

ORIGINAL ARTICLE

Cesare Polito · Giovanni Moggio · Angela La Manna
Fabrizio Cioce · Salvatore Cappabianca
Rosario Di Toro

Cyclic voiding cystourethrography in the diagnosis of occult vesicoureteric reflux

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Abstract Cyclic voiding cystourethrography (CVC) enhances the detection of vesicoureteric reflux (VUR). We investigated whether more-severe VUR may be overlooked, and whether older children are at risk of having their VUR missed with the conventional single-cycle study. Three hundred and seventy patients, 168 boys and 202 girls aged 1 month to 16 years, consecutively admitted over 1 year for suspicion of VUR, underwent two complete cycles of filling and voiding CVC. One hundred and four subjects, 33 boys and 71 girls, were older than 3 years (mean age 5.7 years, range 3.2–16 years). Sixty-six refluxing ureters from 51 patients were identified in the first cycle and 61 refluxing ureters from 45 patients were identified only with the second cycle. Four instances of grade IV VUR in 4 patients and three of grade V VUR in 3 patients were overlooked completely in the first cycle. Seven episodes of VUR \leq grade III from 5 patients diagnosed in the first cycle were upgraded to \geq grade IV at the second cycle. The presence of VUR was identified only in the second cycle in 35 of 74 subjects aged \leq 3 years and in 10 of 22 aged $>$ 3 years (not significant). Of the 10 children aged $>$ 3 years, 2, who had diagnosis only at the second cycle, had \geq grade IV VUR. More-severe VUR may be overlooked or down-graded in a single-cycle study. Two-cycle CVC is also useful in children older than 3 years.

Key words Vesicoureteric reflux · Cyclic voiding cystourethrography · Occult vesicoureteric reflux · Upgrading · Downgrading

Introduction

Over the last decade, cyclic voiding cystourethrography (CVC) has enhanced the detection of vesicoureteric reflux (VUR) in infants and children [1–3]. Up to 12% of subjects with negative cystourethrography in the first cycle of filling and voiding had VUR at the second cycle; hence 26%–42% of the total number of cases of VUR diagnosed by the CVC had been missed with the conventional single-cycle study [1–3]. This could explain, at least in part, the frequency of pyelonephritis and/or of renal scarring with no signs of VUR.

It has been postulated [3] that repeated bladder filling may unmask occult VUR via two mechanisms: (1) bladder mucosal edema due to repeated exposure to contrast material; (2) transient bladder instability due to repeated filling.

A total of 177 [1], 65 [2], and 100 [3] CVC studies have been reported. Because of the limited number of CVC studies reported to date, we do not know whether severe reflux can go undetected and whether older children are at risk of having their VUR missed in the single-cycle study. In the largest series [1], only mild/moderate-grade VUR was missed in the first cycle of CVC, but only a single case of \geq grade IV VUR was found in that study. In the two other series [2, 3], the number of cases of \geq grade IV VUR is not reported. Also, most of the subjects reported were under 3 years. We report a series of 370 unselected infants and children who consecutively underwent two-cycle voiding cystourethrography over a 1-year period.

Patients and methods

Between January 1997 and January 1998 we performed two consecutive bladder fillings and voidings in all patients seen at our institution who needed cystourethrography. There were 370 patients, 168 boys and 202 girls, aged 1 month to 16 years. Patients with neurogenic bladder were excluded from the study. Sixty-three patients (44 boys and 19 girls) underwent CVC at ages 1–3 months to evaluate prenatally detected hydronephrosis. Two hundred and

C. Polito (✉) · A. La Manna · R. Di Toro
Department of Pediatrics, Second University of Naples,
Via S. Andrea delle Dame, 4, I-80138 Naples, Italy
Tel.: +39-081-5665413, Fax: +39-081-5665403

G. Moggio · F. Cioce · S. Cappabianca
Department of Radiological Sciences,
Second University of Naples, Naples, Italy

thirty subjects underwent CVC to evaluate urinary infection, 58 for follow-up of known VUR, and 19 to evaluate various clinical situations (auricular tubercle, multicystic kidney, etc). Of the 370 patients, 6 had a solitary kidney. One hundred and four subjects, 33 boys and 71 girls, were older than 3 years (mean age 5.7 years, range 3.2–16 years).

CVC was performed in all cases with the patient on antibacterial prophylaxis, after the urine had been sterile for at least 3 weeks. The procedure required inserting a 5- or 8-Fr infant feeding tube into the bladder. A 10% solution of iodamide (Opacist, Bracco, Milano, Italy) was administered by drip infusion from a height of approximately 1 m above the table. When the bladder was full, voiding occurred around the catheter. A sustained voiding was necessary for the first cycle to be considered complete. The catheter was left in place for the second cycle. During the second cycle, only fluoroscopy without radiography was performed unless VUR was noted. The additional study prolonged fluoroscopy by an extra 10–30 s.

VUR was graded according to the criteria of the International Reflux Study in Children [4]. Institutional ethical approval had been given for the study and informed consent was obtained from the parents of children who participated.

The chi-squared and the Fisher's test were used for statistical analysis. A *P* value <0.05 was considered significant.

Results

Table 1 reports the findings of the first- and the second-cycle CVC. Sixty-six refluxing ureters from 51 patients were seen in the first cycle and 61 refluxing ureters from 45 patients were identified only in the second cycle. Also some cases of higher-grade VUR (4 grade IV VUR in 4 patients and 3 grade V VUR in 3 patients) were overlooked in the first cycle (Fig. 1).

Of the 96 subjects who were diagnosed for VUR in the first or the second cycle, 47 were boys and 49 girls, 74 were aged ≤3 years and 22 >3 years, 36 had VUR ≥ grade III and 60 < grade III.

The VUR was overlooked in the first cycle in 25 of 45 boys and in 20 of 49 girls [not significant (NS)], in 16 of 36 patients with ≥ grade III VUR and in 29 of 60 with < grade III VUR (NS), in 35 of 74 subjects aged ≤3 years and in 10 of 22 aged >3 years (NS). The mean age of the 10 patients >3 years whose VUR was overlooked in the first cycle was 4.6 years (range 3.2–

Table 1 Reflux grade and ureters identified in the first and second filling cycle in 370 infants and children (VUR vesicoureteric reflux)^a

	VUR identified in the first cycle	VUR identified only in the second cycle
Patients	51 ^b	45 ^c
Refluxing ureters	66 (100)	61 (100)
Grade I	13 (19.7)	16 (26.2)
Grade II	27 (40.9)	24 (39.3)
Grade III	18 (27.3)	14 (22.9)
Grade IV	5 (7.6)	4 (6.6)
Grade V	3 (4.5)	3 (4.9)

^a Percentages are in parentheses

^b 17 patients had bilateral VUR

^c 17 patients had bilateral VUR

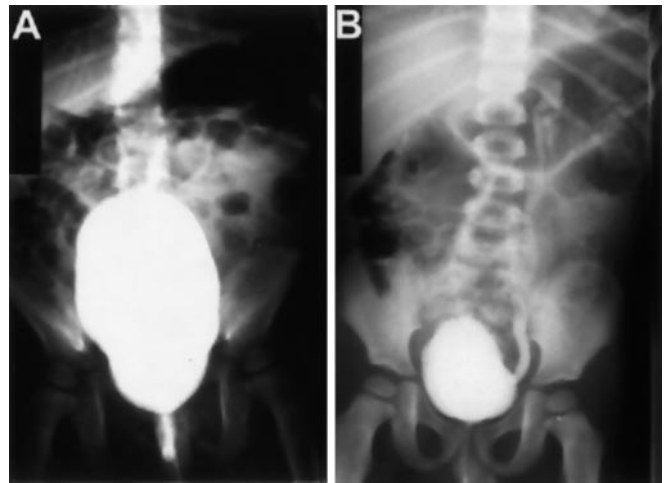


Fig. 1 A, B Two-cycle cystourethrography of a 4-year-old child. No reflux is detected in the first cycle complete filling (A), while grade IV left reflux is seen during the second cycle (B)

Table 2 Discrepancy in reflux grading between the first and the second filling cycle in 14 ureters from 9 patients (M male, F female, R right, L left)

Age (years)	Gender	First cycle	Second cycle
0.2	F	I L	III L
5	M	III R	IV R
3.5	F	II R II L	IV R IV L
0.8	M	III L	V L
5	F	I R I L	III R III L
9	F	III R	IV R
3.5	F	II R II L	IV R IV L
4	F	III R I L	0 R 0 L
5.2	F	IV R II L	III R 0 L

6.9 years). One of these 10 patients had grade IV (Fig. 1) and another grade V VUR.

The second cycle upgraded the VUR in 10 ureters from 7 patients and downgraded it in 4 ureters from 2 patients (Table 2). The percentage of up- or downgrading was significantly (*P*=0.003) higher in subjects aged ≥3 years (7/104) than in those aged <3 years (2/266). The difference in the percentage of up- or downgrading between boys (2/168) and girls (7/204) was not significant (*P*=0.28).

Discussion

In our series we identified VUR in the first-cycle CVC in 51 of 370 patients. Of the 319 subjects whose study was negative in the first cycle, 45 (14%) showed VUR in the second cycle, which is very similar to results reported previously [2, 3]. There was no significant difference between the percentage of VUR of ≥ grade III that we missed in the first cycle (48.6%) and that of <grade III (50.1%). Moreover, 4 episodes of grade IV VUR from 4 patients and 3 episodes of grade V VUR from 3 patients

were completely overlooked in the first cycle. In addition, 7 episodes of \leq grade III VUR from 5 patients identified in the first cycle were upgraded to grade IV or V in the second cycle (Table 2). These findings indicate that even severe VUR may be missed or downgraded in a single cycle study.

The percentage of VUR of each grade identified in the first cycle is very similar to that seen only in the second cycle (Table 1). This indicates that the risk for a VUR being overlooked in the first cycle is almost the same for any grade of reflux.

CVC is chiefly recommended [1, 2] to maximize detection of VUR in infants who typically cannot inhibit voiding until the predicted capacity is reached. The recommendation is also founded on the higher risk for infants and young children of developing renal damage with urinary infection. Our patients over 3 years old showed no different risk of having their VUR missed in the first cycle than younger patients. Of the 22 subjects whose VUR was diagnosed after 3 years of age, 10 had reflux overlooked in the first cycle; 2 of these 10 patients had grade IV and V VUR, respectively (Fig. 1). Our findings indicate that the two-cycle CVC is also useful in children over 3 years old, to avoid missing some patients with VUR, which may be severe.

It is well established [1–3, 5–7] that VUR may be intermittent. Indeed, in the series of Jequier and Jequier [1], an additional 4% of patients showed VUR after three cycles. Three cycles for all children may not be indicated, but it would be reasonable to include a third cycle for patients with a strong clinical suspicion of VUR (marked discrepancy in kidney size and/or intermittent dilatation of the ureters on the sonogram).

Decreased gonadal radiation and continuous monitoring may be provided by cyclic radionuclide cystography as an alternative to CVC [8]. Radionuclide cystography is very sensitive in detecting VUR, but does not allow reliable grading of reflux, nor definition of urethral and bladder morphology. It is therefore better indicated in the follow-up of known VUR.

The overall incidence of VUR in the present series is 25.9%. The reported incidence of VUR is 35% in selected children after a single urinary infection [9], 16%–52% in infants and children screened because of a family history of VUR [10], and 15%–38% in infants referred be-

cause of antenatal renal pelvic dilatation [11–13]. These wide variations in the incidence of VUR mostly depend upon the criteria for referral as well as age and gender. When we are able to better calculate the degree of risk for VUR, according to age, sex, family history, previous urinary infection, renal sonogram, etc., radionuclide CVC would be better indicated in subjects with lower risk for VUR and radiological CVC in those with higher risk.

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