

## Early Performance of Voiding Cystourethrogram after Urinary Tract Infection in Children

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**Key words:** urinary tract infection, children, cystourethrogram

### Abstract

**Background:** Voiding cystourethrogram is performed 3–6 weeks after urinary tract infection. This prolongs the interval of prophylactics, reducing the likelihood of having to perform the procedure.

**Objectives:** To investigate the yield and potential risks/benefits of early compared to late performance of VCUG after UTI.

**Methods:** We conducted a prospective study of 84 previously healthy children < 5 years old admitted from October 2001 to November 2002 with first documented UTI. We then divided the 78 patients who had VCUG into two groups and compared them to a control group: group A – 49 children in whom VCUG was performed within 10 days, group B – 29 children in whom VCUG was performed > 10 days after UTI, and a historical control group C – 82 children in whom VCUG was performed > 4 weeks following UTI.

**Results:** VCUG was performed in 48/48 (100%), 6/35 patients (17.1%) and 34/116 patients (29.3%), and vesicoureteral reflux was demonstrated in 38.8%, 37.9% and 39% in groups A, B and C respectively. No significant difference was found between these groups in terms of incidence of VUR and severity and grading of reflux within each group. One case of UTI secondary to VCUG occurred in a patient in whom the procedure was performed 4 months after the diagnosis.

**Conclusions:** Performing VCUG early does not influence the detection rate, severity of the VUR, or risk of secondary infection; it shortens the period of prophylactic use and increases performance rate of VCUG, thereby minimizing the risk of failure to detect VUR. The traditional recommendation of performing VCUG 3–6 weeks after the diagnosis of UTI should be reevaluated.

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Urinary tract infection occurs in as many as 5% of female and 1–2% of male children [1]. In about 50% of children with their first proven case of symptomatic UTI, a structural abnormality of the urinary tract will be found [2]. The most common abnormality is vesicoureteral reflux, which is diagnosed in 25–40% of children with first documented UTI [1-3]. VUR may be associated with other urinary tract anomalies such as double collecting system, ureterocele or bladder outlet obstruction (i.e., posterior urethral valves) and is common in children with dysfunctional voiding. VUR facilitates the ascent of infected urine to the kidneys, thereby predisposing children to recurrent pyelonephritis [2-4]. Scarring of renal parenchyma, hypertension and renal insufficiency

are well-established complications of VUR and UTI in children [1-5]. Therefore, early diagnosis and proper management of VUR are of crucial importance.

The standard test used to diagnose VUR is voiding cystourethrogram. The generally accepted practice is to perform VCUG in all children younger than 5 years old with first documented UTI. For children older than 5, the recommendations vary according to gender, clinical manifestations and family history of VUR [6-8]. The accepted practice has been to perform VCUG at least 3–6 weeks after a UTI in order to prevent false positive results, which may be caused by UTI-related transient changes in the urinary tract [9,10]. However, the validity of this practice has recently been questioned. Two recent retrospective studies [11,12] and one cross-sectional analysis [13] have shown that the prevalence and severity of VUR in children with UTI were not influenced by the timing of VCUG performance (i.e., early vs. late performance following the diagnosis of UTI).

The purpose of this study was to prospectively evaluate the prevalence and grade of VUR in children with first documented UTI in whom VCUG was performed early (within 10 days) after the diagnosis of UTI, to evaluate whether early VCUG performance poses an increased risk for UTI, and to examine whether early performance of VCUG improves the likelihood of having this study performed.

### Patients and Methods

We prospectively evaluated children of both genders under the age of 5 years who were hospitalized over a 14 month period (October 2001–November 2002) with first documented UTI at Meyer Children's Hospital in Haifa. This tertiary care hospital serves a population of approximately half a million children of various ethnic origins in northern Israel.

Urinary tract infection was diagnosed when a symptomatic child had a culture of a urine specimen obtained by suprapubic aspiration growing any number of colonies, a catheterized specimen growing > 10<sup>4</sup> colonies/ml, or a properly obtained, clean-voided, midstream urine specimen growing ≥ 10<sup>5</sup> colonies/ml. Patients with a previous history of UTI, known VUR or other genitourinary anomalies were excluded from the study.

The original study design was to perform VCUG within 10 days from the diagnosis of UTI in all patients who met the study's inclusion criteria, and in whom parental consent was obtained. In fact, the study group was divided into two subgroups based

VCUG = voiding cystourethrogram

UTI = urinary tract infection

VUR = vesicoureteral reflux

on the timing of VCUG: an "early group" (group A) in which VCUG was performed within 10 days from the occurrence of UTI, and a "late group" (group B) in which VCUG was performed later than 10 days from the diagnosis of UTI (due to delays caused by parents, primary care physicians, or the health management organization). VCUG results of groups A and B were compared with the results of this procedure in a historical control group (group C), which included children with first documented UTI who were hospitalized at Meyer Children's hospital between June 1998 and May 1999 and in whom VCUG was performed more than 4 weeks after the diagnosis of UTI. The data on this group were collected retrospectively (VCUG results) and prospectively (clinical data).

All VCUG studies were performed either at Meyer Children's Hospital or at an adjacent university-affiliated hospital. In both institutions, VCUG was performed in a cyclic manner (i.e., two to three cycles of filling and emptying the bladder), a method previously shown to improve the accuracy and yield of the procedure [14]. Severity of reflux was graded according to the International System of Radiographic Grading of VUR [15].

### Follow-up

Patients in study groups A and B were contacted by telephone several days after the performance of VCUG to check for VCUG-associated sequelae such as fever, chills or other evidence of UTI.

### Statistical analysis

Comparison of categorical variables was performed using the chi-square test. Comparison between continuous variables was performed using the *t*-test and the Mann-Whitney test. Comparisons between group A and group B, as well as between group A and group C were performed by two separate statistical tests with Bonferroni's correction.

### Results

During the study, 84 children under the age of 5 years with first documented UTI who met the inclusion criteria of the study were admitted to Meyer Children's Hospital. VCUG was performed in 78 patients who were divided into two subgroups. Group A comprised patients in whom VCUG was performed within 10 days from the diagnosis (mean 6.4 days, range 3–10 days). Group B comprised patients in whom VCUG was performed more than 10 days after the diagnosis of UTI (mean 51.8 days, range 12–150 days). In 6 of 84 patients (7.1%) who were supposed to be included in the original group B, VCUG was not performed. In five cases, the parents refused to expose the child to this procedure and one patient was lost to follow-up. VCUG was performed in all 49 patients who belonged to original group A. In 6/35 patients (17.1%) who belonged to original group B the procedure was not performed.

Group C comprised a historical control group of children in whom VCUG was performed > 4 weeks from the diagnosis [Table 1]. In 34 of 116 patients (29.3%) who were supposed to be included in the original group C, the procedure was not performed.

**Table 1.** Demographic characteristics of children with urinary tract infection

	Group A n=49	Group B n=35	Group C n=116
Children who had VCUG	VCUG < 10 days n=49 (100%)	VCUG > 10 days n=29 (82.9%)	VCUG > 4 wks n=82 (70.7%)
Ethnicity			
Jews	24 (49%)*	26 (74.3%)	77 (66.4)
Arabs	25 (51%)*	9 (25.7%)	39 (33.6%)
Gender			
Female	34 (71.4%)*	30 (85.7%)	87 (75%)
Male	14 (28.6%)*	5 (14.3%)	29 (25%)
Age (mos)	1–60	0.33–48	0.25–60
Mean ± SD	14.5 ± 16.3*	17.7 ± 13.6	14.7 ± 14.5

n = number of children

\* Not significant vs. groups B and C

**Table 2.** Rates of VUR in children with urinary tract infection

	Group A VCUG < 10 days n=49	Group B VCUG > 10 days n=29	Group C VCUG > 4 wks n=82
Reflux	19 (38.8%)*	11 (37.9%)	32 (39%)
No reflux	30 (61.2%)*	18 (62.1%)	50 (61%)

n = number of children

\* Not significant vs. groups B and C

**Table 3.** Grades of VUR in children with urinary tract infection

	Group A VCUG < 10 days N=30	Group B VCUG > 10 days N=13	Group C VCUG > 4 wks N=51
Grade 1	3 (10%)*	2 (15.4%)	10 (19.6%)
Grade 2	10 (33.3%)*	5 (38.4%)	22 (43.1%)
Grade 3	10 (33.3%)*	3 (23.1%)	12 (23.6%)
Grade 4	6 (20%)*	3 (23.1%)	5 (9.8%)
Grade 5	1 (3.3%)*	0	2 (3.9%)

N = number of kidney units

\* Not significant vs. groups B and C

**Table 4.** Grades of VUR in children with urinary tract infection

	Group A VCUG < 10 days N=30	Group B VCUG > 10 days N=13	Group C VCUG > 4 wks N=51
Low to moderate grade (1,2,3)	23 (76.6%)*	10 (76.6%)	44 (86.3%)
High grade (4,5)	7 (23.3%)*	3 (23.1%)	7 (13.7%)

N = number of kidney units

\* Not significant vs. groups B and C

No statistically significant differences in gender and age were observed between the three study groups [Table 1]. Tables 2, 3 and 4 summarize the rates and grades of VUR within the three study groups. No statistically significant differences were found between groups A and B in term of rate and severity of reflux (chi-square test and Mann-Whitney test).

The findings in both study groups were compared to those in the historical control group (group C) in which VCUg was performed more than 4 weeks after the diagnosis of UTI. No statistically significant differences were found between this group and group A in terms of rate and severity of reflux (chi-square test and Mann-Whitney test). The overall rate of VUR in all patients in group A, B and C combined was 38.5% (30/78).

Early performance of VCUg was safe. Mild sequelae included: a) occurrence of fever without evidence of UTI in two patients in group A (1 and 4 days following the procedure, respectively), and b) the development of UTI caused by *Pseudomonas aeruginosa* in one patient in group B following a VCUg performed 4 months after the initial UTI.

## Discussion

Vesicoureteral reflux, which occurs in 30–40% of children with first documented UTI, facilitates the ascent of infected urine to the kidneys. Children with VUR have a much higher incidence (30–60%) of pyelonephritis scarring than those without reflux, and renal scarring is a predisposing factor to progressive renal failure. Early diagnosis and appropriate management of VUR are therefore of major importance [1,2,4,5].

Voiding cystourethrogram provides both direct detection of VUR and anatomy related to the lower and upper urinary tract. The generally accepted practice has been to perform VCUg at least 3–6 weeks after the diagnosis of UTI. This recommendation is based on two considerations: a) during an acute infection, a transient reflux occurs secondary to inflammatory changes in the vesicoureteral junction, and b) the acute infection may cause transient ureteral dilatations. Therefore, it has been argued that performing VCUg early after a UTI may lead to false positive results [9,10].

However, several recent studies have challenged this view by showing that VUR is a primary renal anomaly that does not occur secondary to infection [11,12]. Hence, it has been suggested that rate and grade of reflux are not influenced by the timing of VCUg [11,12].

McDonald and co-workers [11] showed that there was no difference in the rate and grade of reflux between children in whom VCUg was performed early (within 7 days from the diagnosis of UTI) and children who had VCUg later. In another study, Mahant et al. [12] showed that performing an early VCUg did not influence the rate of detected reflux. It should be noted, however, that both studies were conducted retrospectively.

In our study we prospectively evaluated VCUg findings in children with first documented UTI in our institution. The original design of our study was to perform VCUg within 10 days from the diagnosis of UTI in all children studied and to compare these findings with those of a historical control study group. Nevertheless, in 29 of the 84 children enrolled in the study early VCUg was not performed for various reasons (see Results). Those children in whom VCUg was performed more than 10 days after the diagnosis of UTI constituted a prospective control group, which, together with the historical control group, served to underscore the meaningful findings of this study.

No statistically significant differences in the rate and grade of VUR were found between the group of children in whom VCUg was performed within 10 days of the diagnosis of UTI and those in whom the procedure was performed later. The rate of VUR detection ranged between 38% and 39% in all three study groups, which is similar to the rate found in previous studies [16–18]. Also, the distribution of the severity of reflux within each group was comparable to that reported in the literature [17,19,20].

In this study, we also examined the theoretical risk of ascending secondary infection caused by performing the procedure early after the diagnosis of UTI, when the pathogenic bacteria have not been completely eradicated. Our findings show, for the first time, that early performance of VCUg is not associated with an increased risk of developing UTI. In fact, the only case of secondary UTI in our study was found in a patient in whom VCUg was performed 4 months after the diagnosis of UTI.

An important advantage of performing VCUg early is the ability to discontinue prophylactic antibiotic therapy immediately after the procedure in case of a negative result (i.e., absence of VUR). This not only minimizes the risk of adverse reaction to the therapy but also relieves parents' fear and stress.

McDonald et al. [11] showed in their retrospective study that in 50% of children in whom VCUg was not performed early, the procedure was not performed at all. In our prospective study, 17% of patients in the original group B (the "late group") and 29.3% of patients in the original group C (the historical control group) did not undergo the study. Based on these findings we conclude that postponing the performance of VCUg reduces the likelihood of performing the procedure.

The question whether VCUg should be performed during the initial hospitalization in a child with documented UTI, while receiving the initial antibiotic therapy and following an appropriate clinical response, remains open. The medical and financial implications of such a practice should be investigated.

We conclude that early performance of VCUg (within 10 days) after first documented UTI does not influence the rate or severity of the detected VUR, does not augment the risk of secondary infection, shortens the period during which prophylactic antibiotic therapy is given, and increases the rate performance of the procedure, thereby minimizing the risk of failure to detect VUR. The traditional recommendation of performing VCUg 3–6 weeks after the diagnosis of UTI should be reassessed.

## References

1. Hansson S, Jodal U. Urinary tract infection. In: Avner ED, Harmon WE, Niaudet P, eds. *Pediatric Nephrology*. 5th edn. New York: Lippincott, Williams & Wilkins, 2004:1007–25.
2. Zelikovic I, Adelman RD, Nancarrow PA. Urinary tract infections in children. An update. *West J Med* 1992;157:554–61.
3. Sargent MA. What is the normal prevalence of vesicoureteral reflux? *Pediatr Radiol* 2000;30:587–93.
4. Jacobson SH, Eklof O, Eriksson CG, Lins LE, Tidgren B, Winberg J. Development of hypertension and uraemia after pyelonephritis in childhood: 27 year follow up. *BMJ* 1989;299:703–6.
5. Holland NH, Jackson EC, Kazee M, Conrad GR, Ryo UY. Relation of urinary tract infection and vesicoureteral reflux to scars: follow-up of thirty-eight patients. *J Pediatr* 1990;116:S65–71.

6. Hellerstein S. Urinary tract infections. Old and new concepts. *Pediatr Clin North Am* 1995;42:1433–57.
7. Koff SA. A practical approach to evaluating urinary tract infection in children. *Pediatr Nephrol* 1991;5:398–400.
8. Hellstrom M, Jacobsson B. Diagnosis of vesico-ureteric reflux. *Acta Paediatr Suppl* 1999;88:3–12.
9. Avery M, Mandell J, Simman C, Harmon W, First L. Genitourinary tract infections. In: Avery M, First L, eds. *Pediatric Medicine*. Baltimore, MD: Lippincott, Williams & Wilkins, 1989:611–14.
10. Rushton HG. Vesicoureteral reflux and scarring. In: Avner ED, Harmon WE, Niaudet P, eds. *Pediatric Nephrology*. 5th edn. New York: Lippincott, Williams & Wilkins, 2004:1030–48.
11. McDonald A, Scranton M, Gillespie R, Mahajan V, Edwards GA. Voiding cystourethrograms and urinary tract infections: how long to wait? *Pediatrics* 2000;105:E50–3.
12. Mahant S, To T, Friedman J. Timing of voiding cystourethrogram in the investigation of urinary tract infections in children. *J Pediatr* 2001;139:568–71.
13. Craig JC, Knight JF, Sureshkumar P, Lam A, Onikul E, Roy LP. Vesicoureteric reflux and timing of micturating cystourethrography after urinary tract infection. *Arch Dis Child* 1997;76:275–7.
14. Polito C, Moggio G, La Manna A, Cioce F, Cappabianca S, Di Toro R. Cyclic voiding cystourethrography in the diagnosis of occult vesicoureteric reflux. *Pediatr Nephrol* 2000;14:39–41.
15. Lebowitz RL, Olbing H, Parkkulainen KV, Smellie JM, Tamminen-Mobius TE. International system of radiographic grading of vesicoureteric reflux. International Reflux Study in Children. *Pediatr Radiol* 1985;15:105–9.
16. Sheldon CA, Wacksman J. Vesicoureteral reflux. *Pediatr Rev* 1995;16:22–7.
17. Smellie JM, Barratt TM, Chantler C, Gordon I, Prescod NP, Ransley PG, Woolf AS. Medical versus surgical treatment in children with severe bilateral vesicoureteric reflux and bilateral nephropathy: a randomised trial. *Lancet* 2001;357:1329–33.
18. Ross JH. The evaluation and management of vesicoureteral reflux. *Semin Nephrol* 1994;14:523–30.
19. Elder JS, Peters CA, Arant BS Jr, et al. Pediatric Vesicoureteral Reflux Guidelines: Panel summary report on the management of primary vesicoureteral reflux in children. *J Urol* 1997;157:1846–51.
20. Smellie JM, Jodal U, Lax H, Mobius TT, Hirche H, Olbing H. Outcome at 10 years of severe vesicoureteric reflux managed medically: Report of the International Reflux Study in Children. *J Pediatr* 2001;139:656–63.

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