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ORIGINAL ARTICLE

The Role of Dynamic Renal Scintigraphy in Detecting Vesicoureteral Reflux

Vezikoüreteral Reflü Tanısında Dinamik Böbrek Sintigrafisinin Rolü

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ABSTRACT

Aims: This study aims to evaluate the role of standardized dynamic renal scintigraphy (DRS) in recognizing vesicoureteral reflux (VUR) in patients detected with VUR by voiding cystourethrography (VCUG).
Methods: The data of all pediatric patients who underwent both VCUG and DRS [technetium-99m diethylenetriaminepentaacetic acid (Tc-99m DTPA) or technetium-99m mercaptoacetyltriglycine dynamic renal scintigraphy (Tc-99m MAG-3)] in our hospital between 2013 and 2022 were retrospectively reviewed. Tc-99m MAG-3 was used in infants and Tc-99m DTPA radiopharmaceutical in children over one year old. According to VCUG findings, VUR grades were grouped as grade I-II-III low-grade VUR and IV-V high-grade VUR. The role of DRS in detecting VUR in both low and high-VUR-grade groups was evaluated.
Results: A total of 56 patients (and 69 renal units), 23 girls (%41.1), and 33 boys (%68.9) were included in this study. The median value of the time elapsed between the DRS and VCUG examinations was nine days. According to VCUG, VUR was grade I in five renal units, grade II in 19 renal units, grade III in six renal units, grade IV in six renal units, and grade V in 33 renal units. DRS detected VUR in two of 30 renal units (%6.7) in the low VUR grade group. On the other hand, VUR was observed with DRS in 27 of 39 renal units (%69.2) in the high VUR grade group.
Conclusions: Standardized DRS shows very low sensitivity in recognizing low-grade VUR, and its performance in detecting high-grade VUR is comparatively better. Increasing the awareness of clinicians about the detection of VUR with standardized DRS will benefit patients.

Keywords: Vesicoureteral reflux, scintigraphy, Voiding cystourethrogram

ÖZ

Amaç: Bu çalışmada voidingsistouretrografi (VCUG) ile vezikoüreteralreflü (VUR) saptanan hastalarda standart dinamik böbrek sintigrafisinin (DRS) VUR'u tanımadaki rolünü değerlendirmeyi amaçladık.
Yöntemler: 2013-2022 yılları arasında hastanemizde hem VCUG hem de DRS [teknetyum-99m dietilentriaminpentaasetik asit (Tc-99m DTPA) veya teknesyum-99m merkaptoasetiltriglisin dinamik böbrek sintigrafisi (Tc-99m MAG-3)] yapılan tüm çocuk hastaların verileri geriye dönük olarak incelendi. Bebeklerde Tc-99m MAG-3, bir yaşın üzerindeki çocuklarda ise Tc-99m DTPA radyofarmasötiği kullanıldı. VCUG bulgularına göre VUR dereceleri, derece I-II-III düşük dereceli VUR ve IV-V yüksek dereceli VUR olarak gruplandırıldı. DRS'nin hem düşük hem de yüksek VUR dereceli gruplarda VUR'u tespit etmedeki rolü değerlendirildi.
Bulgular: Bu çalışmaya 23'ü kız (%41.1) ve 33'ü erkek (%68.9) olmak üzere toplam 56 hasta (ve 69 böbrek ünitesi) dahil edildi. DRS ve VCUG incelemeleri arasında geçen sürenin ortanca değeri dokuz gündü. VCUG'a göre VUR beş böbrek ünitesinde grade I, 19 böbrek ünitesinde grade II, altı böbrek ünitesinde grade III, altı böbrek ünitesinde grade IV ve 33 böbrek ünitesinde grade V idi. DRS ile düşük VUR dereceli grupta 30 böbrek ünitesinin ikisinde (%6,7) VUR tespit edildi. Yüksek VUR dereceli grupta ise 39 böbrek ünitesinin 27'sinde (%69,2) DRS ile birlikte VUR gözlendi.
Sonuçlar: Standardize edilmiş DRS, düşük dereceli VUR'u tanımada düşük hassasiyet gösterirken yüksek dereceli VUR'u tespit etmedeki performansı oldukça iyidir. Klinisyenlerin VUR'un standardize DRS ile tespiti konusunda farkındalığının arttırılması hasta yararına olacaktır.

Anahtar Kelimeler: Vezikoüreteral Reflü, Sintigrafi, Voiding sistoüreterografi

Introduction

Vesicoureteral reflux (VUR) is the most common urological abnormality in children. It is seen in 30-40% of children with urinary tract infections and 1-2% of all children(1, 2). The gold standard imaging modality for VUR is voiding cystourethrogram (VCUG) (2, 3). In this examination, filled with iodinated contrast material after a urethral catheter is placed in the bladder and intermittent images are taken both in the filling and voiding phases. According to imaging findings, the degree of VUR is grouped by the International Reflux Scale (IRS) (4). The clinical management of VUR is grade-dependent. A strong correlation exists between grading and VUR prognosis (5). An alternative technique was needed for the detection of VUR due to radiation doses, risk of UTI, and invasive intervention. Although there is no definitive alternative to VCUG in the current literature, the search continues on this issue. Some of these studies investigated the effectiveness of radionuclide cystography applied directly or indirectly to the bladder as an alternative method for the detection of VUR (6, 7). Also, the radiation dose is lower than VCUG (1-5 mSv vs 0.5-0.6 mSv) and has an equal sensitivity for VUR examination (8, 9). However, it cannot provide anatomical details (10, 11). Direct radionuclide cystography provides images during and after voiding, after bladder catheterization, and after filling the bladder with radionuclide material. The second technique, indirect radionuclide cystography helps the diagnosis of VUR seen during urinary drainage as well as the assessment of renal functions

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following intravenous radiopharmaceutical injection into bladder catheterization in children older than 3 years old who have developed sphincter control (12). In standardized DRS, unlike indirect radionuclide cystography, the voiding phase is not examined.

The main aim of this study is to describe the role of standardized DRS in recognizing VUR detected by VCUG. Another purpose is to increase the awareness of nuclear medicine clinicians in recognizing VUR with DRS.

Materials and Methods

The clinical data and DRS findings of pediatric patients diagnosed with VUR by VCUG in our hospital were retrospectively reviewed between January 2013 and January 2022. This study was approved by the local ethics committee (Approval no: 2022/10).

Demographic data, DRS and VCUG reports, and images were interpreted by experienced pediatric surgeons and nuclear medicine physicians for all children. Patients who had undergone VCUG scanning less than 30 days before DRS scanning and patients without a history of VUR-related surgical treatment were included in the study. There were a total of 68 patients who met the inclusion criteria. Twelve patients [with a complex urinary phenotype (n: 3), underwent surgery between two scans (n: 3), with the poor image quality of the scans (n: 2), and had more than 30 days between two scans (n: 4)] were excluded from the study The goal of doing VCUG and DRS images simultaneously was to assess any potential obstruction and urethral dilatation not caused by VUR.

Voiding cystourethrographies were done by a currently accepted standard methodology, and the anticipated bladder capacity for each patient was determined using that formula: 30 mL x [age + 2]. All patients retrospectively evaluated the degree of VUR by the five-level International Reflux Scale (4). Two radiopharmaceutical agents were used for DRS: technetium-99m diethylenetriaminepentaacetic acid (Tc-99m DTPA) or technetium-99m mercaptoacetyltriglycine dynamic kidney scintigraphy (Tc-99m MAG3). Tc-99m DTPA radiopharmaceutical was utilized in children above the age of one, whereas Tc-99m MAG3 was used in infants. Standardized DRS was performed with intravenous (iv) administration of Tc-99m DTPA or Tc-99m MAG3 (3.7 MBq/kg). A dosage of 0.5–1 mg/kg IV furosemide was given 15 minutes after the radiopharmaceutical injection. Flow images were acquired at 2 seconds per frame for the first minute, followed by 1-minute images acquired at 20 minutes on the 64X64 acquisition matrix. Data were analyzed by vendor-supplied kidney processing software, marking the region of interest with kidney and both ureters. Activity stasis in the kidneys and ureters was followed by using the time activity curve created by the integral method.

Interpretation of DRS and VCUG

According to the IRS, the VCUG were rated as zero if they were negative, and one to five if they were positive. Regardless of severe reflux, the DRS findings were classified as negative or positive. The following criteria were sought for DRS positivity; Gradual accumulation of radioactivity in late images in the renogram curves obtained by drawing the kidney area of interest, and progressively increasing radioactivity accumulation in the ureterogram curves obtained by drawing the area of interest including the ureters. The VUR grades were divided into low-grade (grades I–II–III) and high-grade (grades IV–V) VUR. Both renal units in patients with bilateral VUR were assessed individually. VCUG and DRS images were evaluated by pediatric surgeons and nuclear medicine physicians by consensus.

Statistics

The median values of the children's age (months) and the median time elapsed between DRS and VCUG scans (days) were determined. VCUG was used as the gold standard test for the diagnosis of VUR (4). The sensitivity of DRS in detecting VUR was calculated in low-grade VUR (grade I-II-III) and high-grade VUR (grade IV-V) groups classified according to VCUG findings.

Results

A total of 68 children underwent both VCUG and DRS. Twelve children were not included in the research because they met the exclusion criteria. Fifty-six children (median age 56 months, range: 1-181 months), 23 girls (41.1%), and 33 boys (68.9%) were included. Sixty-nine renal units were evaluated. Bilateral VUR was detected in 13 patients. Table 1 contains demographic and clinical information about the children. In Figure 1, DRS and VCUG representative images of a 10-year-old male patient with grade V vesicoureteral reflux in the left kidney are presented.

The median value of the time elapsed between DRS and VCUG examinations was nine days. According to VCUG, VUR was grade I in five renal units, grade II in 19 renal units, grade III in six renal units, grade IV in six renal units, and grade V in 33 renal units (Table 2). There are 30 renal units in the low VUR grade group and 39 renal units in the high-grade VUR group.

When the sensitivity of DRS in detecting VUR was examined; VUR was observed in two of the 30 renal units (6.7%) in the low VUR grade group and 27 (69.2%) of 39 renal units in the high VUR grade group by DRS (Table 3).

Table 1. Demographic data of children.

	Median age at imaging, months (range)	Presence of bilateral VUR (%)	VUR grade I-III (low grade) (%) (renal units)	VUR grade IV-V (high grade) (%) (renal units)
Tc-99m MAG-3 patients	6 (1-12)	7 (30.4%)	9 (13%)	14 (20.2%)
Tc-99m DTPA patients	83 (13-181)	6 (15%)	21 (30.4%)	25 (36.2%)

Tc-99m MAG-3, Technetium-99m mercaptoacetyltriglycine; Tc-99m DTPA, Technetium-99m diethylenetriaminepentaacetic acid; VUR, vesicoureteral reflux.

Table 2. Tc-99m MAG-3 and Tc-99m DTPA scans results in renal units with VUR detected by VCUG

	VCUG				
	Low grade			High grade	
	VUR grade I	VUR grade II	VUR grade III	VUR grade IV	VUR grade V
Tc-99m MAG-3 positive	0	0	1	2	9
Tc-99m MAG-3 negative	1	6	1	1	2
Tc-99mDTPApositive	0	0	1	2	14
Tc-99mDTPAnegative	4	13	3	1	8

Tc-99m MAG-3, technetium-99m mercaptoacetyltriglycine dynamic renal scintigraphy; Tc-99mDTPA, Technetium-99m diethylenetriaminepentaacetic acid; VCUG, voiding cystourethrography; VUR, vesicoureteral reflux.

Table 3. DRS results in renal units with VUR detected by VCUG

	Low-grade VUR (Grade I-II-III)	High-grade VUR (Grade IV-V)
DRS positive	2 (%6.7)	27 (%69.2)
DRS negative	28 (%93.3)	12 (%30.8)
Total	30	39

DRS, dynamic renal scintigraphy; VCUG, voiding cystourethrography; VUR, vesicoureteral reflux.

Discussion

VCUG is regarded as the gold standard for determining VUR (9). It was an invasive procedure with the risk of iatrogenic UTIs and radiation exposure. Also, it is a painful and unpleasant examination. After catheterization, children cannot relax enough to pee. Urinating in front of the camera creates great anxiety for the children and their families (13). Studies are ongoing to develop an alternative non-invasive diagnostic method to VCUG for the detection of VUR (14-18).

While some authors claim more accurate findings with radionuclide cystography, other authors favor the identification of VUR using VCUG (14-17). Unver et al. reported a good agreement between DRS and VCUG in the detection of VUR (17). In our study, we evaluated the detectability of VUR by DRS of 56 children [23 girls (41.1%) and 33 boys (68.9%)], corresponding to 69 kidney units, in whom VUR was detected by VCUG. We sought to evaluate the role of DRS in recognizing VUR detected by VCUG. According to our results, DRS shows very low sensitivity in recognizing low-grade VUR, while its performance in high-grade VUR is comparatively better. DRS detected VUR in 6.7% of the low VUR grade group and 69.2% of the high VUR grade group. In a recent study, Capone et al. (7) evaluated 72% sensitivity and 93% specificity for DRS with indirect cystography in the diagnosis of VUR in 86 pediatric patients. In that study, VUR was detected in 47.5% of the low VUR grade group and 63.3% of the high VUR grade group. Gordon et al. (18) evaluated 74.1% sensitivity and 90.5% specificity for indirect cystography in the diagnosis of VUR in 65 children.

For the detection of VUR, there are two scintigraphic techniques (19). In direct radionuclide cystography, radioactive material is given intravesically. Afterward, the images in the bladder filling and voiding phases are recorded. Bladder catheterization is not applied in indirect radionuclide cystography. In this technique, the radioactive substance is administered intravenously and images are recorded during the bladder filling phase and voiding phase. The disadvantage of both techniques is that reflux grading cannot be done and sufficient anatomical information cannot be obtained.

The main limitations of the study were its retrospective nature and the absence of images of the voiding phase, which is important in detecting VUR. Hinman et al. (20) classified VUR into 3 groups as reflux only during filling (low pressure reflux), reflux during filling and voiding (mixed reflux), and reflux only during voiding (high pressure reflux). The reason for the low detection rate of VUR with DRS in our study might be that some cases had VUR types seen in the voiding phase. In addition to the advantages of DRS such as low radiation dose, non-invasiveness, and information about the functional status of the kidney, adding the voiding phase to the standard procedure for detecting VUR may increase the effectiveness of the scan in detecting VUR.

Conclusion

The sensitivity of DRS was found high, especially in detecting high-grade VUR cases. Increasing the awareness of clinicians that VUR can be observed with DRS will benefit the patient. More comprehensive and prospective studies on the subject are needed.

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Conflict of interest: There is no conflict of interest.

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