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Renal damage detected by DMSA, despite normal renal ultrasound, in children with febrile UTI

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Summary

Objectives
2011 American Academy of Pediatrics guidelines recommended renal-bladder ultrasound (RBUS) as the only evaluation after febrile urinary tract infection (FUTI) in infants aged 2–24 months. We determined the sensitivity, specificity, and false negative rate of RBUS to identify DMSA-detected renal damage in this age group as well as in older children.

Methods
Consecutive patients referred to pediatric urology with a history of FUTI underwent DMSA ≥3 months after FUTI. Abnormal RBUS was defined as: Society of Fetal Urology hydronephrosis grades I–IV; hydroureter ≥7 mm; renal scar defined as focal parenchymal thinning; and/or size discrepancy ≥1 cm between kidneys. Abnormal DMSA was presence of any focal uptake defects and/or split renal function <44%. We calculated sensitivity, specificity, positive and negative predictive values, and false negative rates of RBUS compared to DMSA.

Results
618 patients (79% female), median age 3.4 years, were referred for FUTIs. Of the 512 (83%) with normal RBUS, 99 (19%) had abnormal DMSA. Children with normal RBUS after their first FUTI had abnormal DMSA in 15/151 (10%) aged ≤24 months and 23/119 (19%) aged >24 months. RBUS had poor sensitivity (34%) and low positive predictive value (47%) to identify patients with renal damage. 99/149 (66%) children with renal damage on DMSA had normal RBUS.

Conclusion
After FUTI, 66% of children with reduced renal function and/or renal cortical defects found by DMSA scintigraphy had a normal RBUS. Since abnormal DMSA may correlate with increased risk for VUR, recurrent FUTI and renal damage, our data suggest RBUS alone will fail to detect a significant proportion of patients at risk. The data suggest that imaging after FUTI should include acute RBUS and delayed DMSA, reserving VCUG for patients with abnormal DMSA and/or recurrent FUTI.

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Introduction

The reason for performing imaging studies in children after their initial febrile urinary tract infection (FUTI) is to identify any underlying anatomical abnormalities that might increase risk for FUTI recurrence and/or renal scarring. The 1999 American Academy of Pediatrics (AAP) guidelines recommended renal-bladder ultrasound (RBUS) and VCUG after the first FUTI in children younger than 2 years of age. However, the 2011 guidelines only recommend RBUS unless hydronephrosis, renal scarring or 'other findings that would suggest either high-grade VUR or obstructive uropathy' are found; in which case, cystography is performed [1].

However, previous reports have demonstrated poor correlation between RBUS and renal scarring, compared to the gold standard DMSA scintigraphy, with sensitivity ranging from 5 to 47% [2—4]. Accordingly, RBUS alone may fail to identify patients with underlying renal damage who may benefit from cystography to identify VUR.

Since 2008, the standardized evaluation for children referred for FUTI to a multi-level provider pediatric urology group included both RBUS and DMSA scintigraphy obtained $\geq$3 months after infection to detect renal scarring. Data from some of these patients was previously reported in a cross-sectional study that combined patients with and without FUTIs [5]. The present study included only children with FUTI and focused on the results of RBUS, which have not previously been investigated. The purpose of the study was to determine how well RBUS performed in detecting renal damage that was identified by DMSA performed $\geq$3 months after FUTI.

Methods

In this cross-sectional study, a multi-provider pediatric urology group evaluated the consecutive children for UTI and/or VUR between October 2008 and December 2012 using a standardized protocol. All children aged 0—18 years, with at least one FUTI, who underwent RBUS and DMSA were evaluated. Those with a solitary kidney, ectopic ureter, ureterocele, PUV, prune belly syndrome, and/or neurogenic bladder were excluded. Data sheets were created, which recorded patient age, gender, the number of baseline febrile UTIs ($\geq$38 °C) and non-febrile UTIs ($<$38 °C) at referral, and worst grade of VUR (when present). Results were recorded onto a database, reviewed and analyzed with institutional review board approval.

All children had RBUS and DMSA obtained at or beyond 3 months after the last FUTI. Children referred without cystography and who had normal DMSA had no further radiologic assessment, whereas those with abnormal DMSA underwent VCUG.

Imaging

The RBUS studies were performed using Philips iu22 machines Philips, Andover, MA. Studies were supervised and interpreted by pediatric radiologists. The pediatric urologist independently reviewed the RBUS images. Discrepancies were resolved by consensus after discussion with the pediatric uro-radiology specialist (MY). Renal-bladder ultrasound was defined as abnormal, with the presence of any of the following: hydronephrosis grades I—IV by Society of Fetal Urology criteria (including 'pelviectasis without caliectasis'); hydroureter $\geq$7 mm in transverse diameter; renal scar defined by abnormal focal renal contour with parenchymal thinning; and/or size discrepancy $\geq$1 cm between kidneys [6]. Children with suspected renal duplication anomalies were classified as normal, unless the renal size discrepancy was $\geq$1 cm between the kidneys and/or hydro(uretero)nephrosis was present.

The DMSA scanning was performed according to the institution's standard protocol. The dose was calculated using weight in kg/70 $\times$ standard adult dose = 5 mCi, with a dose range between 1 and 5 mCi. Imaging was performed 1.5—3 h after injection using either a Philips Prism 1500 single head camera or a Philips Axis head camera. The DMSA scans were independently reviewed by two pediatric radiologists, who were blinded to the grade of VUR and other studies except when renal US needed to be reviewed to distinguish a central scar from hydronephrosis. Results were graded using the grading scale adapted from the Randomized Intervention for Children with Vesicoureteral Reflux (RIVUR) trial, as previously described [5]. Patient age (in months) was recorded at the time of the DMSA scan, and times in months were recorded from the last FUTI and RBUS until the date of the DMSA scan.

UTI

Because this protocol began before the 2011 AAP guidelines on UTI, the definition of UTI was according to prior guidelines: a symptomatic child with $>$50,000 colony-forming units (CFU)/ml on catheterized specimens or $>$100,000 CFU/ml in bag or voided specimens. When the new guidelines were released, subset analysis for children with 'confirmed' FUTI was performed as per the new AAP criteria, including a retrospective review of urinalysis results in order to determine who had the pyuria and specimen collection method [1].

Data analysis

The primary outcome was abnormal DMSA. Sensitivity, specificity, positive predictive value, negative predictive value, and false negative rates were calculated for normal and abnormal RBUS, along with 95% confidence intervals (95% CI). Multiple logistic regression was used to estimate the odds of abnormal DMSA with pre-determined risk factors (covariates) included in the model: RBUS (normal/abnormal), number of FUTI (1, 2, $\geq$3), age (months), and gender (binary indicator) [5]. A separate model also included the highest grade of VUR as an additional risk factor (binary indicator compared to no VUR). The 95% profile likelihood ratio confidence intervals were calculated for the adjusted Odds Ratios (OR), and the likelihood ratio Chi-squared statistic was used to test for a significant association between each risk factor and abnormal DMSA. The area under the curve (AUC) for the multiple logistic regression model was reported. Analyses were performed using SAS software, Version 9.2 (SAS Institute, Inc., Cary,