the "single" strategy for abnormalities found on renal sonography and DMSA scanning, dilatation of the renal collecting system, wall thickening of the renal collecting system, and DMSA scans were statistically significant predictors of VUR (Table 2). Dilatation was the most common single finding, with the highest sensitivity and NPV (Figure 2). Wall thickening was the second most common single finding. The specificity of wall thickening was higher than the specificity of dilatation. With the "and" strategy (all 3 abnormal findings present), renal sonography had the lowest sensitivity and the highest specificity and PPV (Table 3). Of the renal units with normal findings on either renal sonography or DMSA scans, 10% (2 of 20 on renal sonography) and 12.1% (7 of 58 on DMSA scans) had VUR, all of low grade. Of the renal units with normal findings on both renal sonography and DMSA scans, 6.3% (1 of 16) had VUR, also of low grade.

Discussion

The children in our study with a first febrile UTI who were younger than 2 years were predominantly boys; this finding was similar to those from other studies. Of the patients in our study, 97.4% (37 of 38) were younger than 1 year.[12,13]

The 2011 AAP guidelines recommend routine renal and bladder sonography for detecting abnormalities of the genitourinary tract in the first febrile UTI in infants and children younger than 24 months.[1] Routine VCUG is no

Table 2. Single Sonographic and DMSA Findings as Predictors of VUR

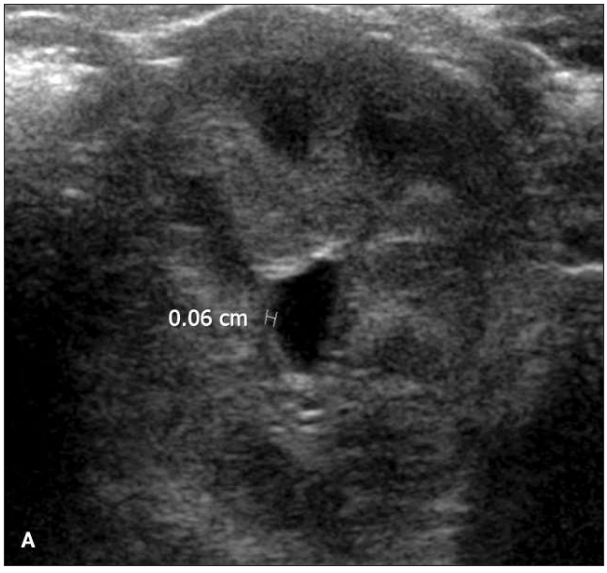
Finding	VUR (n = 14)	Non-VUR (n = 62)	Sensitivity, %	Specificity, %	PPV, %	NPV, %	Odds Ratio (95% CI)	*P*, Pearson χ^2	*P*, Fisher Exact
Sonography									
Dilatation									
Abnormal	12	34	85.7	45.1	26.0	93.3	4.941		.038
Normal	2	28					(1.019–23.948)		
Wall thickening									
Abnormal	9	18	64.2	70.9	33.3	89.7	4.400		.027
Normal	5	44					(1.295–14.949)		
DMSA									
Abnormal	7	11	50.0	82.2	38.8	87.9	4.636	.01	
Normal	7	51					(1.350–15.921)		

CI indicates confidence interval.

longer recommended and is indicated only if renal and bladder sonography reveals abnormalities such as hydronephrosis, scarring, and other findings that would suggest either high-grade VUR or obstructive uropathy.[1] After the guidelines were published, some studies reported renal sonography to be a poor screening test for VUR, raising concerns over missed or delayed diagnoses of clinically important VUR in children with UTI.[9,14,15] Nelson et al[14] reported that renal sonography showed a low sensitivity and PPV for VUR and recommended that VCUG be considered as a complementary diagnostic tool in children with UTI. In these prior studies, abnormal renal and bladder sonographic findings were defined as hydronephrosis and scarring, and the 2011 AAP guidelines do not define the other findings that suggest high-grade VUR.[1] To investigate whether renal pelvic wall thickening could be suggestive of high-grade VUR, we considered the presence of wall thickening of the renal collecting system, in addition to the other findings suggesting VUR, to be an abnormality on renal sonography.

Prior studies have reported the relationship of renal pelvic wall thickening with VUR.[4–6] Sorantin et al[6] reported that VUR and obstruction were the most common findings associated with upper urinary tract wall thickening after excluding UTI, urolithiasis, and rejection after renal transplantation. Tain[5] reported that the sensitivity,

Figure 2. **A**, Transverse sonogram of the right kidney of an 11-month-old boy in the prone position, obtained with a linear array probe, showing only dilatation of the renal pelvis. **B**, Voiding cystourethrography revealed grade II VUR on the right side.



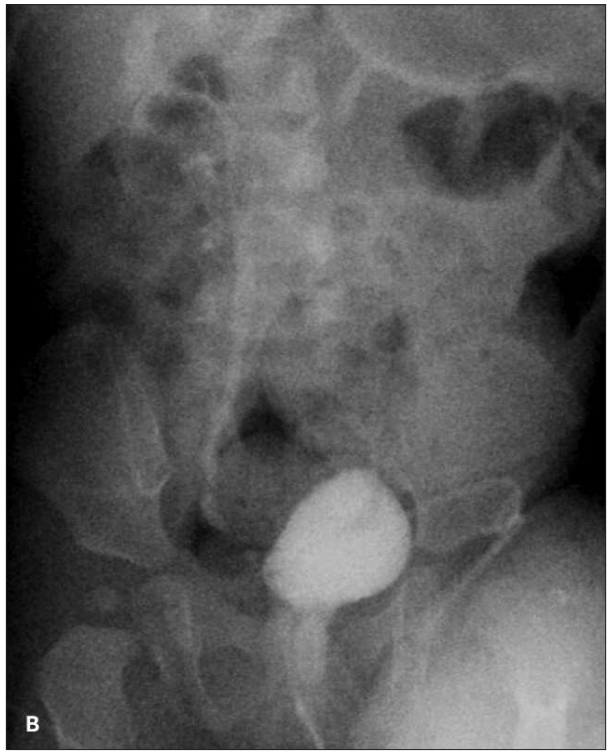


Table 3. Combinations of Findings as Predictors of VUR

Finding	VUR	Non-VUR	Sensitivity, %	Specificity, %	PPV, %	NPV, %	Odds Ratio (95% CI)	*P*, Fisher Exact
All 3 tests								
Abnormal	3	1	21.4	98.3	75.0	84.7	16.636	.018
Normal	11	61					(1.583–174.874)	
Wall thickening and DMSA								
Abnormal	6	3	42.8	95.1	66.6	88.0	14.75	.001
Normal	8	59					(3.068–70.92)	

CI indicates confidence interval.

specificity, and PPV of renal pelvic wall thickening for VUR were 79.4%, 52.1%, and 54%, respectively, and they concluded that renal pelvic wall thickening was inadequate for predicting VUR in acute UTI. Tsai et al[4] included a thickened renal pelvic wall among the abnormal renal sonographic findings considered useful for VUR screening. They reported that hydronephrosis, or calyceal ectasia, was the most common finding (39.1% [86 of 220]), and a thickened pelvic wall was present in 4 infants younger than 3 months presenting with febrile UTI.

Based on our calculated NPV for renal sonography and DMSA scans (Tables 2 and 3), normal findings on renal sonography and DMSA scans can predict the absence of VUR. Normal findings on either or both of these diagnostic tests can exclude a diagnosis of high-grade VUR, as has been previously reported.[8,12,16,17]

Our study had several limitations. First, only a small number of patients were enrolled. Not all of the children with a first febrile UTI underwent renal sonography, DMSA scanning, and VCUG. Second, because our study was retrospective, bias in reviewing the renal sonographic and DMSA scans may have been a factor. Third, we did not analyze clinical symptoms and laboratory findings, such as the white blood cell count, C-reactive protein, and procalcitonin, which correlate with UTI.

In conclusion, our results indicate that normal findings on renal sonography and DMSA scans can predict the absence of high-grade VUR. We propose that renal sonographic findings of wall thickening as well as dilatation of the renal collecting system should be considered predictive of high-grade VUR. In addition, the PPV of wall thickening was higher when this finding was present on both renal sonography and DMSA scans than when it was present on either renal sonography or DMSA scans alone. Further studies of larger patient populations are needed to estimate the efficacy of renal sonography and DMSA scans for predicting VUR in children younger than 2 years with a first febrile UTI.

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