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Critical analysis of the outcome of primary unilateral vesicoureteral reflux in a medium volume center

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Abstract

Background: Vesicoureteral reflux (VUR) is a common finding in pediatric age group. Here in we explored the possible risk factors that affect the rate of resolution in patients with primary unilateral VUR under conservative treatment.

Methods: Between 2006 and 2014, we retrospectively evaluated all VUR patients and included only patients with primary unilateral VUR. Records were reviewed for patient age at diagnosis, antenatal history, patient gender, mode of presentation, side, and grade of VUR, associated hydronephrosis (HN) on renal ultrasound, presence of scarring and split function on dimercaptosuccinic acid (DMSA) scan. Clinical and radiological outcomes were assessed. Both univariate and multivariate analysis were conducted.

Results: A total of 68 patients with primary unilateral VUR were included (32 boys and 36 girls) with a mean age of 10 months (range 1–32). Antenatal HN was detected in 50% of patients. In 15 cases (22%), VUR was of high grade (IV–V). Associated HN was evident in 39 patients (57%). DMSA scans showed renal scarring in 16 patients (23%). After a mean follow-up of 7 years, VUR resolved in 49 patients (72%). Significant predictors for VUR resolution were VUR grade, DMSA split function and associated high-grade HN. High-grade HN with VUR was the only significant independent risk factor.

Conclusions: The rate of resolution in primary unilateral VUR under conservative treatment is significantly affected by VUR grade, DMSA split renal function and the presence of associated HN. Association of high-grade HN with VUR carries a low chance for spontaneous resolution.

Keywords: Vesicoureteral reflux, Unilateral, Scarring, Hydronephrosis, Conservative, Outcome

1 Background

Vesicoureteral reflux (VUR), or the retrograde flow of urine from the bladder into the ureter, is an anatomical and functional disorder that can lead to a significant morbidity from both acute urinary tract infection and reflux nephropathy sequelae [1, 2]. The primary VUR is defined as reflux due to anatomical or functional defect at the vesicoureteric junction [3].

VUR is a common finding in pediatric age with the risk of repeated UTIs and renal scarring. Among normal children, the prevalence of VUR ranges from 0.5 to 3%, while in children with reported UTI, the level increases to 30–40% [2, 4]. Clinical presentation is variable and most children with VUR present with antenatal HN or present later with clinical UTI.

The objectives of VUR patient management are prevention of febrile UTIs, prevention of renal injury, and reduction of treatment morbidity [4, 5]. Different treatment options for VUR include conservative therapy, endoscopic injection of several bulking agents and

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ureteral implantation via different surgical approaches [1, 6, 7].

Early randomized, controlled trials comparing anti-reflux surgery with antimicrobial prophylaxis showed no significant differences in the rates of recurrent UTI and renal scarring; nevertheless, the lack of a placebo or observation group precluded confirmation that either surgery or prophylaxis was effective [8].

Conservative treatment is intended to prevent febrile UTI associated with VUR based on the understanding that in the absence of UTI, VUR will not affect the kidney. Its rationale is that most VUR resolves over time, especially in young patients with low-grade reflux due to elongation and maturation of the ureterovesical junction as the child grows [1, 3, 6].

Several studies have shown that spontaneous VUR resolution depends on multiple factors such as patient's age at presentation, gender, VUR grade, laterality and timing of reflux, mode of clinical presentation, and the existence of anatomic abnormalities or associated voiding dysfunction [1, 9–12].

In our study, we explored the possible risk factors that could influence the rate of resolution in patients with primary unilateral VUR under conservative treatment.

2 Methods

We retrospectively reviewed the medical records of all patients diagnosed with VUR between 2006 and 2014 after receiving the approval of the institutional review board at our hospital. Only patients with primary unilateral VUR have been included, whereas patients with bilateral VUR, secondary VUR, associated urinary anomalies, patients who underwent prior surgical intervention for VUR, and patients who missed follow-up were excluded from the study.

Records were reviewed for patient age at diagnosis, antenatal history, patient gender, mode of presentation, side and grade of VUR, associated hydronephrosis (HN) on renal ultrasound, presence of renal scarring and split renal function (SRF) on dimercaptosuccinic acid (DMSA) scan. The society for fetal urology (SFU) grading system was used to classify HN into low grade (SFU grade 1 and 2) or high grade (SFU grade 3 and 4) [13].

Vesicoureteral reflux was diagnosed with micturating cystourethrogram (MCUG) in all children and graded according to the International Classification System [1, 14]. For statistical analysis, the VUR grades were then classified as mild/moderate (grades I–III) and severe (grades IV–V).

All UTIs were confirmed by quantitative urine culture results in addition to evidence of pyuria and/or bacteriuria according to clinical guidelines from The American Academy of Pediatrics [15]. For neonates born at

our institution with antenatal HN, antibiotic prophylaxis was initiated using amoxicillin at doses of 100 mg/day. Starting at 3 months of age, the drug used for chemoprophylaxis was nitrofurantoin (1–2 mg/kg/day) or trimethoprim (1–2 mg/kg/day) [12]. The same protocol of prophylaxis was applied to all other patients referred from other hospitals with VUR diagnosis. After the age of toilet training, we stopped the antibiotic prophylaxis in all boys and in girls with low-grade VUR and these cases were not excluded from our study. This issue also depended on the family compliance with CAP.

Follow-up of patients was carried out every 3 months in the first 2 years and every 6 months thereafter by clinical examination, renal bladder ultrasound, and urine analysis at each visit. Urine cultures were performed if there were any suspected symptoms of UTIs. If any febrile urinary tract infection was documented, it was recorded. Additional follow-up imaging studies included either VCUG or DMSA were done when necessary. A new VCUG was requested 1–2 years from initiation of conservative management to assess VUR resolution while a follow-up DMSA scan was indicated if patient developed repeated febrile UTIs or any renal abnormalities in RBUS during follow-up. Indications for surgical intervention were breakthrough repeated febrile UTIs (two or more attacks), deterioration of SRF >5% on DMSA scans or development of new renal scarring.

Clinical and radiological outcomes were assessed in relation to patients' variables on initial presentation. Primary outcomes were status of reflux at last clinical follow-up; resolution, persistence or the child underwent surgical intervention, and time to resolution. We considered downgrading of high-grade reflux to grade I or II as resolution while grade I and II were considered complete resolution when VUR disappeared; otherwise, if persisted, it was considered persistent. We choose a cutoff of 40% for SRF based on our mean SRF that was nearly 40%. Also, from previous studies in which a SRF below 40% means that there is a renal function impairment.

2.1 Statistical analysis

Statistical analysis was performed using SPSS version 22 (SPSS Inc., Chicago, IL, USA). Values are shown as mean \pm SD unless otherwise reported. Both univariate and multivariate analyses were conducted. For categorical variables, Chi-square test was executed. A univariate survival analysis using a log-rank test was performed to identify predictors of reflux resolution. Estimates from Kaplan–Meier were used to demonstrate the effect of VUR grade, side, presentation mode, gender, associated HN and SRF on initial DMSA over the study period on the VUR resolution rate. To adjust for other significant characteristics, a Cox proportional hazards model was

utilized. Only variables that showed a statistically significant effect on survival were included in the multivariate analysis. A *p* value of less than 0.05 was considered statistically significant.

3 Results

A total of 68 patients with primary unilateral VUR were enrolled in the study (32 boys and 36 girls) with a mean age at diagnosis of 10 ± 8.5 months (range, 1–32). In 50% of patients, antenatal HN was observed, while the other half presented with UTI. VUR was of high grade (IV–V) in 15 patients (22%). Associated HN of various grades was evident in 39 patients (57%). DMSA scans showed

renal scarring in 16 patients (23%) and a mean split function of $39\% \pm 12$ (range, 21–59). Patients' demographics and imaging characteristics are shown in Table 1.

After a mean follow-up of 7.5 ± 3 years (range, 3–16), VUR was resolved in 49 patients (72%) with a mean time for resolution of 2.5 ± 1.2 years (range, 1–5). Surgical intervention was necessary in 11 patients (16%) during conservative treatment due to repeated breakthrough febrile UTIs in 6 and deterioration of SRF and/or development of new renal scarring in 5.

Univariate analysis showed that VUR grade (low vs. high), DMSA split renal function on initial assessment and associated HN were significant predictors for VUR

Table 1 Patient demographics, imaging characteristics and clinical outcome of 68 children with primary unilateral vesicoureteral reflux

Variable at initial presentation	Number = 68	Percentage (%)	Resolution no. (%)	Persistent no. (%)	<i>p</i> value
Gender					
Boy	32	47	24 (75)	8 (25)	0.610
Girl	36	53	25 (69)	11 (31)	
Mode of presentation					
Antenatal HN	34	50	29 (85)	5 (15)	0.092
UTI	34	50	20 (59)	14 (41)	
VUR side					
Right	29	43	22 (76)	7 (24)	0.547
Left	39	57	27 (69)	12 (31)	
VUR grade					
Grade I	11	16	9 (82)	2 (18)	0.048*
Grade II	22	32	18 (81)	4 (19)	
Grade III	20	30	15 (75)	5 (25)	
Grade IV	8	12	4 (50)	4 (50)	
Grade V	7	10	3 (43)	4 (57)	
VUR group					
Low grade	53	78	42 (79)	11 (21)	0.021*
High grade	15	22	7 (46)	8 (54)	
Renal scarring on DMSA					
No scars	52	76.5	40 (77)	12 (23)	0.107
Renal scars	16	23.5	9 (56)	7 (44)	
Split renal function					
Above 40%	57	84	44 (77)	13 (23)	0.032*
Below 40%	11	16	5 (45)	6 (55)	
Renal US					
No HN	29	43	24 (83)	5 (17)	0.027*
Hydronephrosis	39	57	25 (64)	14 (36)	
Fate of VUR					
Resolution	49	72%			
Persistent	8	12%			
Surgery	11	16%			

* Significant

p value was calculated using Chi-Square test

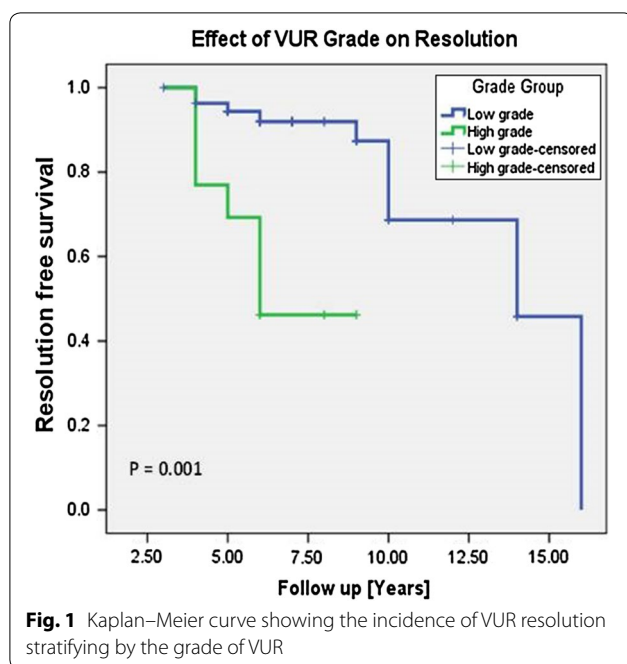


Fig. 1 Kaplan–Meier curve showing the incidence of VUR resolution stratifying by the grade of VUR

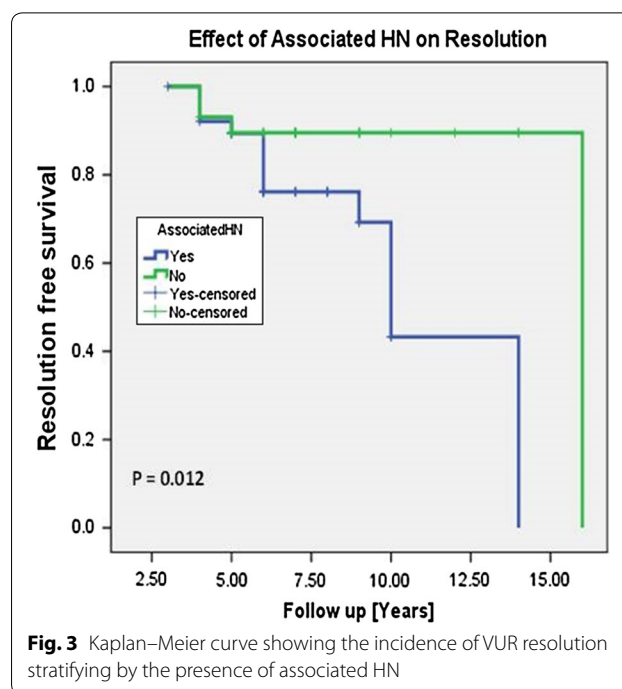


Fig. 3 Kaplan–Meier curve showing the incidence of VUR resolution stratifying by the presence of associated HN

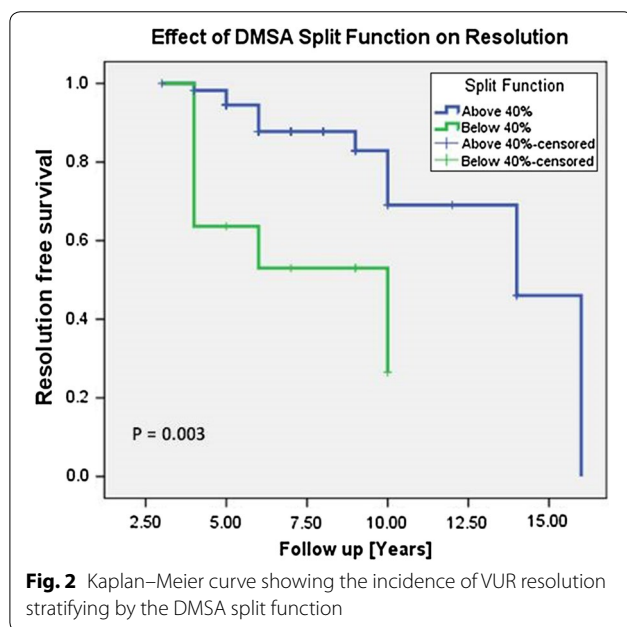


Fig. 2 Kaplan–Meier curve showing the incidence of VUR resolution stratifying by the DMSA split function

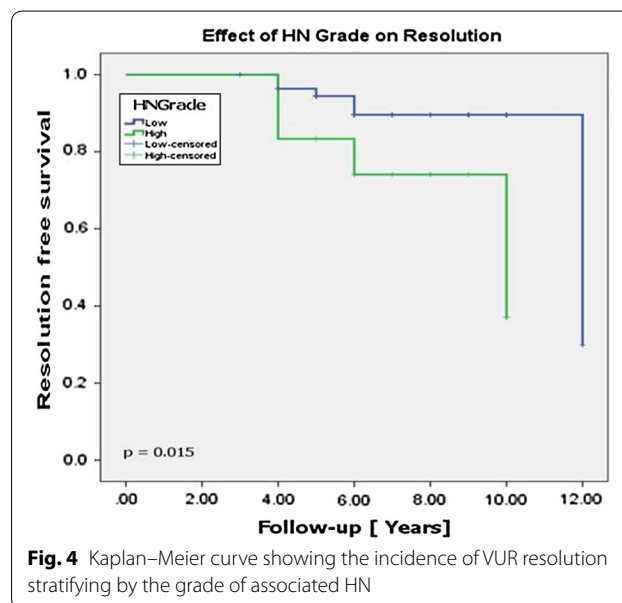


Fig. 4 Kaplan–Meier curve showing the incidence of VUR resolution stratifying by the grade of associated HN

resolution (Figs. 1, 2, 3). Besides, when we divided associated HN into low- and high-grade HN; the presence of high-grade HN was correlated significantly with a low probability of VUR resolution ($p=0.015$), Fig. 4. Meanwhile, the patient's age at diagnosis, gender, mode of presentation, VUR side and presence or absence of renal scarring on DMSA were not statistically significant factors in the prediction VUR resolution (Table 1).

The presence of associated high-grade HN with VUR was the only significant independent risk factor affecting the resolution rate on multivariate analysis (Table 2).

4 Discussion

Patients with VUR demonstrate a wide range of severity, and a good percentage of reflux patients do not develop renal scars and do not need any intervention as VUR

Table 2 Multivariate analysis of factors predicting resolution in 68 children with primary unilateral vesicoureteral reflux

Factor	B	SE	Exp (B)	95% CI for Exp (B)		p value
				Lower	Upper	
Associated hydronephrosis	1.79	0.59	5.97	1.84	19.39	0.003*
Hydronephrosis grade	0.69	0.32	1.99	1.07	3.69	0.026*
VUR grade group low versus high	1.91	1.11	6.75	0.77	59.29	0.085
Split function on DMSA	1.01	0.54	2.76	0.96	7.94	0.060

* Significant

Statistical analysis using Cox proportional hazards model

tends to resolve spontaneously over time [4, 7]. Improved ability to predict individualized early reflux resolution will assist the parent and physician with VUR management decisions. In our study, we aimed to identify the potential prognostic factors that affect primary VUR resolution in a cohort of conservatively managed patients.

The main objective of VUR treatment is to avoid the occurrence of febrile UTIs and subsequent renal scarring [2, 4]. Conservative therapy requires diligent waiting, intermittent or continuous antibiotic prophylaxis, and bladder rehabilitation in cases with bladder dysfunction [1].

In 2015, de Bessa et al.'s meta-analysis findings endorsed continuous antibiotic prophylaxis (CAP) in all children with VUR regardless of reflux grade. For asymptomatic patients, the correct length of antibiotic prophylaxis is uncertain. Annual performance of a VCUG control is a choice. Prophylaxis may be discontinued if VUR is not observed in the control imaging after the first year. If breakthrough infections occur under this antibiotic prophylaxis, surgical treatment should be attempted [16].

In our study, spontaneous resolution including improvement was 72%, persistent VUR in 12% while the surgical intervention was indicated in 16%. Comparable results were reported in the Arlen et al. 2016 study where spontaneous resolution including improvement was 56.5%, persistent VUR in 26% while surgical intervention was necessitated in 17.5% [17].

A decreasing incidence of VUR with age reflects spontaneous resolution in many patients. As expected, VUR grade was significantly associated with resolution. Children with high-grade VUR have a higher risk of renal scarring after a febrile UTI, and the possibility of spontaneous VUR resolution is low [10]. VUR has a high spontaneous resolution rate within the first 4–5 years of life (80% VUR grade III, 30–50% VUR grade IV–V). The anatomic maturation probability is highest during these years [4, 10].

The rate of spontaneous resolution depends not only on the degree of reflux, but also on clinical presentation, patient age, sex, laterality, and associated LUT dysfunctions [10, 12]. Several variables were identified as negative predictive factors for VUR resolution [11, 12]. Sjostrom and her colleagues evaluated the predictive factors for the resolution of congenital high-grade VUR in infants [11]. They reported an overall spontaneous reflux resolution rate of 38%, including cases downgraded to grade I to II. Variables that were substantially associated with VUR resolution were breakthrough febrile UTI, bladder dysfunction, higher grade of reflux, and renal abnormality. There were no differences in VUR resolution depending on gender, or prenatal or postnatal diagnosis. These findings were consistent with our current study.

Knudson et al. analyzed the predictive factors for spontaneous primary VUR resolution and found that initial VUR grade, bladder volume at reflux onset, age at diagnosis and history of prenatal HN were independent factors affecting VUR resolution rate [18]. After an average follow-up of around 2 years, 60% achieved spontaneous resolution (64% for grade I–III vs. 17% for grades IV and V). Those findings were also comparable to our study in terms of high spontaneous VUR resolution rate.

In their study, they found that VUR during the filling phase of VCUG or passive VUR is a negative predictor for VUR resolution. When bladder volume at VUR onset was greater than 50% of predicted bladder capacity, improved resolution was observed. They also found that VUR resolution was higher in patients with prenatal HN than those presented later, and this might due to patients with early VUR diagnosis are more likely to have transient VUR that resolves rapidly. After early infancy period, the VUR chance for resolution will be like those presenting at older age. They also compared children younger versus older than 2 years of age and they found that diagnostic age is an important factor affecting the annual resolution rate of VUR; however, the overall resolution rate was not significantly affected [18].

Similar to our study findings, spontaneous resolution rates have been shown to be significantly higher in grade I–III VUR, whereas high-grade reflux is much less likely to resolve irrespective of long-term monitoring and antibacterial therapy [11]. In their long-term follow-up, Schwab et al. 2002 recorded a 68% overall rate of VUR resolution and found that grades I to III VUR resolved at the same rates and significantly more rapidly than grades IV to V (76% vs. 35%) [19].

Spontaneous VUR resolution was observed in 25 out of 56 renal units (45%) after a median follow-up of 5.5 years of conservative treatment in another study by Silva et al. 2006; 75% for moderate reflux (I–III) and 37% for severe reflux (IV–V) [12]. Furthermore, Estrada et al. conducted a study of 2462 VUR patients and found an overall resolution rate of 51% [55% for grades I–III vs. 32% for grade IV and V]. They reported that VUR resolution is influenced by a combination of factors that include gender, age at presentation, laterality and grade of reflux, ureteral anatomy and mode of presentation [10].

Yeung et al. reported that 70% of the cases of mild reflux and 43% of the cases of severe reflux resolved by 15 months of follow-up [20]. A low-resolution rate has been reported for grade V reflux [0–30%] during a follow-up of 2–5 years, whereas grade IV was often reported to have a resolution rate of more than 50%. In contrary, Garcia Roig and colleagues reported that high-grade (IV or V) reflux was not associated with a resolution at any point [9].

The presence of renal damage is an additional variable examined in relation to spontaneous resolution of VUR [10, 12, 21]. Among 506 Brazilian children with VUR, Silva et al. performed a multivariate study and found that VUR resolution was predicted among other variables by the absence of renal scars [12]. The survival study found that VUR resolves in only 17% of children with renal damage versus 62% of children without renal damage. In our study, we discovered that kidneys with split renal function less than 40% had a lower VUR resolution rate than those above 40% (77% vs. 45%).

The presence of associated HN with VUR was also studied. In the classical study of Edwards et al., VUR was resolved in more than 80% of undilated ureters but only in 40% of dilated units after 7–15 years of follow-up [22]. In our research, we observed that VUR associated with HN has a lower probability of resolution than non-dilated systems.

We recognized from previous studies that impaired bladder function adversely affected VUR resolution rate, we likewise did not use voiding dysfunction as a factor in our statistical analysis, and we omitted children with secondary VUR because of underlying bladder pathology.

There should be recognition of several limitations of our study. It is a retrospective analysis and selection bias can occur because the decision on care relied on the choice of pediatric urologists and parents. The sample size was relatively small because our center has a medium volume that could predispose the results to statistical errors of type I and type II and restricted our ability to perform subgroup analyses. We excluded patients with bladder dysfunction from the study based on clinical history, but some patients with irregular bladder function may not have been detected and included in our research. Nonetheless, we believe that in the treatment of unilateral primary VUR, our study provided valuable information to enable risk stratification. By identifying the predictive factors, pretreatment counseling could be also improved. Patients with high-grade VUR associated with high-grade HN might benefit from early active intervention to minimize the need for repeated VCUG and protect future renal damage.

5 Conclusions

The rate of resolution in primary unilateral VUR under conservative treatment is significantly affected by the grade of VUR, split renal function on DMSA and the presence of high-grade HN. Association of high-grade HN with VUR carries a low chance for spontaneous resolution. These factors are very useful in parent counseling.

Abbreviations

VUR: Vesicoureteral reflux; HN: Hydronephrosis; VCUG: Voiding cystourethrogram; DMSA: Dimercaptosuccinic acid; UTI: Urinary tract infection; CAP: Continuous antibiotic prophylaxis; SRF: Split renal function.

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Authors' contributions

OS designed the study, prepared the manuscript, and analyzed the data. AE collected the data and helped with manuscript preparation. AA and MA helped with drafting of the manuscript, literature search and supervised the study. ZN and FA contributed to statistical analysis and revised the final manuscript. All authors read and approved the manuscript.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

This study was approved by the ethics committee of Prince Sultan Military Medical City on 04/2017. Written informed consent to participate in the study was provided by all participants' parents before inclusion.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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References

1. Tekgöl S, Riedmiller H, Hoebeke P, Kočvara R, Nijman R, Radmayr C, Stein R, Dogan H, European Association of Urology (2012) EAU guidelines on vesicoureteral reflux in children. *Eur Urol* 62:534–542
2. Tokat E, Gurocak S, Ure I, Acar C, Sinik Z, Tan M (2019) Did our current initial treatment practice change after EAU/ESPU vesicoureteral reflux risk grouping? *J Pediatr Surg* 54:1477–1480
3. Radmayr C, Schwentner C, Lunacek A, Karatzas A, Oswald J (2009) Embryology and anatomy of the vesicoureteric junction with special reference to the etiology of vesicoureteral reflux. *Ther Adv Urol* 1:243–250
4. Hajiyev P, Burgu B (2017) Contemporary management of vesicoureteral reflux. *Eur Urol Focus* 3:181–188
5. Peters C, Skoog S, Arant B Jr, Copp HL, Elder JS, Hudson RG, Khoury AE, Lorenzo AJ, Pohl HG, Shapiro E, Snodgrass WT, Diaz M (2010) Summary of the AUA guideline on management of primary vesicoureteral reflux in children. *J Urol* 184:1134–1144
6. Routh J, Bogaert G, Kaefer M, Manzoni G, Park J, Retik A, Rushton HG, Snodgrass W, Wilcox D (2012) Vesicoureteral reflux: current trends in diagnosis, screening, and treatment. *Eur Urol* 61:773–782
7. Silay MS, Turan T, Kayali Y, Başibüyük I, Gunaydin B, Caskurlu T, Karaman M (2018) Comparison of intravesical (Cohen) and extravesical (Lich-Gregoir) ureteroneocystostomy in the treatment of unilateral primary vesicoureteral reflux in children. *J Pediatr Urol* 14:65.e1–65.e4
8. RIVUR Trial Investigators, Hoberman A, Greenfield S, Mattoo T, Keren R, Mathews R, Pohl H, Kropp B, Skoog S, Nelson C, Moxey-Mims M, Chesney R, Carpenter M (2014) Antimicrobial prophylaxis for children with vesicoureteral reflux. *N Engl J Med* 370:2367–2376
9. Garcia-Roig M, Ridley D, McCracken C, Arlen AM, Cooper C, Kirsch A (2017) Vesicoureteral reflux index: predicting primary vesicoureteral reflux resolution in children diagnosed after age 24 months. *J Urol* 197:1150–1157
10. Estrada C Jr, Passerotti C, Graham D, Peters C, Bauer S, Diamond D, Cilento B Jr, Borer J, Cendron M, Nelson C, Lee R, Zhou J, Retik A, Nguyen H (2009) Nomograms for predicting annual resolution rate of primary vesicoureteral reflux: results from 2,462 children. *J Urol* 182:1535–1541
11. Sjöström S, Sillén U, Jodal U, Sameby L, Sixt R, Stokland E (2010) Predictive factors for resolution of congenital high grade vesicoureteral reflux in infants: results of univariate and multivariate analyses. *J Urol* 183:1177–1184
12. Silva J, Diniz J, Lima E, Vergara R, Oliveira E (2006) Predictive factors of resolution of primary vesico-ureteric reflux: a multivariate analysis. *BJU Int* 97:1063–1068
13. Nguyen HT, Herndon CD, Cooper C, Gatti J, Kirsch A, Kokorowski P, Lee R, Perez-Brayfield M, Metcalfe P, Yerkes E, Cendron M, Campbell JB (2010) The Society for Fetal Urology consensus statement on the evaluation and management of antenatal hydronephrosis. *J Pediatr Urol* 6:212–231
14. Lebowitz R, Olbing H, Parkkulainen K, Smellie J, Tamminen-Möbius T (1985) International system of radiographic grading of vesicoureteric reflux. International reflux study in children. *Pediatr Radiol* 15:105–109
15. Subcommittee on Urinary Tract Infection, Steering Committee on Quality Improvement and Management, Roberts KB (2011) 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* 128:595–610
16. de Bessa Jr J, de Carvalho Mrad F, Mendes EF, Bessa M, Paschoalin V, Tiraboschi R, Sammour Z, Gomes C, Braga L, Netto J (2015) Antibiotic prophylaxis for prevention of febrile urinary tract infections in children with vesicoureteral reflux: a meta-analysis of randomized, controlled trials comparing dilated to nondilated vesicoureteral reflux. *J Urol* 193:1772–1777
17. Arlen A, Garcia-Roig M, Weiss A, Leong T, Cooper C, Kirsch A (2016) Vesicoureteral reflux index: 2-institution analysis and validation. *J Urol* 195:1294–1299
18. Knudson M, Austin J, McMillan Z, Hawtrey C, Cooper C (2007) Predictive factors of early spontaneous resolution in children with primary vesicoureteral reflux. *J Urol* 178:1684–1688
19. Schwab C Jr, Wu H, Selman H, Smith G, Snyder H 3rd, Canning D (2002) Spontaneous resolution of vesicoureteral reflux: a 15-year perspective. *J Urol* 168:2594–2599
20. Yeung C, Godley M, Dhillon H, Gordon I, Duffy PG, Ransley PG (1997) The characteristics of primary vesico-ureteric reflux in male and female infants with pre-natal hydronephrosis. *Br J Urol* 80:319–327
21. Nepple K, Knudson M, Austin J, Wald M, Makhoul A, Niederberger C, Cooper C (2008) Adding renal scan data improves the accuracy of a computational model to predict vesicoureteral reflux resolution. *J Urol* 180:1648–1652
22. Edwards D, Normand IC, Prescod N, Smellie J (1977) Disappearance of vesicoureteric reflux during long-term prophylaxis of urinary tract infection in children. *Br Med J* 2:285–288

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