Evaluation of Prenatal Hydronephrosis: Novel Criteria for Predicting Vesicoureteral Reflux on Ultrasonography

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Abbreviations and Acronyms

HN = hydronephrosis
US = ultrasonography
UTI = urinary tract infection
VCUG = voiding cystourethrogram
VUR = vesicoureteral reflux

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See Editorial on page 640.

Purpose: Radiographic evaluation for prenatal hydronephrosis often includes voiding cystourethrography to ascertain whether vesicoureteral reflux is present. We sought to determine whether use of voiding cystourethrography could be limited to those patients at greatest risk for vesicoureteral reflux. We hypothesized that vesicoureteral reflux could be predicted by findings on renal/bladder ultrasonography of hydroureter, renal dysmorphia and/or duplication.

Materials and Methods: We reviewed the records of patients with prenatal hydronephrosis who underwent initial postnatal ultrasonography and voiding cystourethrography during a 3-year period. The presence of vesicoureteral reflux on voiding cystourethrogram was correlated to ultrasound findings, including hydronephrosis grade, presence of hydroureter, renal dysmorphia or duplication, with ultrasound considered positive for any of the latter 3 findings.

Results: Of 262 patients 47 (18%) had vesicoureteral reflux. Ultrasound was positive in 24 of 29 patients (83%) with high grade reflux and 12 of 18 (67%) with low grade reflux. If ultrasonography showed any of the 3 positive findings, the odds ratio of detecting vesicoureteral reflux was 8.07 (95% CI 3.86, 16.87). Using these criteria, among all cases of prenatal hydronephrosis 5 (2%) with high grade vesicoureteral reflux and 6 (2%) with low grade reflux would have been missed. Among the 47 cases of reflux overall 5 of 29 high grade (17%) and 6 of 18 low grade cases (33%) would have been missed.

Conclusions: By using ultrasonography criteria of hydroureter, duplication and renal dysmorphia for patients with prenatal hydronephrosis, vesicoureteral reflux can be detected more specifically. Using our criteria, 165 of 262 voiding cystourethrograms (63%) could have been avoided in patients with prenatal hydronephrosis during a 3-year period. Reducing these evaluations may decrease risks regarding radiation exposure, family anxiety and health care costs.

Key Words: hydronephrosis, prenatal diagnosis, urination, vesico-ureteral reflux

The 2010 Pediatric Vesicoureteral Reflux Guidelines Panel Summary Report revealed the paucity of data to support evaluation for detection of vesicoureteral reflux in patients with prenatal hydronephrosis.[1] Much debate has been ongoing regarding who may benefit from voiding cystourethrography and whether detection of reflux in asymptomatic patients will ultimately be clinically significant. The natural history of vesicoureteral reflux diagnosed during evaluation of prenatal hydronephrosis

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differs from reflux diagnosed following symptomatic urinary tract infection. Prenatally detected reflux is more commonly seen in males and demonstrates more rapid resolution rates of even high grade disease.[2,3] Studies have additionally shown that up to 1.8% of urologically normal children may have reflux, although the incidence may be higher in normal newborns.[4] These undiagnosed cases reflect that under certain circumstances vesicoureteral reflux is a benign entity.

Several studies correlating the degree of HN with VUR prevalence suggest that only higher grades of HN may warrant evaluation. However, results have been inconsistent and trend toward no association between HN grade and VUR prevalence.[5–8] It has been our observation that VCUG is still performed at a high rate with a large number of negative examinations. Therefore, we conducted a retrospective review of patients with prenatal HN to investigate whether VUR can be predicted primarily with renal/bladder ultrasound revealing hydroureter, renal dysmorphia and/or duplication, as opposed to HN grade alone.

MATERIALS AND METHODS

Following institutional review board approval, we retrospectively reviewed all patients younger than 4 months who had undergone VCUG for prenatal HN between January 1, 2010 and December 31, 2012. All VCUGs were performed at our institution and were identified through our radiographic software system, Montage (Montage Healthcare Solutions, Inc, Philadelphia, Pennsylvania). Initial postnatal renal/bladder US had to be done within 3 months of VCUG and available for review within our institution. US from the prenatal period was not evaluated given the limited accessibility to these studies performed elsewhere. Additionally we do not routinely screen patients with a history of prenatal HN who do not have HN on postnatal US. Exclusion criteria consisted of posterior urethral valves, spina bifida, initial UTI as presentation, lack of associated US in our system and presence of hydronephrosis on postnatal US performed for other disorders. The lack of associated US was due to these images being performed elsewhere and/or lack of importation to our system for review.

HN was graded based on Society for Fetal Urology criteria. Low grade VUR was defined as grades I to III and high grade VUR as grade IV or V. VUR was correlated to US findings including hydronephrosis grade, hydroureter, renal dysmorphia and duplication. Hydroureter included any degree of ureteral dilatation that was visualized on US and was located proximally, distally or both. Dysmorphia was defined as an echogenic kidney on US or renal hypotrophy of 3 cm longitudinal length or less (normal kidney size 4.5 to 6 cm).[9] Multicystic dysplastic kidneys were not considered dysmorphic since we identify these as separate entities not secondary to reflux nephropathy. Ureteroceles were not excluded from the cohort, but were not analyzed given that they are associated with duplication anomalies and not directly with VUR.

US findings were considered positive or predictive of VUR if there was evidence of hydroureter, dysmorphia and/or duplication. US was considered positive even if there was discordance between the side of the US finding and the side of VUR.

Circumcision status, prophylactic antibiotics, development of febrile UTI, surgical intervention and VUR status at followup were also analyzed to attempt to assess clinical outcomes. Febrile UTI was defined as a positive urine culture of greater than 50,000 cfu/ml obtained from a catheterized specimen and a fever of greater than 38.5C. Children were routinely placed on prophylactic antibiotics at initial diagnosis of prenatal HN until VCUG was performed. Antibiotic prophylaxis was continued if VUR was diagnosed and for other urological conditions on an individualized basis, and was reported as positive if usage continued after VCUG was performed. Additionally we routinely repeat VCUG at 12 to 18-month intervals to evaluate for persistence or resolution of VUR.

Categorical data were analyzed using Fisher exact test or chi-square test with Yates continuity correction. Normally distributed nominal data were analyzed using Student t-test. Sensitivity, specificity, likelihood ratios, post-test probabilities and univariate odds ratios were calculated using standard formulas with confidence intervals calculated using the Wald method. Statistical analysis was performed using SigmaPlot for Windows 12.5 (Systat Software, Inc, San Jose, California). A p value of less than 0.05 was considered statistically significant.

RESULTS

During a 3-year period 377 patients were identified as having undergone VCUG before age 4 months for prenatal HN and 262 were included in the study. The 115 excluded patients had posterior urethral valves (7), spina bifida (3), UTI on presentation (13) or incidentally detected HN (12), or did not have postnatal US available for review (80).

Of the study patients 47 (18%) had VUR (tables 1 and 2). There was no difference in detection of VUR based on HN grade except with grade II ($p = 0.011$), which was significantly associated with

Table 1. *US findings in patients with prenatal HN*

	High Grade VUR	Low Grade VUR	All VUR	No Reflux	p Value*
Male-to-female ratio	21:8	8:10	29:18	170:45	0.020
No. SFU grade (%):					
I	1 (3)	1 (6)	2 (4)	10 (5)	0.789
II	4 (14)	4 (22)	8 (17)	79 (37)	0.011
III	16 (55)	6 (33)	22 (47)	70 (33)	0.092
IV	8 (28)	7 (39)	15 (32)	56 (26)	0.523
No. hydroureter (%)	17 (59)	10 (56)	17 (36)	56 (26)	<0.001
No. renal dysmorphia (%)	3 (10)	0 (0)	3 (6)	3 (1)	0.125
No. duplication (%)	11 (38)	5 (28)	16 (34)	15 (7)	<0.001
No. any of 3 positive US findings (%)	24 (83)	12 (67)	36 (77)	61 (28)	<0.001

*For high and low grade VUR combined vs no reflux.