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Time to resolution: A prospective evaluation from the Society for Fetal Urology hydronephrosis registry

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Summary

Introduction
The resolution rate of prenatal urinary tract dilation (UTD) has been documented in several retrospective studies. The present study analyzed prospective observational registry data, with the aim of determining time to resolution among patients prenatally identified with mild postnatal UTD.

Materials and methods
A total of 248 subjects, from four centers, were prospectively enrolled from 2008 to 2015. Exclusion criteria included other anomalies ($n = 69$), fewer than two ultrasounds, and/or <3 months follow-up ($n = 26$). Resolution was defined as Outcome A (SFU 0) and Outcome B (SFU 0/1). Fisher's exact test, Mann–Whitney U or Kruskal–Wallis test and Kaplan–Meier were used for analysis.

Results/discussion
The median follow-up for 179 ($n = 137$ males) subjects was 15 months (IQR 7–24), range 0–56 months. VCUG was performed in 100 (57%) and VUR identified in 15 (15%). There was no association with reflux and resolution ($P = 0.72$). For resolution assessment ($n = 153$), lower grades were likely to resolve and demonstrated a higher rate in the Outcome B classification. Time to resolution also favored lower grades, with the majority resolving within 2 years (Figure). Surgical intervention was performed in 14 (8%). It is interesting to note that regardless of grade of UTD, there was no difference in frequency of US or the time that RUS was first performed. Practitioners performed the first RUS of life within a narrow window ranging from 0.27 RUS/month for Grade 1 UTD to 0.30 RUS/month for Grade 4 UTD. It was speculated that this practice pattern occurrence likely reflected the deficiency in knowledge by primary care providers, and identified a potential opportunity for education. The SFU registry substantiates that the vast majority of patients will demonstrate transient UTD and most cases that do not resolve will improve within 2 years of life. This data could be used to further an evidenced-based approach towards the evaluation and management of prenatal UTD, as outlined in the multidisciplinary consensus statement for prenatal urinary tract dilation.

Conclusions
This prospective registry confirms that the majority of prenatal UTD is transient, resolution occurs within the first 3 years of life, and most patients will not need intervention. Redefining SFU 1 as normal increased the resolution rate. A large proportion of patients were not evaluated with a VCUG, therefore impact of VUR could not be determined.

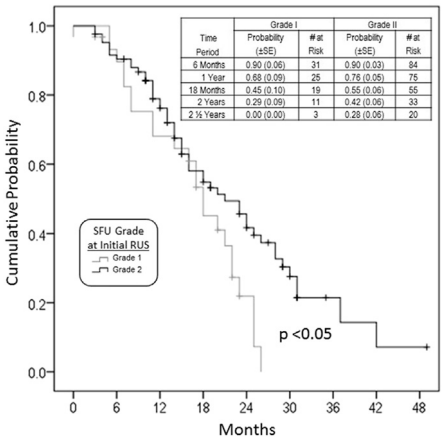

Figure Kaplan–Meier curve depicting resolution for patients initially presenting with SFU Grade 1 (grey) or Grade 2 (black) hydronephrosis censored for follow-up and surgical intervention. At 6 months, the probability of resolution for both grades is 10%. At 2 years, the probability of resolution for Grade 1 is 71% and Grade 2 is 58%. At 2.5 years, the probability of resolution is 100% for Grade 1 and 72% for Grade 2.

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Introduction

Prenatal urinary tract dilation (UTD) is a common condition that occurs in 1–3% of pregnancies [1]. Historically, the prenatal identification of these children dictated a comprehensive postnatal evaluation, with many patients being placed on prophylactic antibiotics. However, several centers have demonstrated that a minority of patients will have significant disease and, thus, many of these children are no longer completely postnatally evaluated with lower urinary tract imaging [2,3]. This creates a slightly different population in comparison with the group that has had the identification of VUR afforded to them through aggressive screening. Nonetheless, it appears that, despite this less aggressive approach towards the identification of VUR, most patients do well and demonstrate transient urologic disease [2,4,5].

Defining rates of intervention and resolution of patients with prenatal UTD could assist in the development of a treatment algorithm in order to appropriately frame parental expectation based on initial degree of UTD [6]. Furthermore, lack of standardization of imaging protocols to follow these patients likely contributes to significant expenditure of healthcare dollars that may not alter patient management. Indeed, data suggest that prenatal ultrasound imaging has minimal impact on patient outcomes, despite costing upwards of $90 million annually [7]. Elucidation of resolution and intervention rates could result in streamlining the costs associated with postnatal imaging studies and alleviating parental concerns.

The present study examined patients enrolled in the prospective, multi-institutional Society for Fetal Urology (SFU) registry, with the primary aim being to assess probability and timing for resolution of mild postnatal UTD. This information could be used to better define follow-up frequency and duration, as well as expectations for families of neonates with prenatally detected UTD. Secondary aims were to determine rates of intervention and imaging utilization.

Materials and methods

The SFU registry records were reviewed for subjects enrolled between September 2008 and September 2015. All participating centers obtained Institutional Review Board approval at their center. Four academic centers participated in the study, including: University of Virginia, Connecticut Children's Medical Center, University of Wisconsin School of Medicine, and the University of California, Davis. Subjects were eligible for enrollment if they had been prenatally diagnosed with hydronephrosis, presented within 2 years of life, and all postnatal records and imaging were available ($n = 248$). Children with a diagnosis of a renal anomaly (dilated ureter, duplex kidney, multicystic dysplastic kidney, renal cyst, ureterocele, ectopic ureter, PUV, solitary kidney, horseshoe kidney and bladder diverticulum) were excluded from the cohort ($n = 69$). To ensure that minimal imaging and follow-up were available for analysis of the primary aim (probability/timing of resolution), children with fewer than two postnatal ultrasounds and/or <3 months of follow-up ($n = 26$) were excluded, in addition to those with a renal anomaly for the resolution analysis only.

The primary outcome was resolution of prenatally identified hydronephrosis. Initial SFU grade was defined as SFU grade by the first renal ultrasound (RUS) after birth. If the first RUS reported SFU Grade 0, then the results of the second RUS after birth were used. If a subject reported bilateral hydronephrosis, the highest grade was reported. Resolution was defined as Outcome A (SFU Grade 0 of both renal moieties at most recent ultrasound) or Outcome B (SFU Grade 0/1 of both renal moieties at most recent ultrasound) to assess whether there was any between-group difference. Improvement was defined as improved hydronephrosis by at least 1 SFU grade in the highest grade moiety at the most recent follow-up compared to initial US. Stable was defined as: no change in SFU grade in either moiety during the study period. Worsening was defined as: increase by at least 1 SFU grade in the highest grade moiety or development of bilateral hydronephrosis from initial postnatal RUS at most recent follow-up. Secondary outcomes were: surgical intervention related to hydronephrosis, utilization of RUS and other diagnostic imaging such as VCUG, and/or functional radionuclide scan, as well as VUR. Imaging utilization was reported as average per month of life, due to variation in length of follow-up. The renal pelvic anterior posterior diameter measurement was not uniformly recorded in all patients prior to 2014.

Follow-up duration was defined as date of birth to most recent clinic visit. As per registry protocol, subjects were followed until discharged from clinical care, most recent follow-up visit, or until the study endpoint at 5 years of age.

Analyses were performed using SPSS 17.0 (IBM Corporation, Armonk, NY). Comparisons were made using Fisher's exact test, Mann–Whitney U test, or Kruskal–Wallis test. A Kaplan–Meier survival curve was calculated to determine time to resolution and 95% confidence intervals for initial SFU Grades 1 and 2. Follow-up was defined as date of birth to date of most recent clinic visit, and resolution defined as Grade 0 or 1 at most recent RUS. Differences between SFU hydronephrosis Grades 1 and 2 were compared using the log-rank test. All statistical tests were two-tailed with a P-value <0.05 considered significant.

Results

Four academic centers recruited 248 patients from September 2008 to September 2015. After diagnosis exclusion criteria were applied, 179 patients (137 male and 42 females) were eligible for analysis of secondary outcomes. Of the males, 103 (75%) were circumcised. Median follow-up was 15 months (IQR 7–24 months), range 0–56. The majority (52%) reported initial bilateral hydronephrosis, with 56% of subjects having initial SFU Grade 2, 24% ($n = 42$) having Grade 0 or 1, 13% ($n = 23$) having Grade 3, and 7% ($n = 13$) having Grade 4.

Resolution data

One hundred and fifty-three patients were included in the resolution analysis after applying the exclusion criteria of fewer than two RUS or <3 months follow-up. Of the 153