The Role of Videourodynamic Studies in Diagnosis and Management of Vesicoureteral Reflux

Vezikoüreteral Reflünün Tanısı ve Takibinde Videoürodinamik Çalışmaların Rolü

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ABSTRACT Objective: Increased incidence of lower urinary tract dysfunction (LUTD) has been reported in older children with vesicoureteral reflux (VUR), and its treatment affects patient outcome. The optimal initial imaging method is often difficult for clinicians to select in this patient group. The aim of the study was to investigate the value of videourodinamic studies (VUD) in the detection and management of VUR in children with recurrent urinary tract infections and lower urinary tract symptoms such as urge, urge incontinence, weak stream, and frequency. **Material and Methods:** The study included 117 children with 234 kidney-ureter units (KUUs). The clinical patient records of DMSA scintigraphy, voiding cystouretrography (VCUG), and VUD were reviewed retrospectively. **Results:** Vesicoureteral reflux was identified in 108 of 234 KUUs (46%). In 55% of refluxing KUUs, VUR was exhibited by both techniques while 25% of refluxing KUUs were exhibited by only VCUG, and 19% of refluxing KUU by only VUD. Bladder instability was detected in 55 of 74 (74%) patients with VUR, and in 34 of 43 (79%) patients without VUR. There was moderate concordance in the diagnosis of VUR by VUD and VCUG (κ=0.55±0.05), but the difference in reflux detection rate between VUD and VCUG was not statistically significant (p=0.47). **Conclusion:** Our findings indicated that VUD and VCUG techniques exhibit equal reliability in the diagnosis of VUR, and VUD provides additional information concerning LUTD.

Key Words: Vesico-ureteral reflux; urinary tract infections; urinary bladder, neurogenic

ÖZET Amaç: Vezikoüreteral reflüsü (VUR) olan büyük çocuklarda alt üriner sistem disfonksiyonu insidansı artmıştır ve tedavi edilmesi prognozu etkiler. Klinisyenler için bu hasta grubunda en uygun başlangıç görüntüleme metoduna karar vermek genellikle zordur. Bu çalışmanın amacı, tekrarlayan idrar yolu enfeksiyonu ve idrar kaçırma, zayıf akım ve sık idrara çıkma gibi alt üriner sistem disfonksiyonu semptomları olan çocuklarda videoürodinamik çalışmaların (VUD) VUR tanısı ve tedavisindeki yerini incelemektir. **Gereç ve Yöntemler:** Çalışmada 117 çocuğa ait böbrek-üreter ünitesi (BÜÜ) incelendi. Hastaların DMSA sintigrafisi, işeme sistografisi (VSUG) ve videoürodinami kayıtları retrospektif olarak tekrar değerlendirildi. **Bulgular:** 234 BÜÜ'nin 108 (%46)'inde VUR saptandı. Reflülü BÜÜ'lerinin %55'inde reflü her iki yöntemde de görülürken,%25'inde sadece VSUG'de, %19'unda da sadece VUD'de reflü görülmüştü. Reflüsü olan 74 hastanın 55'inde (%74) ve reflüsü olmayan 43 hastanın 34 (%79)'ünde mesane instabilitesi vardı. Vezikoüreteral reflü tanısı açısından VSUG ve VUD teknikleri birbiri ile orta derecede uyumluydu (κ=0,55±0,05), ancak reflüyü tespit etme oranları açısından istatistiksel olarak anlamlı fark yoktu (p=0,47). **Sonuç:** Bizim bulgularımıza göre VSUG ve VUD teknikleri reflü tanısında eşit derecede güvenilirdir ve VUD mesane fonksiyonu hakkında ilave bilgiler sağlar.

Anahtar Kelimeler: Vezikoüreteral reflü; üriner kanal enfeksiyonları; mesane, nörojenik

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Urinary tract infections (UTIs) can cause significant morbidity, particularly when associated with anatomic abnormalities or lower urinary tract dysfunction (LUTD). Vesicoureteral reflux is the

most commonly associated abnormality, and reflux nephropathy is an important cause of end stage renal disease (ESRD) in children.[1] The role of LUTD in the evaluation and management of VUR is still an active topic of discussion.[2-5] It has been reported that the incidence of detrussor overactivity, higher intravesical pressure, detrussor-sphincter dyssynergia, or incomplete voiding is increased in children with VUR. Moreover, urodynamic abnormality can affect ureterotrigonal structure and cause VUR.[6] Additionally, the presence of LUTD may prevent spontaneous resolution of VUR or may reduce the success of surgical correction. Detection of LUTD is essential in the management of children with VUR.[7] Therefore, it is important to investigate the presence of lower urinary tract symptoms; identification of LUTD is particularly important in patients with recurrent UTI or VUR.

Due to the necessity of invasive procedures, the diagnosis and management of VUR is particularly challenging. Currently, VCUG, the commonly performed diagnostic procedure in children with febrile UTI or recurrent UTI, is considered the gold standard for detection and grading of VUR. In the presence of VUR, VCUG provides detailed anatomic information about bladder, urethra, and ureters. However, this technique does not satisfactorily evaluate LUTD. Videourodynamic study is able to demonstrate detrusor overactivity, increased intravesical pressure, detrusor-sphincter dyssynergia, and incomplete voiding in addition to the presence of reflux. Therefore, the optimal selection of initial technique sometimes remains unclear for clinicians. The primary aim of our study was to investigate the reliability of VUD in the diagnosis of VUR, and to determine whether VUD is the optimal initial technique for patients with recurrent UTIs and voiding dysfunction symptoms.

MATERIAL AND METHODS

This study is a retrospective evaluation of children older than 5 years of age with recurrent urinary tract infections and lower urinary tract symptoms including urge, urge incontinence, weak stream, and increased voiding frequency. We reviewed hospital records of these patients who were admitted to Başkent University Adana Hospital, Pediatric Nephrology Department between 2009 and 2011. One hundred seventeen children (86 girls and 31 boys) were eligible for the study. The mean age was 8.4±2.9 (min 5-max 11) years. DMSA renal scan was obtained from all of the patients to assess renal cortical abnormalities. Hypoactive areas, contour defects and low differential renal function (<45%) were defined as renal cortical abnormalities.

Videourodynamic study provided detailed information concerning detrusor pressure, sensation, bladder capacity and compliance, and presence of uninhibited detrussor contractions during bladder filling and subsequent voiding phase. Bladder and detrussor instability definitions were in concordance with the standards recommended by the International Continence Society.[8] Videourodynamic study was performed by pediatric urology department.

The presence of at least one of the following signs-detrussor overactivity, hypocompliance, elevated detrussor pressure, detrussor sphincter dyssynergy, spinning top, low bladder capacity-was considered LUTD.

Male patients underwent VCUG to image posterior urethra; patients with VUR using VUD also underwent VCUG to grade VUR. VCUG was also utilized to confirm whether the presence of VUR in patients without VUR using VUD, but with recurrent UTIs and/or renal scar. The International Reflux Study Classification was used to grade reflux on VCUG.[9] Grade I and II reflux were considered low grade and grade III-IV and V reflux were considered high grade reflux.

Children with urogenital anatomical disorders (e.g., posterior urethral valves, ureterocele, meatal stenosis, anorectal malformation) and neurogenic bladder were excluded from the study. The majority of patients suffered from recurrent urinary tract infections, but they received antibacterial prophylaxis and were free of UTI for a period of at least 8 weeks preceding the VUD.

STATISTICAL ANALYSIS

The data were analyzed using SPSS version 17.0. Categorical variables were compared using the chi-square test. The Student's t-test was used for comparison of continuous variables when the data followed normal distribution. The comparability and applicability of the statistical methods were analyzed by the kappa method, and calculated manually according to Landis and Koch.[10] The assessment of inter-rater agreement is described in detail in the footnote of Table 1. McNemar's test was used to establish the statistical significance of the differences. A p value of less than 0.05 was considered to indicate a statistically significant result.

RESULTS

A total of 117 children [234 kidney-ureter units (KUUs)] were examined. VUR was demonstrated in 108 (46%) of 234 KUUs (in 74 patients); 60 (55%) of them were assessed by both VCUG and VUD (Group A). In 21 KUUs (19 %), reflux was identified by VUD only (Group B), and in 27 KUUs (25 %) by VCUG only (Group C). In 126 out of 234 KUUs, reflux was not observed by both techniques (Group D) (Table 1).

In group B, VCUG missed reflux in 21 ureters (in 17 patients) (19% of 108 ureters with VUR); 9 of these patients exhibited renal scar. In group C, VUD missed reflux in 27 ureters (in 21 patients) (25% of 108 ureters with VUR); 6 were high grade reflux, 21 were low grade reflux, and 12 exhibited renal scars. The sensitivity and specificity of VUD were 68% and 86%, respectively, and the positive predictive value was 75% and the negative predictive value was 82%. There was a moderate agreement between the two evaluation methods; the differences in the detection rate of reflux between VUD and VCUG was statistically insignificant according to McNemar's test (p=0.47). The assessment of inter-rater agreement is described in detail at the footnote of Table 1.

In addition to these data, VUD revealed detrussor overactivity in 52%, hypocompliance in 68%, elevated detrussor pressure in 57%, detrussor sphincter dyssynergy in 3%, and significant residual urine in 25% of all patients. According to these findings, LUTD was detected in 55 patients with VUR (74%), and in 34 patients without VUR (79%) (Table 2).

Lower urinary tract dysfunction was detected in 13 of 17 patients (76%) in group B, and 17 of 21 patients (80%) in group C (Table 3).

TABLE 1: Refluxing ureters diagnosed by videourodynamic study (VUD) and voiding cystourethrography (VCUG).

		VCUG		
	VUR	VUR (+)	VUR (-)	Total
VUD	VUR (+)	60 (A)	21(B)	81
	VUR (-)	27 (C)	126 (D)	153
	Total	87	147	234

VUR+, positive diagnosis of vesicuretral reflux; VUR -, negative diagnosis of vesicouretral reflux

Calculation of kappa: 1. Number of agreements for the proportion of diagonal to total observation: a) (60+126)/234=0.794 (observed proportion)

2. Total of the relevant row divided by the relevant column (number and proportion to the total of agreement just by chance): a) 81x87/234=30.08; b) 147x153/234=96.11; c) 30.08 + 96.11=126.19

d) 126.16/234= 0.539 (expected proportion)

3. κ= (0.794-0.539)/(1.00-0.539)=0.555 (standard error [κ]=0.057)

4. When κ has a maximum of 1.00, the agreement is perfect. A value of 0 indicates agreement only by chance, negative value shows worse than chance (unlike in this context).

Strength of agreement: <0.2: poor, 0.21-0.4: fair, 0.41-0.6: moderate, 0.61-0.8: good, >0.8: very good.

5. Conclusion: There was a ''moderate'' agreement between the two evaluation methods.

TABLE 2: Bladder instability and renal scar rates in VUR+ and VUR- patients.

	Renal scar (+)	Renal scar (-)	Normal bladder	Unstable bladder	Total
VUR+ (74)	44 (59%)	30 (41%)	19 (26%)	55 (74%)	74
VUR- (43)	15 (34%)	28 (66%)	9 (21%)	34 (79%)	43
Total	59 (50%)	58 (50%)	28 (23%)	89 (76%)	117

TABLE 3: Clinical findings in patients with VUR missed by VCUG and by VUD.

	Group B (VUR missed by VCUG) (21 ureters in 17 patients)	Group C (VUR missed by VUD) (27 ureters in 21 patients)	p
Bladder dysfunction	13/17 (76%)	17/21 (80%)	NS
Renal scar	9/21 (42%)	12/27 (44%)	NS
Surgical correction	4/21 (20%)	7/27 (25%)	NS

NS: Non-statistically significant.

Sixty kidneys of 108 refluxing KUUs (55%) exhibited renal scar formation. Renal scar was detected in 9 of 21 (42%) refluxing KUUs in group B, and 12 of 27 (44%) refluxing KUUs in group C (Table 3).

Forty-three of the 108 (39%) refluxing ureters were treated with surgical procedures. A total of 21 (19%) ureters (13 patients) were administered subureteric injection and 22 (20%) ureters (14 patients) underwent ureteroneocystostomy. The remaining 47 patients (63%) with VUR were given conservative treatment, including anticholinergic agents, antibacterial prophylaxis, and strict voiding regimen. Four ureters in group B and 7 in group C underwent surgical repair (Table 3). There was no statistically significant difference between group B and C concerning renal scar formation and surgical repair rate.

DISCUSSION

VUR is a common abnormality of the urinary tract in children. In addition to abnormal implantation of the ureter into the bladder, urinary tract infections, lower urinary tract dysfunction, and elevated bladder pressure are important in the development of reflux.[11] Bladder instability is a frequent finding in children with VUR. The relationship between voiding dysfunction and VUR in neurologically normal children has been reported for many years in urological literature.[2,3,4,5,6,12-14] In this study, we found VUR in 74 of 117 patients (63%) with recurrent UTIs and voiding dysfunction symptoms. Videourodynamic examination of all children suspected of having reflux showed that LUTD in 89 of 117 (76%) children. Bladder dysfunction was detected in 55 of 74 (74%) patients with VUR. Our rates of bladder instability were similar to the study by Karami et al., but higher compared to other studies in literature, in which it has been reported in approximately 30-40% of patients with VUR.[2,3,12-14] This difference may be due to patient selection. Our patients exhibited marked LUTD symptoms, such as incontinence and frequency.

The ideal method for the evaluation of VUR should be safe, non-invasive, and accurate. Until the present time, VCUG has been accepted as the gold standard for the detection and grading of VUR; however, this method causes significant ionizing radiation exposure despite the use of digital and pulsed fluoroscopy. Radionuclide cystography is highly sensitive, with a lower radiation dose, but is lacking in grading and anatomic detail. Voiding urosonography is also more sensitive for detection and grading of reflux compared with VCUG.[15] Because of the high bladder instability rate in this patient population, VCUG and other methods that show reflux only are insufficient for evaluation of recurrent UTIs and dysfunctional voiding. The appearance of "spinning top" and abnormal trabeculation in the bladder wall on VCUG may suggest the presence of bladder instability, but this technique is not adequate for monitoring the detrussor pressures, detrussor-syfincter dyssynergy, reduced detrussor compliance, and uninhibited detrussor contractions. Videourodynamic assessment, however, identifies the characteristics of the bladder wall, bladder neck, posterior urethra anomalies during filling and voiding phase, and evaluates the function of the lower urinary tract; this method can obtain detailed information about the parameters of LUTD and it can aid in determining the ap-

propriate usage of anticholinergic and/or α1 receptor blocker therapy.

In our study, VUD was in agreement with VCUG in 186 of 234 KUUs (79%), and the missing rate of reflux (false negativity rate) for both techniques was similar. LUTD was detected in 79% of patients without VUR; VCUG was normal in these patients, but they received anticholinergic and/or α1 receptor blocker therapy. VCUG was also unsatisfactory in detecting VUR in 17 patients (21 KUUs) with VUR identified by VUD, and there was bladder dysfunction in 76% of these patients. However, VUD did not detect VUR in 21 patients, but demonstrated instable bladder findings; anticholinergic and/or α1 receptor blocker therapy was prescribed to these patients. Only four of these patients (19%) underwent surgical treatment, eight developed spontaneous resolution, and the others are still being followed-up.[10]

Strict voiding regimen and anticholinergic medication and/or α1 receptor blocker therapy are very important in addition to antibiotic prophylaxis in the management of VUR, if it is associated with LUTD. On the other hand, treatment of LUTD can increase surgical repair success; can even provide spontaneous resolution in some patients.[6] Approximately 30-70% of the patients with VUR exhibit bladder instability; thus, bladder instability most likely plays an important role in the development of VUR. Patients with bladder instability, female patients in particular, are at risk for recurrent urinary tract infections. Detection of functional anomalies is very important; a videourodynamic study with simultaneous VCUG is the most suitable initial investigation to diagnose VUR and bladder dysfunction in one combined study because this is an easy and reliable procedure.[3,14]

In conclusion, currently there is no consensus concerning the optimal management and investigational procedures for patients with VUR. Based on our findings, we recommend VUD primarily for children with recurrent UTI associated with dysfunctional voiding. In patients without reflux during VUD, VCUG can be performed to ensure the presence of reflux if there is severe renal scar, or if UTIs recur insistently. Additionally, when there is a suspicion of posterior urethral valve in male patients, VCUG can be applied for investigation of urethra.

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