The Predictive Value of Renal Ultrasound of Vesicoureteral Reflux After First Urinary Tract Infection in Neonates and Infants 0-24 Months

Richard J. Mazzaccaro MD
Lehigh Valley Health Network, Richard.Mazzaccaro@lvhn.org

Michael J. Weiss MPH
Lehigh Valley Health Network, Michael_J.Weiss@lvhn.org

The Predictive Value of Renal Ultrasound for Vesicoureteral Reflux After First Urinary Tract Infection in Neonates and Infants 0-24 Months

Richard J. Mazzaccaro, MD, PhD, Department of Pediatrics; **Michael J. Weiss, MPH,** Network Office of Research and Innovation

Lehigh Valley Health Network, Allentown, PA

Purpose:

In 2011, the American Academy of Pediatrics (AAP) revised its Urinary Tract Infection (UTI) clinical practice guideline[1]. A significant change to prior practice is the recommendation of a renal ultrasound (RUS) to determine whether to perform a voiding cystourethrogram (VCUG) for detection of vesicoureteral reflux (VUR) after initial UTI in infants 2-24 months old. The new recommendation has generated controversy, however, due to concerns that the RUS is not an ideal screening tool for detecting VUR[2,3,4,5], which may lead to potential delays in diagnosis of VUR, recurrence of UTI, and the possibility of renal scarring and long-term renal disease.

Additionally, the current AAP recommendation applies only to infants 2-24 months old and few studies have focused on neonates 0-2 months of age[6]. It is unclear if predictive characteristics of RUS can or should be applied to infants 0-2 months old presenting with a first episode of UTI.

Study Objectives:

The objective of this study was to evaluate the effectiveness of a RUS as a screening tool for detecting VUR in neonates and infants after initial UTI.

Methods:

- We conducted an IRB-approved, retrospective chart review of 91 infants 0-24 months of age who were admitted to the inpatient pediatrics unit with a diagnosis of first UTI between January 1, 2006 and December 31, 2010.
- All infants had a RUS and VCUG.
- Sensitivity, specificity, positive and negative predictive values were calculated for the ability of a non-normal RUS to predict VUR. Specific analyses distinguished between grades of detected VUR, as well as subject age.

Table 1. Study Subject Characteristics

	Number (%)
Number of Subjects	
Total	91 (100%)
0-60 Days	39 (42.9%)
2 months to 24 months	52 (57.1%)
Collection Method	
Straight Catheter	74 (81.3%)
Clean Catch	4 (4.4%)
Urine Bag	3 (3.3%)
Not Specified	10 (11.0%)
CFU/ml	
10,000-50,000 cfu/ml	14 (15.4%)
50,000-100,000 cfu/ml	5 (5.5%)
>100,000 cfu/ml	68 (74.7%)
Not Reported	4 (4.4%)
Bacterial species Isolated	
Escherichia coli	69 (75%)
Enterobacter spp.	7 (7.6%)
Group B Streptococcus	5 (5.4%)
Klebsiella spp.	3 (3.3%)
Enterococcus	3 (3.3%)
MRSA	1 (1.1%)
Not identified, other or negative	4 (4.3%)
Renal Ultrasound	
Normal	54 (59.3%)
Non-normal	37 (40.7%)
Highest VUR Grade	
No VUR	69 (75.8%)
I	6 (6.6%)
II	3 (3.3%)
III	9 (9.9%)
IV	1 (1.1%)
V	3 (3.3%)

Results:

- Ninety-one infants, including 39 neonates (5 days to 2 months old), admitted with first episode of UTI were included in our study.
- Most of the infants in our study had culture-confirmed UTI (87%) following objective signs of infection (fever in 90%) and appropriate urine collection methods (81%). **Table 1** summarizes the characteristics of the infants in this study.
- Overall, 37% of our study group had a RUS reading other than normal (i.e. renal fullness, pelviectasis, hydronephrosis), and 25% of infants were found to have VUR of any grade.
- The performance of RUS in predicting VCUG was highly dependent on VUR grade. In detecting any grade VUR, sensitivity, specificity, PPV and NPV were generally low. In restricting analysis to grades III-V VUR only, RUS performance was not significantly better in any age group. However, the optimal effectiveness of RUS as a screening tool was in detecting grades IV and V VUR only, with sensitivity and NPV of 100% in both neonates and older infants. **Table 2** summarizes the predictive characteristics of a RUS for detecting varying grades of VUR in neonates 0-2 months-old and older infants, 2-24 months-old.

Table 2. Performance Characteristics of a RUS in Detecting Varying Grades of VUR by Age Group

	Sensitivity (%)	PPV (%)	Specificity (%)	NPV (%)
0-2 Months Old (n=39)				
Any VUR	57.1	19.1	46.9	83.3
Grade III, IV, V VUR Only	60	14.3	47.1	88.9
Grade IV or V VUR Only	100	14.3	50	100
2-24 Months Old (n=52)				
Any VUR	33.3	31.2	70.3	72.2
Grade III, IV, V VUR Only	37.5	18.6	70.5	86.1
Grade IV or V VUR Only	100	6.3	70.6	100

Discussion:

Until the recent AAP UTI CPG revision, it had been standard practice to perform both a RUS and VCUG on infants after initial UTI to detect renal abnormalities that could predispose to recurrent infection and potential chronic renal disease. More recently, concerns of increasing bacterial resistance[7] and the overall effectiveness of prophylactic antibiotics[8] in VUR have been raised, prompting the change in the AAP's position to perform VCUG only after an abnormal RUS. This has been controversial as the effectiveness of RUS as a screening tool has not been established.

We evaluated RUS as a screening tool for VUR in infants after their first UTI. Overall, sensitivity, specificity, PPV and NPV were low in both neonates and older infants. This suggests that there will be a significant number of false-negative RUS leading to undiagnosed VUR. However, with effectiveness of prophylactic antibiotics still unresolved and the expectation that lower-grade VUR usually resolves spontaneously, then perhaps the benefit of both detection and prophylactic antibiotics may be experienced with only the highest grades of VUR (e.g, III to V). Although RUS was no better at detecting grades III to V VUR than any VUR, sensitivity and NPV increased to 100% for grades IV or V only in all age groups. Therefore, RUS may be effective as a screening tool if future research demonstrates benefit of prophylactic antibiotics for only the highest grades of VUR. Additionally, because the predictive characteristics for RUS were similar in both neonates and older infants, a further finding of this study suggests that current AAP recommendations can be extended to neonates 0-2 months old.

Conclusion:

- As a screening tool, RUS demonstrated poor sensitivity, specificity, PPV and NPV for any grade of VUR, or for grades III, IV and V VUR in infants after initial UTI.
- Sensitivity and NPV are significantly increased when limited to the highest, and perhaps more clinically relevant, grade IV or V VUR only. These results should be considered when applying the revised AAP UTI CPG.
- The performance of RUS as a screening tool appears to be similar in neonates as in older infants, suggesting that the scope of the AAP's UTI CPG can include neonates.

References:
1. Urinary Tract Infection: Clinical Practice Guideline for the Diagnosis and Management of the Initial UTI in Febrile Infants and Children 2 to 24 Months. *Pediatrics*. 2011. 128(3): 595-619.
2. Alshamsam, L, et al. The value of renal ultrasound in children with a first episode of urinary tract infection. *Ann Saudi Med*. 2009.29(1):46-9.
3. Hoberman A, et al. Imaging studies after a first febrile urinary tract infection in young children. *N Engl J Med*. 2003. 348(3):195-202.
4. Mahant S, et al. Renal ultrasound findings and vesicoureteral reflux in children hospitalised with urinary tract infection. *Arch Dis Child*. 2002. 86(6):419-20.
5. Blane, CE, et al. Renal sonography is not a reliable screening examination for vesicoureteral reflux. *J Urol*. 1993. 150(2 Pt 2):752-5.
6. Goldman M, et al. Imaging after urinary tract infection in male neonates. *Pediatrics*. 2000. 105(6):1232-5.
7. Cheng, et al. Antibiotic resistance patterns of community-acquired urinary tract infections in children with vesicoureteral reflux receiving prophylactic antibiotic therapy. *Pediatrics*. 2008. 122(6):1212-7.
8. Montini, et al. Prophylaxis After First Febrile Urinary Tract Infection in Children? A Multicenter, Randomized, Controlled, Noninferiority Trial. *Pediatrics*. 2008. 122(5):1064-71.

children's hospital
LEHIGH VALLEY HEALTH NETWORK
a service of Lehigh Valley Hospital