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RESEARCH ARTICLE / *ARAŞTIRMA MAKALESİ*

Can Impaired Distal Ureteral Contraction Detected by Urinary Ultrasonography Indicate Presence of VUR?

Üriner Ultrasonografide Tespit Edilen Bozulmuş Distal Üreter Kontraksiyonu Vezikoüreteral Reflüyü Gösterebilir mi?

Avni Merter Keçeli[1], Muhammet İrfan Dönmez[2]

[1]Ankara Bilkent City Hospital, Department of Pediatric Radiology, Ankara, Turkiye
[2]Istanbul Faculty of Medicine, Department of Urology, İstanbul, Turkiye

ORCID ID: A.M.K. 0000-0002-9412-6733; M.İ.D. 0000-0002-2828-7942

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ABSTRACT

Objective: The aim of this study was to determine if impaired distal ureteral contraction detected by urinary ultrasonography (US) could predict presence of vesicoureteral reflux (VUR).

Materials and Methods: A Retrospective analysis of patients' files between November 2016 and September 2020 was performed. A total of 248 children with demonstrated VUR on voiding cystourethrogram (VCUG) and who underwent urinary US within one week of the VCUG examination were included in the study. The degree of hydronephrosis was classified as per Society for Fetal Urology grading system and grading of VUR was done by the International Reflux Study Group grading system. The impaired distal ureteral contraction was defined as the reduced movement of the distal ureter as well as the deficiency of urine discharge into the bladder.

Results: There was a significant correlation between the grade of VUR and the grade of hydronephrosis (p=0.0028). Also, the presence of distal ureteral dilation was related to increasing grades of VUR (p=0.001). The impaired distal ureteral contraction was present only in children with dilating VUR (grades III IV V) while its relationship between VUR grade was significantly high for grades IV and V VUR (p=0.001).

Conclusion: In children, the impaired distal ureter contraction as well as the increase of grades of hydronephrosis, and the presence of distal ureteral dilation may aid decision-making in terms of requesting VCUG to detect dilating VUR.

Keywords: VUR, VCUG, ultrasonography, children, radiation exposure

ÖZ

Amaç: Bu çalışmanın amacı, üriner ultrasonografi (US) ile saptanan bozulmuş distal üreter kontraksiyonunun vezikoüreteral reflü (VUR) varlığını tahmin edip edemeyeceğini belirlemekti.

Gereç ve Yöntem: Kasım 2016 ile Eylül 2020 arasındaki hasta dosyalarının retrospektif analizi yapıldı. İşeme sistoüretrogramında (VCUG) VUR gösterilen ve VCUG muayenesinden sonraki bir hafta içinde üriner US yapılan toplam 248 çocuk çalışmaya dahil edildi. Hidronefroz derecesi, Society for Fetal Urology derecelendirme sistemine göre sınıflandırıldı ve VUR derecelendirmesi, International Reflux Study Group derecelendirme sistemine göre yapıldı. Bozulmuş distal üreter kontraksiyonu, distal üreterin hareketinin azalması ve mesaneye idrar çıkışının olmaması olarak tanımlandı.

Bulgular: VUR derecesi ile hidronefroz derecesi arasında anlamlı bir ilişki vardı (p=0,0028). Ayrıca distal üreter dilatasyonu varlığı artan VUR derecesi ile ilişkiliydi (p=0,001). Bozulmuş distal üreter kontraksiyonu sadece dilate VUR'lu (derece III-V) çocuklarda mevcutken, derece IV ve VUR için VUR derecesi arasındaki ilişki anlamlı olarak yüksekti (p=0,001).

Sonuç: Çocuklarda bozulmuş distal üreter kontraksiyonu, artan hidronefroz dereceleri ve distal üreter dilatasyonunun varlığı, dilatasyon yapan VUR'u saptamak için VCUG talep etme konusunda karar vermeye yardımcı olabilir.

Anahtar Kelimeler: Vezikoüreteral reflü, ultrasonografi, üreteral kontraksiyon

Corresponding Author/Sorumlu Yazar: Muhammet İrfan Dönmez **E-mail:** m_irfan83@yahoo.com

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INTRODUCTION

Vesicoureteral reflux (VUR) is described as the non-physiologic retrograde flow of urine from the bladder to the ureter, renal pelvis, and collects system during filling of the bladder or micturition, and it is closely related to urinary tract infections (UTI). Also, reflux nephropathy is one of the common causes of renal failure in children. Thus, early diagnosis of VUR is important to prevent its consequences such as recurrent febrile UTIs requiring hospitalization and subsequent renal scarring (1,2).

The American Academy of Pediatrics (AAP) 2016 guidelines do not recommend performing voiding cystourethrography (VCUG) in the absence of sonographic findings after the first febrile UTI. It is stated that VCUG is required after a febrile UTI if hydronephrosis, renal scar formation, and/or ureteral dilatation in urinary ultrasonography (US) is present in children between 2 and 24 months (3). Likewise, there are studies suggesting that the US may be used as a screening method (4,5). On the other hand, some studies reveal the risks that may occur in children that do not undergo VCUG after the first febrile UTI (6,7).

The US is a non-invasive method to evaluate the size, contour, parenchyma, and collecting system of the kidney. Mild to moderate hydronephrosis can be seen in urinary tract infections however, this may or may not be accompanied by VUR. While the US is a safe method, it is not diagnostic for VUR and, VCUG or radionuclide studies should be performed for a definitive diagnosis of VUR (8).

The shortening of the longitudinal muscle layer in the submucosal and transmural part of the ureter with active contraction ensures the transmission of urine from the ureter to the bladder. Functional and structural changes of the distal end of the ureter disrupt of the active valve mechanism in the vesicoureteral junction (9,10). Defective development in the distal end of the ureter and dysplasia, atrophy, or structural irregularity in smooth muscle cells at the lower end of the ureter may be the underlying reasons for the development of vesicoureteral reflux (11).

Urine is transported through the ureter via rhythmic contractions that are initiated at the renal pelvis by the pacemaker atypical smooth muscle cells and maintained by more distally located interstitial Cajal cells (12). Loss of Cajal cells at the vesicoureteral junction causes uncoordinated contractions in the distal ureter resulting in disturbance of the anti-reflux mechanism. These impaired distal ureteral contractions can be defined as the reduced movement of the ureter in addition to the lack of urine discharge in the bladder may be observed by the US. Subsequently, impaired ureteral contraction and pressure changes in patients with higher grades of VUR are shown in manometric studies (13,14).

In this study, we aimed to investigate the diagnostic value of impaired distal ureter contraction and the presence and degree of hydronephrosis detected by the US in the children with confirmed VUR diagnosis.

MATERIALS AND METHODS

After obtaining the approval of the local ethics committee (2021/3222), the hospital records of patients (aged 0-15 years) who underwent VCUG examination in our radiology department between November 2016 and September 2020 were retrospectively re-evaluated. 332 children underwent the urinary US within one week before VCUG. In this group, children with ureteropelvic or ureterovesical junction obstruction, ectopic ureter, genitourinary anomalies such as hypospadias or epispadias, posterior urethral valve, previous surgery on the urinary system, history of urogenital trauma, renal scars, congenital or acquired renal parenchymal disease, and dysplastic kidney were excluded from the study. US examinations that had been performed when the bladder was empty or insufficiently filled (less than half of the estimated bladder capacity for age) and VCUG examinations that were not performed following the institutional protocol were excluded. Thus, the total number of VCUGs included in the study was 248. Each kidney of each participant was counted as a single urinary unit. As a result, the number of urinary units examined was 496.

Reassessment of VCUG examination images obtained from hospital records were done by the joint decision of a pediatric radiologist and a pediatric urologist. Hydronephrosis and distal ureter findings were reviewed and recorded after the re-evaluation of US examination reports, most of which was made by the same pediatric radiologist or other general radiologists of the same imaging department. Reflux grading was done by using the International VUR Grading System (15). The degree of hydronephrosis in the US reports was stated as per the Society of Fetal Urology Association (SFU) System (16).

Intact distal ureteral contraction was described upon dynamic evaluation of the distal ureter within 1 minute in the longitudinal plane, which was stated as a distally movement of the ureter and a flow into the bladder. The presence or absence of ureteral dilatation and the presence/absence of glare indicating the passage of urine from the ureter to the bladder due to non-rhythmic movement of the distal ureter (lower 1/3 of the ureter) described in imaging reports were recorded. In our radiology protocol, when the urine jet flowed from the lower ends of the ureter into the bladder could not be determined on a grayscale US, it is re-evaluated with Color Doppler US. However, this finding was not graded.

The ureteral dysfunction was evaluated together with the presence and grade of hydronephrosis. The grade of HN specified in the US was determined separately from both kidneys. The distal ureteral width was not included in the parameters since the width of the lower end of the ureter in our department had not been reported with metric values regularly in all US reports. Similarly, the anteroposterior diameter measurement of the renal pelvis, which is used for hydronephrosis evaluation in the US, was not included in the parameters since it has not been described standardized in the radiological reports most of the time.

Table 1: The distribution and relationship between the grade of hydronephrosis (as per SFU grading system) and the grade of VUR.

			SFU Grade of Hydronephrosis					*p
			0	1	2	3	4	
Grade of VUR	0	N	153	13	27	26	9	***0.001***
		%	67.1%	5.7%	11.8%	11.4%	3.9%	
	1	N	44	0	1	0	0	
		%	97.8%	0.0%	2.2%	0.0%	0.0%	
	2	N	13	29	10	3	0	
		%	23.6%	52.7%	18.2%	5.5%	0.0%	
	3	N	11	22	36	36	0	
		%	10.5%	21.0%	34.3%	34.3%	0.0%	
	4	N	0	6	22	14	4	
		%	0.0%	13.0%	47.8%	30.4%	8.7%	
	5	N	0	0	1	5	11	
		%	0.0%	0.0%	5.9%	29.4%	64.7%	
	**p		***0.001***	***0.001***	***0.001***	***0.001***	*0.197*	

** Significance level according to the results of the chi-square test*
*** Significance levels according to one sample Chi-square test results*

The Power (Power of Test) for each variable was determined by taking at least 80% and Type-1 error as 5%. The statistical significance level was taken as (α) 5%. Categorical variables were expressed as numbers and percentages. The Chi-square test was used to detect the relationship between categorical variables. For statistical analysis, IBM SPSS for Windows (ver. 24) and Minitab (Statistical Software for Windows, ver.17) were used.

RESULTS

One hundred and sixty (64.5%) of the children were girls and 88 (35.5%) were boys. The age range was between 1 month and 15 years (mean age: 6 ± 2.12 years; median age: 7 years). Of the total 496 renal units, 268 (54%) had VUR. In 268 urinary units with VUR, 45 were grade I (17%), 55 were grade II (20%), 105 were grade III (%39), 46 were grade IV (18%), and 17 were grade V (%6) VUR. The presence of hydronephrosis was detected in 275 urinary units in the US. Among patients with VUR, 70 had grade I HN (25%), 97 had grade II HN (36%), 84 had grade III HN (30%), and 24 had grade IV HN (9%). No hydronephrosis was present in 221 (44.5%) renal units and no VUR was detected in 153 renal units (69%) in this group (Table 1). On the other hand, 68 renal units had VUR on VCUG but no hydronephrosis, non-rhythmic movement of the distal ureter, and absence of a urine jet stream from the lower end of the ureter to the bladder (impaired distal ureteral contraction) in the US.

In patients without VUR, no distal ureteral dilation was present in 212 (93%). In addition, distal ureteral dilation was not found in 191 patients (43%) with VUR (Table 2). However, there was a correlation between distal ureteral dilation and the degree of hydronephrosis (p<0,05).

Impaired distal ureteral contraction was not detected in patients without VUR or those with grade I and II VUR. However, the impaired distal ureteral contraction was associated with dilating VUR (grade III-V). In addition, there was a statistically significant relationship between impaired distal ureteral contraction and grade IV & V VUR (p<0.05) (Tables 3-4). In multiple regression analyses based on VUR grading, hydronephrosis grade and impaired distal ureteral contraction were better in predicting VUR when compared to distal ureteral dilation (Table.4).

Table 2: Distribution and relationship between distal ureteral dilation and grade of VUR.

			Distal Ureteral Dilation		*p
			No	Yes	
Grade of VUR	0	N	212	16	***0.001***
		%	93.0%	7.0%	
	1	N	45	0	
		%	100.0%	0.0%	
	2	N	54	1	
		%	98.2%	1.8%	
	3	N	82	23	
		%	78.1%	21.9%	
	4	N	10	36	
		%	21.7%	78.3%	
	5	N	0	17	
		%	0.0%	100.0%	
	**p.		***0.001***	***0.001***	

** Significance level according to the results of the chi-square test*
*** Significance levels according to one sample Chi-square test results*

Table 3: The distribution and relationship between impaired distal ureteral contraction and grade of VUR.

			Impaired Distal Ureteral Contraction		*p
			No	Yes	
Grade of VUR	0	N	228	0	
		%	100.0%	0.0%	
	1	N	45	0	
		%	100.0%	0.0%	
	2	N	55	0	
		%	100.0%	0.0%	
	3	N	96	9	***0.001***
		%	91.4%	8.6%	
	4	N	21	25	
		%	45.7%	54.3%	
	5	N	3	14	
		%	17.6%	82.4%	
	**p.		***0.001***	***0.005***	

** Significance level according to the results of the chi-square test*
*** Significance levels according to one sample Chi-square test results*

With regards to the use of the US in VUR, a previous study reported that hydronephrosis defined in the US performed with a full bladder can be used in the prediction of grade V VUR (17). In the same study, it showed that the power of the examination was increased as the fullness of the bladder increases. Under the US protocol, all our participants were examined with at least half full bladder (expected volume per age). However, it should be noted that the effect of bladder fullness findings and diagnosis was not investigated in this study.

In another study, the researchers obtained normal US results in 4 of 8 patients with grade V VUR and 27 of 37 participants with grade IV VUR (6). In another study evaluating hydronephrosis and distal ureter width, the normal US rates in the presence of high-grade VUR were determined as 9% for stage V and 39% for stage IV (18). The results of our study supported that hydronephrosis was a helpful finding in the presence of high-grade VUR (grades IV-V).

As previously stated, functional and anatomical problems contributed to the etiology of vesicoureteral junction problems in children. Accordingly, distal ureter dilation and impaired distal ureteral contraction might be considered as a relatively reliable indicators of vesicoureteral junction problems. Our

Table 4: Multiple regression analysis results (grade of VUR as the dependent factor)

Model	Unstandardized Coefficients		Standardized Coefficients	t	p.	95.0%CI.	
	B	Std. Error	Beta			Lower	Upper
(Constant)	0.756	0.078		9.745	***0.001***	0.604	0.909
Grade of Hydronephrosis	0.389	0.054	0.317	7.188	***0.001***	0.283	0.496
Distal Ureteral Dilatation	0.495	0.219	0.121	2.255	***0.025***	0.064	0.926
Impaired Distal Ureteral Contraction	1.661	0.260	0.307	6.387	***0.001***	1.150	2.172
Summary							
R		R^2	*Adjusted* R^2		*Anova p.*		
0.629		*0.395*	*0.392*		*0.001*		

DISCUSSION

VCUG is the most commonly used method to diagnose VUR. However, this method is invasive and hazardous due to bladder catheterization and ionizing radiation. Further, VUR can be detected in 35% of children with febrile UTIs. Therefore, it is recommended that children with UTI should be evaluated with noninvasive methods such as the US beforehand (3).

This study investigated the value of sonographic findings, including the presence and grade of hydronephrosis, distal ureteral dilation, and impaired distal ureteral contraction in predicting VUR. In radiology practice, evaluation of the distal ureter is usually overlooked in the urinary US. In our imaging unit, distal ureteral evaluation has been standardized since 2015 and it is included in the reports. Therefore, distal ureter findings are considered reliable.

results indicated that impaired distal ureteral contraction may be used as a surrogate for the diagnosis of possible VUR. Multiple regression analysis revealed that impaired distal ureter contraction and presence of hydronephrosis are stronger findings than distal ureteral dilatation in the prediction of VUR (Table 4). In other words, impaired distal ureteral contraction seems to be a better determinator, especially in high-graded VUR whereas distal ureteral dilation may be a more prominent sign with increasing grades of VUR. Our results indicated that the distal ureteral contraction might be included in the US protocols to increase the sensitivity of US for the susception of VUR.

In the study by Nelson et al. (19) investigating the value of US in VUR screening in children with UTI younger than 60 months;

US findings were found to be normal in 75% of the patients. In the group of patients limited by the presence of UTI, US findings were abnormal in only 5% of patients in the presence of VUR. When evaluating in terms of the presence and stage of hydronephrosis in the prediction of VUR, the results of our study did not support the results of the mentioned study, like many studies.

This study has some limitations. Firstly, the number of examined urinary units remained lower than in many previous studies. The exclusion of patients with insufficient bladder fullness, those who did not undergo the interpretation of the ureter, and those from whom the sonographic and fluoroscopic examinations were not obtained under the appropriate protocol decreased the number of participants in the study. Moreover, the measurement of the intramural ureter would have provided further information on the assessment of patients with suspected VUR. These were regarded as handicaps of a retrospective study and possible unintended selection bias might have occurred. Also, the bladder volume during the examination was not routinely calculated in reports. Additionally, interobserver variability was an issue even though US and VCUG examinations were performed with a standard protocol.

CONCLUSION

Our study showed that sonographic parameters could be used as a guide in VUR screening. Hydronephrosis, distal ureteral dilation, and impaired distal ureter contraction defined in the US were useful in determining the presence of VUR as the grade of VUR advances. Considering these parameters while carrying out urinary US in clinical suspicion of VUR and if present, performing VCUG even after the first febrile UTI may reduce comorbidities related to late diagnosis.

Ethics Committee Approval: This study was approved by the Necmettin Erbakan University Ethics Committee 2021/3222 (07.05.2021).

Informed Consent: Written consent was obtained from the participants.

Peer Review: Externally peer-reviewed.

Author Contributions: Conception/Design of Study- A.M.K., M.İ.D.; Data Acquisition- A.M.K., M.İ.D.; Data Analysis/Interpretation- A.M.K., M.İ.D.; Drafting Manuscript- A.M.K., M.İ.D.; Critical Revision of Manuscript- A.M.K., M.İ.D.; Final Approval and Accountability- A.M.K., M.İ.D.

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