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Original Article

An evaluation of ureteral diameter ratio and vesicoureteral reflux index in the treatment of primary vesicoureteral reflux

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Abstract *Objective:* Vesicoureteral reflux (VUR) index is a simple, validated tool that reliably predicts significant improvement and spontaneous resolution of primary reflux in children. The aim of this study was to evaluate and compare the ureter diameter ratio (UDR) and VUR index (VURx) of patients treated with endoscopic injection (EI) and ureteroneocystostomy (UNC) methods in the pediatric age group due to primary VUR.
Methods: Patients under the age of 18 years old who underwent EI and UNC with the diagnosis of primary VUR between January 2011 and September 2021 were determined as the participants. The UDR was assessed using voiding cystourethrography, and the VURx score was determined prior to treatment based on hospital records included in the study.
Results: A total of 255 patients, 60 (23.5%) boys and 195 (76.5%) girls, with a mean age of 76.5 (range 13.0–204.0) months, were included in the study. EI was applied to 130 (51.0%) patients and UNC was applied to 125 (49.0%) patients due to primary VUR. The optimum cut-off for the distal UDR was obtained as 0.17 with sensitivity and specificity of 73.0% and 63.0%, respectively. The positive and negative predictive values were 66.0% and 70.0%, respectively.
Conclusion: When the UDR and VURx score are evaluated together for the surgical treatment of primary VUR in the pediatric age group, it is thought that it may be useful in predicting the clinical course of the disease and evaluating surgical treatment options.

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1. Introduction

Vesicoureteral reflux (VUR) is one of the most common urological diagnoses in the pediatric age group. While the incidences of VUR in the general pediatric population are 0.4%—1.8%, the incidences in children with a history of febrile urinary tract infection rise to approximately 30%—40% [1]. Voiding cystourethrography (VCUG) provides the diagnosis and grading of VUR [2]. Ureterovesical junction anatomy plays an important role in the development of primary VUR [2]. Although many factors play a role in the clinical course of VUR, the most determining factor in predicting regression or improvement of reflux is still the degree of reflux. Distal ureter dilatation may be a determining factor in the clinical course of primary VUR compared to upper urinary tract dilatation [3]. Major factors affecting the decision for anti-reflux surgery are the risk of pyelonephritis, new renal parenchymal scar formation, and the degree of ongoing VUR [4]. Surgery is indicated to preserve kidney function in children with persistent VUR, recurrent urinary tract infections (UTIs), or intermittent progression of renal scarring. In recent years, endoscopic injection (EI) has become the first treatment for children with VUR due to its high success rates and very low incidences of complications [5].

The aim of this study was to compare ureter diameter ratio (UDR) and VUR index (VURx) of patients treated with ureteroneocystostomy (UNC) and EI method due to primary VUR in the pediatric age group, and discuss in the light of current literature.

2. Patients and methods

2.1. Patients and design

We evaluated patients under 18 years of age who underwent EI and UNC method with the diagnosis of primary stroke between January 2011 and September 2021. Written consents were obtained from the parents of all patients for the publication of patient information. Demographic characteristics of the patients, reflux time on VCUG, degree and the side of VUR, constipation and urinary incontinence were recorded. The VUR was graded by a radiologist through VCUG, International Reflux Study classification system for children before the treatment. The UDR was calculated by measuring the largest ureter diameter in the pelvis in the pre-treatment VCUG in millimeters and dividing this measurement result by the distance from the bottom of the L1 vertebral body to the top of L3. The highest VUR grade was used in the analysis of the UDR in bilateral reflux cases. The timing of VUR in VCUG was determined as filling or voiding. The patients included in the study were divided into two groups as EI group and UNC group. The reflux grading of the cases in both groups were performed by VCUG. The reflux grades of the patients in both groups were evaluated as grades I—III VUR and grades IV—V VUR. The demographic data of the patients who had UNC and EI, the VURx, and UDR results were compared. For this study, the permission of Cukurova University Ethics Committee with the decision number 118 dated 7 January 2022 was obtained.

2.2. Inclusion criteria

Patients who underwent EI and open surgery for primary VUR and whose UDR and VURx could be calculated by VCUG before treatment were included in the study.

2.3. Exclusion criteria

Cases with neurogenic bladder, ectopic ureter, ureterocele, accompanying ureteropelvic or ureterovesical junction obstruction, missing clinical information, and the UDR not calculated with VCUG before the procedure were excluded from the study.

2.4. Statistical analysis

Categorical variables were represented using numerical values and percentages, whereas continuous variables were summarized using measures such as mean, standard deviation (SD), and median, depending on the specific context. Chi-square test was used to compare categorical variables between the groups. The normality of distribution for continuous variables was confirmed with the Shapiro—Wilk test. For comparison of continuous variables between two groups, Mann—Whitney *U* test was used. An analysis of the characteristic curve was conducted to identify the most effective threshold for the UDR. Logistic regression analysis was performed to determine the likelihood of undergoing UNC. In univariate analysis, variables significant at the $p<0.25$ level were entered in logistic regression analysis. All analyses were performed using SPSS statistics version 20.0 (IBM Corp, Armonk, NY, USA). The statistical level of significance for all tests was considered to be less than 0.05.

3. Results

A total of 255 patients, 60 (23.5%) boys and 195 (76.5%) girls, with a mean age of 76.5 (SD 42.6) months, were included in the study. One hundred and thirty (51.0%) patients had EI and 125 patients (49.0%) had UNC because of primary VUR. While 88 (67.7%) of the patients who had EI were grades I—III VUR, 42 (32.3%) patients were grades IV—V VUR; 57 (45.6%) patients who had UNC were grades I—III VUR, and 68 (54.4%) patients were grades IV—V VUR. UNC was performed in 21 (16.2%) of 130 patients who underwent EI due to the lack of regression in the degree of reflux and the occurrence of recurrent UTIs.

The demographic information of the patients who had UNC and EI, as well as the VURx, is presented in Table 1. When the UNC and EI groups were compared, age, gender, body mass index, complete blood count, blood creatinine level, incidence of renal scarring, and technetium-99m-labeled dimercaptosuccinic acid are presented in Table 2. Results were not significant.

The comparison of EI and UNC groups according to the degree of reflux in the pre-treatment VCUG revealed that the incidence of grades I—III reflux was 67.7% ($n=88$) in the EI group and 45.6% ($n=57$) in the UNC group. The incidence of grades IV—V reflux was 32.3% ($n=42$) in the EI group and 54.4% ($n=68$) in the UNC group. The grades I—III reflux

Table 1 The demographic information of the patients and VURx.

Variable	Score
Gender	
Girl	1
Boy	0
VUR timing	
Early-moderate filling	3
Late filling	2
Voiding phase	1
Ureteral abnormality	
Yes	1
No	0
VUR incidence	
Grades I–III	0
Grades IV–V	1

VUR, vesicoureteral reflux; VURx, VUR index.

incidence was significant in favor of the EI group, and the grades IV–V reflux incidence was significant for the UNC group ($p<0.001$) (Table 3).

The incidence of unilateral reflux was 69.2% ($n=90$) in the EI group, 32.8% ($n=41$) in the UNC group; the incidence of bilateral reflux was 30.8% ($n=40$) in the EI group, 67.2% ($n=84$) in the UNC group. The incidence of bilateral reflux was statistically significant in favor of the UNC group ($p<0.001$) (Table 3).

While 56.2% ($n=73$) of the patients in the EI group had reflux in the VCUG during the voiding phase, 56.0% ($n=70$) of the patients in the UNC group had reflux in the filling phase. There was no statistical significant difference between the two groups in terms of the time of reflux on voiding cystography ($p=0.138$) (Table 3).

The prevalence of constipation was 17.7% ($n=23$) in the EI group, and 26.4% ($n=33$) in the UNC group. There was not any statistically significant difference between both

Table 3 Comparative results of EI and UNC groups.

Variable	EI ($n=130$)	UNC ($n=125$)	p-Value
Location			<0.001
Right	36 (27.7)	15 (12.0)	
Left	54 (41.5)	26 (20.8)	
Bilateral	40 (30.8)	84 (67.2)	
Bilateral reflux			<0.001
No	90 (69.2)	41 (32.8)	
Yes	40 (30.8)	84 (67.2)	
Constipation			0.093
No	107 (82.3)	92 (73.6)	
Yes	23 (17.7)	33 (26.4)	
Urinary incontinence[a]			<0.001
No	96 (75.0)	33 (26.8)	
Yes	32 (25.0)	90 (73.2)	
Reflux incidence			<0.001
Low-grade	88 (67.7)	57 (45.6)	
High-grade	42 (32.3)	68 (54.4)	
Reflux time			0.138
Voiding phase	73 (56.2)	55 (44.0)	
Filling phase	57 (43.8)	70 (56.0)	

EI, endoscopic injection; UNC, ureteroneocystostomy.
Note: data are presented as *n* (%).
[a] Information regarding urinary incontinence could not be obtained in the post-procedure follow-up of a total of four patients.

Table 2 Findings of the patients who had EI and UNC because of primary vesicoureteral reflux.

Variable	EI ($n=130$)	UNC ($n=125$)	p-Value
Age, month	68.0 (13.0–190.0)	72.0 (25.0–204.0)	0.835
Distribution age			0.801
≤24 months	18 (13.8)	0	
>24 months	112 (86.2)	125 (100.0)	
Height, cm	116.1±21.5	112.5±22.5	0.191
Weight, kg	28.5±12.9	24.6±11.9	0.120
BMI, kg/m^2	20.07 (11.11–21.67)	16.64 (12.10–19.67)	0.175
Gender			0.110
Boy	36 (27.7)	24 (19.2)	
Girl	94 (72.3)	101 (80.8)	
Hemoglobin, g/dL	11.9±1.3	12.2±1.5	0.139
Blood urea nitrogen, mg/dL	12.9±8.1	14.2±8.2	0.160
Blood creatinine, mg/dL	0.5±0.5	0.5±0.4	0.958
Renal scarring incidence			0.428
No	73 (56.2)	64 (51.2)	
Yes	57 (43.8)	61 (48.8)	
Kidney function distribution, %			
Right kidney	51.6±20.1	49.6±21.3	0.610
Left kidney	48.4±20.1	50.1±21.2	0.748

EI, endoscopic injection; UNC, ureteroneocystostomy; BMI, body mass index.
Note: data are presented as median (range), *n* (%), or mean±standard deviation.

groups for constipation prevalence ($p=0.093$). The incidence of urinary incontinence concomitant with constipation was 25.0% ($n=32$) in the EI group and 73.2% ($n=90$) in the UNC group. The incidence of urinary incontinence concomitant with constipation was statistically significant in favor of the UNC group ($p<0.001$) (Table 3).

The mean UDR in grades I–III reflux cases was 0.14 (SD 0.06) in the EI group and 0.19 (SD 0.09) in the UNC group; in grades IV–V reflux cases, it was calculated as 0.21 (SD 0.09) in the EI group and 0.26 (SD 0.08) in the UNC group. The UDR was significant in favor of the group UNC when EI and UNC groups were compared ($p<0.001$) (Table 4 and Fig. 1).

The receiver operator characteristic curve analysis revealed good discriminatory power for UDR in predicting units, with an area under the curve of 0.750 (95% confidence interval [CI]: 0.690–0.810, $p<0.001$) (Fig. 2). The optimal cut-off for the UDR was obtained as 0.17 with a sensitivity and specificity of 73.0% and 63.0%, respectively. The positive and negative predictive values were 66.0% and 70.0%, respectively.

The mean UDR value of 21 patients who had UNC due to reflux that did not improve in the follow-up after EI treatment was calculated as 0.25 (SD 0.12).

The mean VURx score in grades I–III reflux patients was 2.4 (SD 0.7) in the EI group and 2.6 (SD 0.7) in the UNC group; it was calculated as 3.5 (SD 0.7) in the EI group of grades IV–V reflux patients and 3.9 (SD 0.7) in the UNC group. The VURx was significant in favor of the UNC group when EI and UNC groups were compared for VURx ($p<0.001$) (Table 4).

As a result of multivariate logistic regression analysis of the findings of 21 patients who had UNC during follow-up after EI treatment, bilateral reflux (OR=4.90, 95% CI: 2.45–9.79, $p<0.001$), presence of urinary incontinence (OR=8.88, 95% CI: 4.45–17.76, $p<0.001$), and UDR ($\geq$0.17) (OR=5.53, 95% CI: 2.62–11.66, $p<0.001$) were important factors for UNC (Table 5).

Table 5 Multivariate logistic regression analysis results of the patients who had UNC after EI ($n=21$).

Variable	OR (95% CI)	p-Value
Age (>24 months)	0.99 (0.37–2.64)	0.981
Gender (girl)	2.09 (0.87–5.03)	0.099
Bilateral reflux	4.90 (2.45–9.79)	<0.001
Urinary incontinence	8.88 (4.45–17.76)	<0.001
UDR ($\geq$0.17)	5.53 (2.62–11.66)	<0.001
VUR (high-grade)	1.67 (0.73–3.81)	0.223
Constipation	1.06 (0.46–2.45)	0.888
Reflux time (filling)	0.51 (0.23–1.14)	0.100

OR, odds ratio; CI, confidence interval; UNC, ureteroneocystostomy; EI, endoscopic injection; UDR, ureteral diameter ratio; VUR, vesicoureteral reflux.

4. Discussion

A review of the literature has highlighted the need for individualized and selective treatment in the treatment of children with VUR during the last decade [6]. While the current VUR grading system mainly focuses on the radiographic appearance of the upper tract, primary VUR treatment success depends on the structure of the ureterovesical junction. The UDR which is used to measure the vesicoureteral structure more objectively has become one of the most researched parameters in recent years for predicting surgical outcomes as well as spontaneous regression or resolution of reflux [7–9].

Helmy et al. [9] reported that UDR alone was superior to the degree of reflux in predicting EI success. The same study showed a significant relationship between the EI success rate and UDR, and reported that the degree of reflux was not a significant predictor of success after EI. Arlen et al. [10] reported an increased permanent VUR score by 2.6 for increased UDR.

Mendez et al. [11] in their study evaluating clinical factors for successful endoscopic correction of primary VUR, reported that UDR is the main factor determining outcome. Cooper et al. [12] reported that 2.4 times more surgical intervention is required in case of increased UDR in primary reflux.

In our study, UDR was found to be significantly lower in EI group than in UNC group (Fig. 1). In addition, UDR was significantly higher in patients who failed injection therapy and underwent open surgery ($p<0.001$). Our study revealed that UDR was significant in favor of the UNC group in cases of low-grade and high-grade primary VUR who underwent EI and UNC ($p<0.001$). In our study, the optimal cut-off for the distal UDR was obtained as 0.17. Sensitivity was 73.0% and specificity was 63.0%; positive and negative predictive values were 66.0% and 70.0%, respectively (Fig. 2).

Reflux occurring earlier at the beginning of the bladder filling phase of VCUG has been associated with anatomically inadequate ureteral orifices [13]. Reflux detected in the early phase during VCUG has lower resolution rates [14].

Table 4 VURx score and UDR comparison between EI and UNC groups.

Variable	EI			UNC		
	Grades I–III	Grades IV–V	p-Value	Grades I–III	Grades IV–V	p-Value
VURx score	2.4±0.7	3.5±0.7	<0.001	2.6±0.7	3.9±0.7	<0.001
UDR	0.14±0.06	0.21±0.09	<0.001	0.19±0.09	0.26±0.08	<0.001
UDR			<0.001			<0.001
<0.17	67 (76.1)	14 (33.3)		27 (47.4)	7 (10.3)	
≥0.17	21 (23.9)	28 (66.7)		30 (52.6)	61 (89.7)	

VUR, vesicoureteral reflux; VURx, VUR index; EI, endoscopic injection; UNC, ureteroneocystostomy; UDR, ureter diameter ratio.
Note: data are presented as mean±standard deviation or n (%).

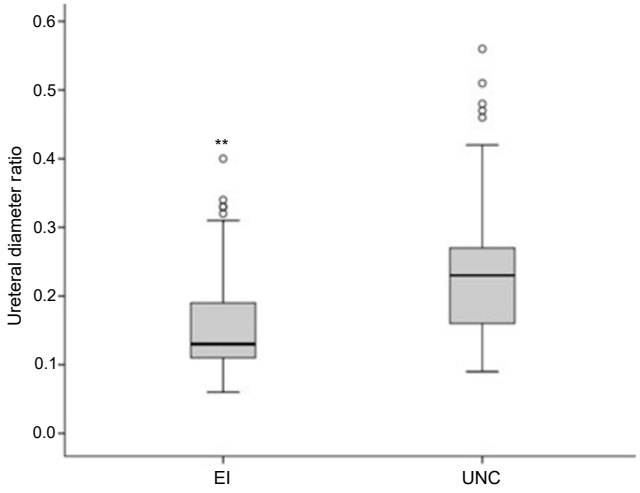

Figure 1 The box plot of ureteral diameter ratio in UNC and EI groups. UNC, ureteroneocystostomy; EI, endoscopic injection. ** $p<0.001$.

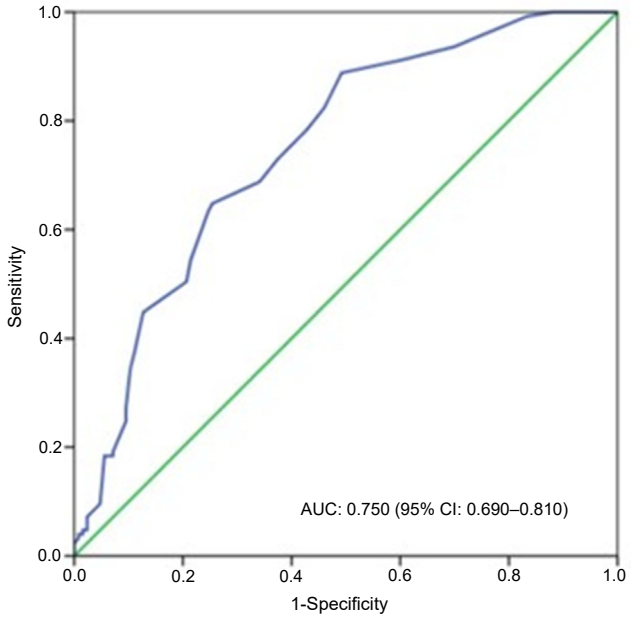

Figure 2 The receiver operating characteristic curve analysis of ureter diameter ratio predicts ureteroneocystostomy AUC. AUC, area under the curve; CI, confidence interval.

In our study, although the time to detect reflux was higher in the UNC group in both the filling phase and the voiding phase in the EI group, there was no statistical difference between the two groups ($p=0.138$) (Table 3).

Han et al. [15] reported that the success rate of EI was 3.2 times higher in patients with reflux in the voiding phase. Lee et al. [16] suggested that high-grade VUR patients with reflux during the voiding phase may experience a similar success rate for EI compared with low-grade VUR patients.

The VURx is a simple computational index that includes initial voiding cystography finding, patient sex, and reliably predicts resolution and spontaneous resolution of primary reflux in children [15]. Kirsch et al. [14] showed that the VURx significantly predicted the time to radiological VUR resolution. The reflux recovery rate was reported as 11.1% in patients with a VURx score of 5–6 and 88.9% in patients with a VURx score of 2–4 [14]. One study reported earlier surgical treatment in patients with a high VURx score [17].

In our study, when the VURx results of low-grade and high-grade VUR patients in the EI and UNC groups were compared, it was shown that the VURx score was significantly higher in favor of the UNC group ($p<0.001$) (Table 4).

The term bladder–bowel dysfunction (BBD) is used to describe lower urinary tract symptoms accompanying bowel discomfort, such as constipation and/or encopresis [18]. In a meta-analysis of the literature, the prevalence of BBD was found to be higher in UTI patients without VUR than in the general population [19,20].

Also, there was a strong association between recurrent UTI and BBD. Patients with primary VUR with BBD have a higher risk of UTI than patients with VUR alone [21]. The American Urological Association guidelines on primary VUR management have shown that the presence of BBD significantly delays the healing of VUR [22,24]. The Swedish study showed that patients with both VUR and BBD are at increased risk of kidney damage after treatment and their association should be investigated in patients with VUR [23,24].

Although there was no statistically significant difference in the incidence of constipation between the two groups in our study ($p=0.093$), the incidence of urinary incontinence was significant in favor of the UNC group ($p<0.001$).

Furthermore, as a result of multivariate logistic regression analysis, bilateral reflux, presence of urinary incontinence, and higher UDR were important factors for UNC (Table 5).

5. Study limitations

Our study has a few deficiencies and limitations. Our study was designed as retrospective and had limited number of patients. We believe that the result of the evaluation of the distal UDR and VURx together in pediatric patients diagnosed with primary VUR requires a prospective study with a larger number of patients to draw an exact conclusion.

6. Conclusion

The optimum management of the patients with primary VUR remains to be contradictory. The decision of which patient group would benefit from conservative treatment and which group would need surgical treatment is the most important part of management. When the increased distal UDR and VURx are evaluated together for surgical treatment of primary VUR in the pediatric group, it is believed that it may be useful in prediction of the clinical course of the disease and evaluation of the surgical treatment options.

Author contributions

Study conceptand design: Yusuf Atakan Baltrak, Nebil Akdoğan, Nihat Satar.
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Conflicts of interest

The authors declare no conflict of interest.

References

[1] Stull TL, LiPuma JJ. Epidemiology and natural history of urinary tract infections in children. Med Clin 1991;75:287—97.
[2] Stephens FD, Lenaghan D. The anatomical basis and dynamics of vesicoureteral reflux. J Urol 1962;87:669—80.
[3] Cooper CS, Birusingh KK, Austin JC, Knudson MJ, Brophy PD. Distal ureteral diameter measurement objectively predicts vesicoureteral reflux outcome. J Pediatr Urol 2013;9:99—103.
[4] Swanton AR, Arlen AM, Alexander SE, Kieran K, Storm DW, Cooper CS. Inter-rater reliability of distal ureteral diameter ratio compared to grade of VUR. J Pediatr Urol 2017;13:207.e1—5. https://doi.org/10.1016/j.jpurol.2016.10.021.
[5] Biočić M, Todorić J, Budimir D, Cvitković Roić A, Pogorelić Z, Jurić I, et al. Endoscopic treatment of vesicoureteral reflux in children with subureteral dextranomer/hyaluronic acid injection: a single-centre, 7-year experience. Can J Surg 2012;55:301—6.
[6] Cooper CS, Birusingh KK, Austin JC, Knudson MJ, Brophy PD. Distal ureteral diameter measurement objectively predicts vesicoureteral reflux outcome. J Pediatr Urol 2013;9:99—103.
[7] Estrada CR Jr, Passerotti CC, Graham DA, Peters CA, Bauer SB, Diamond DA, et al. Nomograms for predicting annual resolution rate of primary vesicoureteral reflux: results from 2462 children. J Urol 2009;182:1535—41.
[8] Arlen AM, Alexander SE, Wald M, Cooper CS. Computer model predicting break through febrile urinary tract infection in children with primary vesicoureteral reflux. J Pediatr Urol 2016;12:e1—5. https://doi.org/10.1016/j.jpurol.2016.03.005.
[9] Helmy T, Sharaf D, AbdelHalim A, Hafez A, Dawaba M. Can distal ureteral diameter predict reflux resolution after endoscopic injection? Urology 2015;85:896—9.
[10] Arlen AM, Kirsch AJ, Leong T, Cooper CS. Validation of the ureteral diameter ratio for predicting early spontaneous resolution of primary vesicoureteral reflux. J Pediatr Urol 2017;13:e1—6. https://doi.org/10.1016/j.jpurol.2017.01.012.
[11] Mendez R, Somoza I, Tellado MG, Liras J, Sanchez A, Pais E, et al. Predictive value of clinical factors for successful endoscopic correction of primary vesicoureteral reflux grades III—IV. J Pediatr Urol 2006;2:545—50.
[12] Cooper CS, Alexander SE, Kieran K, Storm DW. Utility of the distal ureteral diameter on VCUG for grading VUR. J Pediatr Urol 2015;11:183. e1—6. https://doi.org/10.1016/j.jpurol.2015.04.009.
[13] Arlen AM, Broderick KM, Huen KH, Leong T, Scherz HC, Kirsch AJ. Temporal pattern of vesicoureteral reflux on voiding cysto urethrogram correlates with dynamic endoscopic hydro distention grade of the ureteral orifice. J Urol 2014;192:1503—7.
[14] Kirsch AJ, Arlen AM, Leong T, Merriman LS, Herrel LA, Scherz HC, et al. Vesicoureteral reflux index (VURx): a novel tool to predict primary reflux improvement and resolution in children less than 2 years of age. J Pediatr Urol 2014;10:1249—54.
[15] Han DS, Cambareri G, Alagiri M, Chiang G. Reflux timing is a predictor of successful endoscopic treatment of vesicoureteral reflux. Urology 2019;124:237—40.
[16] Lee JN, Lee SM, Ha YS, Kim BS, Kim HT, Kim TH, et al. VUR timing on VCUG as a predictive factor of VUR resolution after endoscopic therapy. J Pediatr Urol 2016;12:e16. https://doi.org/10.1016/j.jpurol.2016.04.002.
[17] Garcia-Roig M, Ridley DE, Mc CrackenC, Arlen AM, Cooper CS, Kirsch AJ. Vesicoureteral reflux index: predicting primary vesicoureteral reflux resolution in clinic diagnosed after age 24 months. J Urol 2017;197:1150—7.
[18] Vaz GT, Vasconcelos MM, Oliveira EA, Ferreira AL, Magalhães PG, Silva FM, et al. Prevalence of lower urinary tract symptoms in school-age children. Pediatr Nephrol 2012;27:597—603.
[19] Conway PH, Cnaan A, Zaoutis T, Henry BV, Grundmeier RW, Keren R. Recurrent urinary tract infections in children: risk factors and association with prophylactic antimicrobials. JAMA 2007;298:179—86.
[20] Van Gool JD, Hjälmås K, Tamminen-Möbius T, Olbing H. Historical clues to the complex of dysfunctional voiding, urinary tract infection and vesicoureteral reflux. The ınternational reflux study in children. J Urol 1992;148:1699—702.
[21] Yang S, Chua ME, Bauer S, Wright A, Brandström P, Hoebeke P, et al. Diagnosis and management of bladder bowel dysfunction in children with urinary tract infections: a position statement from the International Children's Continence Society. Pediatr Nephrol 2018;33:2207—19.
[22] Mattoo TK, Chesney RW, Greenfield SP, Hoberman A, Keren R, Mathews R, et al. RIVUR trial investigators. Renal scarring in the randomized intervention for children with vesicoureteral reflux (RIVUR) trial. Clin J Am Soc Nephrol 2016;11:54—61.
[23] Läckgren G, Cooper CS, Neveus T, Kirsch AJ. Management of vesicoureteral reflux: what have we learned over the last 20 years? Front Pediatr 2021;9:650326. https://doi.org/10.3389/fped.2021.650326.
[24] RIVUR trial investigators; Hoberman A, Greenfield SP, Mattoo TK, Keren R, Mathews R, Pohl HG, et al. Antimicrobial prophylaxis for children with vesicoureteral reflux. N Engl J Med 2014;370:2367—76.