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Original Article

Predict the spontaneous resolution of vesicoureteral reflux by direct radionuclide cystography

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ABSTRACT

Objectives: To evaluate the prognostic value of initial direct radionuclide cystography (DRC) for spontaneous resolution of vesicoureteral reflux (VUR).
Methods: Fifty-one children with initial diagnosis and 1–6 years' follow-up of VUR by DRC were enrolled in this study. VUR was graded according to the anatomic grading as (1) mild reflux corresponding to tracer just in ureter, (2) moderate reflux with accumulation of activity in a non-dilated collecting system and ureter, and (3) severe reflux equated with a dilated ureter and collecting system. The severity of VUR was also expressed according to the functional classification as (1) transient reflux, which occurred at filling or voiding phase only and (2) persistent reflux, present in both filling and voiding phases.
Results: Twenty-nine of the 51 children had unilateral VUR, and the other 22 had bilateral VUR. In the total of 73 refluxing ureters, there were 12 mild, 49 moderate and 12 severe VUR according to anatomic grading, and 30 transient and 43 persistent VUR according to the functional grading. After follow-up, resolution of VUR was found in 92% (11/12) of mild, 59% (29/49) of moderate and 25% (3/12) of severe VUR ($P = .04$, mild vs. moderate; $P = .003$, mild vs. severe). Eighty percent (24/30) of transient and 44% (19/43) of persistent reflux showed spontaneous resolution ($P = .003$).
Conclusions: DRC allows anatomic and functional classification of VUR. It is an ideal method for the diagnosis, staging and follow-up of VUR, and provides valuable information to predict the patient's outcome.

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Predicción de la resolución espontánea del reflujo vesicoureteral mediante cistografía isotópica directa

Palabras clave:
Pielonefritis aguda
Cistografía isotópica directa
Reflujo vesicoureteral
Infección del tracto urinario

RESUMEN

Objetivos: Evaluar el valor pronóstico de una cistografía isotópica directa (CID) inicial para la resolución espontánea de reflujo vesicoureteral (RVU).
Métodos: Se incluyeron 51 niños con un diagnóstico inicial y con 1 a 6 años de seguimiento de RVU mediante CID. Los RVU fueron clasificados según los grados anatómicos de la manera siguiente: *(1)* reflujo leve que corresponde a trazador solamente en el uréter, *(2)* reflujo moderado con acumulación de actividad en un sistema colector sin dilatar y uréter, y *(3)* reflejo severo con un uréter y sistema colector dilatados. La severidad del RVU también se expresó según la clasificación funcional como: *(1)* reflujo transitorio, que ocurre solo en la fase de llenado o vaciado, y *(2)* reflujo persistente, presente tanto en las fases de llenado como de vaciado.
Resultados: Veintinueve de los 51 niños presentaron RVU unilateral y los otros 22 tuvieron RVU bilateral. De los 73 uréteres con reflujo, hubo 12 con RVU leves, 49 moderados y 12 severos, según la clasificación anatómica, y 30 transitorios y 43 persistentes según la clasificación funcional. Después del seguimiento, se observó resolución de RVU en el 92% (11/12) de los leves, en el 59% (29/49) de los moderados y en el 25% (3/12) de los severos ($p = 0{,}04$, leve vs moderado; $p = 0{,}003$, leve vs severo). El 80% (24/30) de los reflujos transitorios y el 44% (19/43) de los persistente demostraron resolución espontánea ($p = 0{,}003$).
Conclusiones: Una CID hace posible la clasificación anatómica y funcional del RVU. Es un método idóneo para el diagnóstico, estadificación y seguimiento de RVU, y proporciona información valiosa para predecir el resultado del paciente.

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Introduction

Vesicoureteral reflux (VUR) is one of the most common diseases in infancy and childhood that affects approximately 1–2% of all children.[1] About one third (25–40%) of the children who have urinary tract infection (UTI) are accompanied with the presence of VUR.[2] The principal long term consequence of VUR, particularly when associated with infection, is the development of acute pyelonephritis (APN), which may lead to serious renal sequelae, such as renal scarring, hypertension and chronic renal failure.[3,4]

Early investigation of VUR is essential for the accurate assessment of pathology and hence appropriate management to prevent progression to renal parenchymal damage.[5] Radiographic voiding cystourethrogram (VCUG), the fluoroscopic contrast X-ray of bladder and lower urinary tract, has been frequently used for detection of VUR. It can provide detailed anatomic information for the definition of VUR, but its high radiation limits the availability of continuous monitoring and close follow-up. Direct radionuclide cystography (DRC) has gained increasing acceptance as a useful method to detect VUR during the past several years. It is shown to be more accurate than VCUG for the diagnosis of VUR in children[6] and provide better sensitivity, especially in detecting transient reflux.[7,8] Because of its safety, high sensitivity and minimal radiation exposure, DRC has been suggested for the initial diagnosis and follow-up of VUR.[9]

There are two ways to treat VUR. Children can receive non-invasive medical treatment with a regimen of long-term antibiotic prophylaxis to prevent UTI and renal damage till the spontaneous resolution as they grow up. Surgical treatment of VUR offers an invasive but immediate correction of the anatomic problem and is often recommended in children with recurrent UTI despite antibiotic prophylaxis, especially in high grade VUR. Since there is still difficulty in making a decision for optimal treatment, we hope to predict the prognosis at initial diagnosis of VUR, and offer a better therapeutic strategy as soon as possible. Therefore, the aim of the study was to evaluate the prognostic value of initial DRC for spontaneous resolution of VUR.

Materials and methods

Patients

Eight hundred and thirty-eight children were referred to our department for initial DRC due to various urinary tract diseases (mostly UTI). VUR was diagnosed in 135 of them (16%). In our hospital, the goal of treatment for VUR was to prevent kidney damage, and the plan of treatment was made according to severity of reflux, breakthrough infection and patient age. Therefore, antibacterial prophylaxis with a yearly DRC follow-up was the first choice for children with mild to moderate VUR because it was more likely to resolve spontaneously. Surgical correction was indicated in children with breakthrough infection and those with severe VUR older than 1 year, since infants with severe VUR had higher resolution rate in the first year.[10] In the 135 children with VUR, 44 underwent corrective reflux surgery soon due to congenital abnormality of ureters, severe VUR beyond infancy or breakthrough UTI despite prophylactic antibiotics. Another 40 children were lost to follow-up. Finally 51 children with VUR (including 8 infants with severe VUR) were enrolled in this study, identified with an initial DRC and on a yearly follow-up schedule. Twenty-three were boys and 28 were girls. VUR was detected at a mean age of 17 ± 20 months (range 5 days to 5 years). At the time of the first DRC, the clinical diagnosis was febrile UTI in 46 children, meningocele with neurogenic bladder in 2, prenatal hydronephrosis in 2 and chordee penile in 1. All children with VUR were given prophylactic antibiotics treatment after diagnosis and underwent a mean of 2 years (ranged from 1 to 6 years) of follow-up DRC. This study was approved by the Institutional Review Board and the Hospital Ethics Committee.

DRC protocol

All patients underwent Foley catheterization before the DRC. Imaging acquisition was started at the beginning of administration of 18.5 MBq (0.5 mCi) ^{99m}Tc-DTPA via indwelling catheter, and then followed by instillation of optimal amount of normal saline. The expected bladder capacity (ml) was body weight (kg) $\times$ 7 for infants and (age in years +2) $\times$ 30 for children over 1 year of age. Once the instilled saline was sufficient to fill the bladder, Foley catheter was removed and the patients were asked to void as much as possible. Sequential images were continuously recorded with the patient supine in the posterior view on a gamma camera (Siemens orbiter 75; Siemens Corp., Hoffman Estates, IC) with a low-energy, parallel-hole and all-purpose collimator in a 64×64 matrix at the frame rate of 15 s per image. The bladder and both kidneys were within the field of view throughout the whole course.

Image interpretation

VUR was graded anatomically as (1) mild reflux corresponding to tracer just in ureter, (2) moderate reflux that is the accumulation of activity in a non-dilated collecting system and ureter, and (3) severe reflux that is equated with a dilated ureter and collecting system.[11] The severity of VUR was also expressed according to the functional classification as (1) transient reflux occurring at filling or voiding phase only, or (2) persistent reflux present in both filling and voiding phases.

Statistical analysis

Chi-square test was used to determine the significance of difference between groups. Differences were considered significant at $P < 0.05$. Cox regression curve was derived from Kaplan–Meier method. All of the calculations were performed using SPSS version 12.0 (SPSS, Chicago, IL).

Results

The initial DRC showed unilateral VUR in 29 of the 51 children and bilateral VUR in the other 22 children, making a total of 73 refluxing ureters. Anatomic grading showed 12 of them to be mild, 49 to be moderate and 12 to be severe VUR. Transient VUR according to functional classification was seen in 30 refluxing ureters (28 at voiding and 2 at filling phase) (Fig. 1), and persistent VUR in 43 refluxing ureters (Fig. 2).

The follow-up DRC showed resolution of VUR in 43 of the 73 (59%) refluxing ureters, including 11 of the 12 (92%) mild VUR, 29 of the 49 (59%) moderate VUR and 3 of the 12 (25%) severe VUR. The mean times to resolution were 12.3 months (ranged from 9 to 15 months) for mild VUR, 20.4 months (ranged from 13 to 42 months) for moderate VUR and 45.7 months (ranged from 35 to 55 months) for severe VUR (Fig. 3). Spontaneous resolution was obviously associated with the degree of reflux ($P = 0.04$, mild vs. moderate; $P = 0.003$, mild vs. severe). Transient VUR resolved in 24 of the 30 (80%) refluxing ureters, and persistent VUR in 19 of the 43 (44%) refluxing ureters. The mean times to resolution were 14.7 months (ranged from 9 to 29 months) for transient VUR and 27.0 months (ranged from 14 to 55 months) for persistent VUR (Fig. 4). Transient VUR was nearly twice more likely to resolve than the persistent VUR ($P = 0.003$). Combined analysis of anatomic and functional classification found resolution in all of the 8 mild transient VUR and only 3 of 12 severe persistent VUR ($P < 0.001$).

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