Cyclic voiding cystourethrography without the use of fluoroscopic monitoring

Alev Kadioglu a,*, Ismail Mihmanli b, Fatih Kantarci b, Aylin Tekes a, Omer Uysal c

a ALKA Medical Imaging Center, Buyukdere Cad. Levent Apt. No: 36/16, 06200-Mecidiyekoy, Istanbul, Turkey
b Istanbul University, Cerrahpasa Medical Faculty, Department of Radiology, 34300-Istanbul, Turkey
c Istanbul University, Cerrahpasa Medical Faculty, Department of Biostatistics, 34300-Istanbul, Turkey

Received 1 March 2005; received in revised form 17 June 2005; accepted 21 June 2005

Abstract

Purpose: To determine whether cyclic voiding cystourethrography (VCUG) examinations can be performed without using real-time fluoroscopic monitoring.

Materials and methods: VCUG examinations were performed in 209 children (133 girls and 76 boys). In each child, it was performed in a cyclic manner (three consecutive cycles) without using fluoroscopic monitoring and one radiograph was taken in each cycle of the examination. All patients were sedated by midazolam prior to examination. The degree of vesicoureteric reflux (VUR) was graded for each of the kidney ureter units (KUU) (total 418 KUU) separately. Statistical analysis included the comparison of the presence and absence of VUR and three ordinal-matched comparisons of each cycle.

Results: VCUG was detected in 37.3% of the children (78/209) and 28.7% (120/418) of the KUU. The absence of or same degree of VUR in three consecutive cycles were obtained in 345 KUU and the agreement was calculated as 82.5%. The same degree and presence of reflux were found in 85 and 89 refluxing KUU, the same negative findings (absence of VUR) in 306 and 298 KUU, and discordant findings in 27 and 31 KUU (between the first and second and between first and third cycles), respectively. Therefore, the agreement was 93.5 and 92.5% between the first and second cycles (p = 0.70) and between the first and the third cycles (p = 0.15), respectively.

Conclusion: Both the cyclic nature of this study and the results indicated that VCUG without real-time fluoroscopic monitoring could be used where adequate fluoroscopic examination is not possible for children in whom VUR detection is necessary and impacts treatment. However, the responsibility of pediatric radiologist always must also include the task to provide proper equipment for imaging children with suspected VUR.

© 2005 Elsevier Ireland Ltd. All rights reserved.

Keywords: Vesicoureteric reflux; Voiding cystourethrography; Midazolam; Children; Radiation dose; Fluoroscopy

1. Introduction

Artificial (man-made) sources of radiation account for approximately 15% of the radiation exposure of the general public [1]. Diagnostic procedures represent the main source of medical radiation exposure. Since the use of radiation in medicine appears to be increasing, efforts to reduce the radiation dose are an important aspect of diagnostic imaging, especially in children. There is a large body of epidemiological data on medically irradiated populations [2,3] and dose reduction is the major concern of these studies. Pediatric radiologists, especially, are faced with the ALARA principle, which states that the amount of radiation used should be no more than is required to achieve a satisfactory diagnosis. It is the responsibility of the pediatric radiologist to determine the appropriate radiological examination technique in children.

Conventional fluoroscopy employs a relatively large radiation dose and approximately 25% of the genetically significant radiation dose in children arises from imaging of the urinary tract [4]. Vesicoureteric reflux (VUR) is probably the most common urinary tract disease a pediatric radiologist...
encounters. Therefore, voiding cystourethrography (VCUG) is the most common fluoroscopic procedure performed in children during routine clinical practice. Sonographic cystography and radionuclide cystography are other common diagnostic methods for the detection of VUR.

Generally, the fluoroscopic dose is estimated to be 80% of the entire radiation dose in a VCUG examination [5]. Many reports exist concerning the use of modern X-ray equipment, the determination of the best technique to be used, and the necessity of lower radiation doses. Additionally, a large body of literature is available regarding whether VCUG should be performed cyclicly or not and/or via various fluoroscopic methods [5–10]. To the best of our knowledge, there is no published data regarding VCUG examinations done with standard radiographs, in which real-time fluoroscopic monitoring was not used. The background of our hypothesis comes from intravenous urography, which generally does not necessitate the use of fluoroscopic monitoring. It was our hypothesis that if we could document VUR by VCUG examination with standard radiographs, without using real-time fluoroscopic monitoring, and obtain a diagnostic quality comparable to that of VCUG with real-time fluoroscopic monitoring, as reported in the literature, children may not have to face an unnecessary dose of X-ray radiation. This postulation encouraged us to undertake this prospective study and add our own material in the evaluation of whether VCUG examination can be performed without using real-time fluoroscopic monitoring as well as to determine the prevalence of intermittent VUR.

2. Materials and methods

The study group initially chosen included 225 children scheduled to undergo VCUG examination for the first time, between September 2003 and November 2004. Inclusion criteria was urinary tract infection. Exclusion criteria were as follows: patients with history of antenatal hydrocephalus (n = 2), urogenital malformation (n = 1), meningomyelocele (n = 1), extrophy vesical (n = 1), horseshoe kidney (n = 1), pelvic renal ectopy (n = 3), and multicystic dysplastic kidney (n = 1). All of these patients chose not to participate in the study who met the inclusion criteria. And no studies were performed in which laboratory examinations disclosed an acute infection (n = 2). All of the children’s renal sonographic examinations were done on the same day as their VCUG examinations, but prior to VCUG.

Institutional review board approval was deemed not necessary, although the study was performed according to the guidelines of the Helsinki declaration. Informed consent was obtained from the parents of the children participating in the study.

A total of 209 patients (133 girls, 76 boys), 1 month to 132 months old (40.09 ± 36.67 months) fulfilled the above-mentioned criteria. The VCUG examination in each child was performed in a cyclic manner (three consecutive cycles) without using fluoroscopic monitoring. First radiograph was taken during the filling period in order to detect VUR, trabeculation, diverticula of the bladder, and functional disturbances such as spinning top urethra. One radiograph was taken in each cycle of the examination and the final radiograph was obtained just after the third micturition. Each radiograph included kidneys, ureters, bladder, and urethra. Children who were less than 3 years old were restricted from fluid intake 2 h before the examination and those who were more than 3 years old were restricted for 4 to 5 h.

The same radiology technician performed all VCUGs with the same standard technique, as previously explained. A pediatric radiologist performed catheterization of the bladder in all the patients. A 5-, 6-, or 8-F feeding tube was used in all cases and a 15% solution of diatrizoate meglumine and diatrizoate sodium, at room temperature, was introduced by drip infusion from a height 1 m above the table top at a rate of 5% of the expected age-matched volume per minute. The amount of the solution to be infused was determined by predicting bladder capacity, which was estimated in milliliters by the following formulas: for under the age of 1, [(weight (kg) × 7) and for over the age of 1, [(age in years + 2) × 30]. The technician maintained visual contact with each child and with the infusion bottle at all times. When the infusion flow was seen to be slowing, the filling phase radiographs were taken. Infusion was continued until each child became uncomfortable or started to void. During voiding the technician would expose a radiograph. The amount of the solution infused during each cycle of VCUG was marked on the bottle. The catheter was left in place during voiding to be used for the second and third cycles of VCUG, which were performed immediately after the end of voiding by repeating the same processes as mentioned above. At the end of each cycle, the volume of contrast medium introduced was calculated by subtracting the residual volume in the bottle from the marked volume at the beginning. The fluid that was voided was also measured to determine if the bladder was completely emptied prior to the start of the next filling cycle. For the following cycle, approximately the same amount of voided contrast medium was infused. The amount of solution left in the connecting tube was not measured because it was constant in each of the three cycles. The bladder capacity did not exceed more than 20% of the expected capacity.

All patients were sedated by midazolam prior to examination. The routes of administration of this sedative drug were rectal for patients younger than 3 years and nasal for those older than 3 years (0.2 mg/kg, with a maximum dose of 15 mg).

Fluoroscopic monitoring was not used during the examination. The radiographs taken for each cycle were as follows: one anteroposterior projection for the first cycle and both one right and one left oblique projection for the second and third cycles, respectively. Each patient was in a recumbent position during the examination. Skin entrance dose of the whole examination was calculated by using dosimetry.
VUR was graded for each kidney ureter unit (KUU) using the International Grading Scale of 0–5 described by Lebowitz et al. [11].

The statistical analysis included the comparison of presence or absence of VUR that was tested with McNemar $X^2$ and three ordinal-matched comparisons of the cycles were performed with Friedman $X^2$. All agreements were evaluated with Kappa test. $P$ values of less than 0.05 were accepted as statistically significant.

3. Results

The skin entrance doses for the children in whom dosimetry was placed just next to the child, grouped according to age, were as follows: children younger than 1 year = 47.25 mRAD, children between 1 and 2 years of age = 56.7 mRAD, children between 2 and 3 years of age = 66.15 mRAD, children between 3 and 4 years of age = 75.6 mRAD, children between 4 and 5 years of age = 94.5 mRAD, children between 5 and 7 years of age = 141.75 mRAD, and children between 7 and 11 years of age = 170.1 mRAD.

VUR was detected in 120 of 418 KUU (28.7%) in 78 of 209 children (37.3%) (49 females, 29 males) during the first, second, and third cycles. The VUR was $\leq$ grade 2 in 67 KUU (54 children) and $\geq$ grade 3 in 53 KUU (24 children). The same degree and absence of VUR in three consecutive cycles was obtained in 345 KUU and agreement among the three consecutive cycles was calculated to be 82.5%. The numbers of refluxing KUU and degree of grade among the three cycles were not statistically significant (Friedman $X^2 = 3.70$, $p = 0.16$). Unchanged in the presence and degree of reflux from the first to the second cycle and from the first to the third cycle were 365 KUU (87.3%, $\kappa = 0.68$, $p < 0.001$), respectively. However, comparing the first cycle, VUR was upgraded in 33 KUU and was downgraded in 20 KUU in the second cycle and upgraded in 51 KUU and downgraded in 16 KUU in the third cycle. In the presence of reflux in the first cycle, discordant findings were 41 of 100 KUU (41%) in the second cycle and 47 of 100 KUU (47%) in the third cycle. In the absence of VUR in the first cycle, the reflux was detected in 12 KUU in the second cycle and 20 KUU in the third cycle.

The same degree and presence of reflux were found in 85 refluxing KUU and the same negative findings (absence of VUR) were found in 306 KUU between the first and second cycles. Discordant findings were found in 27 KUU; two of them were $\geq$ grade 3 while the remaining 25 were $\leq$ grade 2. Eighty-nine same refluxing KUU and 298 same negative findings were found between the first and third cycles. Discordant findings were found in 31 KUU; six of them were $\geq$ grade 3 while the remaining 25 were $\leq$ grade 2. Therefore, the agreement between the first and second cycles was 93.5%

### Table 1

<table>
<thead>
<tr>
<th>A</th>
<th>Presence and grade of VUR on the first, second, and third consecutive cycles of VCUG in 418 kidney ureter units</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>First cycle</strong></td>
<td><strong>Second cycle</strong></td>
</tr>
<tr>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>0</td>
<td>306</td>
</tr>
<tr>
<td>I</td>
<td>11</td>
</tr>
<tr>
<td>II</td>
<td>4</td>
</tr>
<tr>
<td>III</td>
<td>1</td>
</tr>
<tr>
<td>IV</td>
<td>3</td>
</tr>
<tr>
<td>V</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>321</td>
</tr>
<tr>
<td>B</td>
<td>First cycle</td>
</tr>
<tr>
<td>0</td>
<td>298</td>
</tr>
</tbody>
</table>

*a* Two KUU showed intrarenal reflux.

**(McNemar $X^2 = 0.14$, $p = 0.70$)** and the agreement between the first and third cycles was 92.5% (McNemar $X^2 = 2.06$, $p = 0.15$) (Table 2A and B).

VUR in 11 KUU was detected only in the first cycle (eight KUU in 7 of 49 girls and three KUU in 3 of 29 boys); 9 of 11 KUU showed grade 1 reflux while the remaining two were grade 2. VUR in eight KUU was detected only in the third cycle (five KUU in 5 of 49 girls and three KUU in 3 of 29 boys); seven of them showed grade 1 reflux while one was grade 3. Apparently, these differences were not statistically significant

### Table 2

<table>
<thead>
<tr>
<th>A</th>
<th>Comparison of positive or negative results for the first to the second (A) and the first to the third (B) cycles in 418 kidney ureter units</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>First cycle</strong></td>
<td><strong>Second cycle</strong></td>
</tr>
<tr>
<td>Positive</td>
<td>Negative</td>
</tr>
<tr>
<td>85</td>
<td>15</td>
</tr>
<tr>
<td>12</td>
<td>306</td>
</tr>
<tr>
<td>Total</td>
<td>97</td>
</tr>
<tr>
<td>B</td>
<td>First cycle</td>
</tr>
<tr>
<td>Positive</td>
<td>Negative</td>
</tr>
<tr>
<td>89</td>
<td>11</td>
</tr>
<tr>
<td>20</td>
<td>298</td>
</tr>
<tr>
<td>Total</td>
<td>109</td>
</tr>
</tbody>
</table>
significant \( (p > 0.05) \). Similarly, no significant difference was found either in mean bladder capacity between the first, second, and third cycles (124.49 ± 86.60, 122.72 ± 86.30, and 122.44 ± 86.71 ml, respectively; \( p > 0.05 \)). There was also no significant difference in the mean age of children who had constant findings in the three consecutive cycles and those with intermittent reflux \( (p > 0.05) \).

The negative predictive value of the first cycle for all children was 96.2% considering the second cycle as the standard of reference, and was 93.7% considering the third cycle as the standard of reference.

VUR during filling phase was as follows: right side eight KUU grade 1, 12 KUU grade 2, one KUU grade 3, one KUU grade 4, one KUU grade 5; left side nine KUU grade 1, 18 KUU grade 2, two KUU grade 3, two KUU grade 4, one KUU grade 5. When compared to the VUR detected during voiding, none of the VUR grades detected during the filling phase was greater than that detected during the cyclic phase.

In addition to VUR, over the course of this study, two patients had ectopic ureterocele without associated reflux, 89 patients had trabeculated bladders, four patients had posterior urethral valve (one of them without associated reflux), two patients had spinning top urethra, two patients had peri-ureteral diverticula, two patients had ureteropelvic junction obstruction, and one patient had refluxing megaureter.

Figs. 1–6 are representative images.

4. Discussion

In our study, the overall prevalence of vesicoureteral reflux (37.3% of patient population and 27.8% of all KUU) was comparable to that found by other authors who used fluoroscopy during their studies [12–16]. The results agreement we obtained between the first and second cycles (93.5%) and the first and third cycles (92.5%) are similar to studies of Jequier and Jequier [17] and Polito et al. [9]. Additionally, the agreement between the first and second cycles of our study was similar to the study of Papadopoulou et al. [18], who performed only two successive cycles in their study. It is well known that several factors can influence the occurrence of reflux and affect the sensitivity and reliability.
Fig. 2. Bilateral grade 4 reflux is seen in a boy. The wall of the bladder is thickened with irregular inner contours. Also note a left periureteral diverticulum (arrow). Urethra is normal throughout its course.

of VCUG, such as bladder dysfunction [19] or neurogenic disorders [20]. There are also technique-related variables that affect the accuracy of VCUG [21]. Bladder catheterization done by inadequately trained personnel, use of different types and sizes of catheters, hand injection of contrast media increasing the intravesical pressure, differences in temperature, and concentration of contrast media are all variables that might cause bladder irritation and intermittent reflex affecting the outcome of VCUG [22]. In addition, the state of hydration could affect the result of VCUG. It has been suggested that ureteral peristalsis related to diuresis can affect the frequency of reflex detection [23]. In our study, particular attention was paid to standardize the above variables. We also used midazolam in our patients. Midazolam is a benzodiazepine that can be administered orally, nasally, rectally, intramuscularly, or intravenously because of its water-soluble properties. It is an ideal sedative drug, providing rapid onset, short recovery time, no side effect, and it is also safe and easy to administer [24,25]. Sedating a child for a VCUG is not a common practice, and even upon parents’ requests, sedation is usually discouraged. Bozkurt et al. [26] found that midazolam administered before urodynamic studies had no effect on urodynamic variables. Recently, Stokland et al. [27] reported on their experience concerning sedation with midazolam for VCUG, and they found that midazolam reduces patients’ stress. We also share the authors opinion, that catheterization of the bladder was easier in sedated children. Additionally, catheters were not retracted spontaneously or by the children and there was no need for recatheterization. The use of sedation probably increased our success and helped us to avoid unnecessary motion artifacts.

VCUG has been accepted as the standard for both detecting and grading VUR. It is also considered as the standard for comparison with other imaging modalities, such as radionuclide cystography and voiding urosonography (VUS). Radionuclide technique is limited by its low resolution and anatomic detail, possible failure to depict grade I reflux, as well as its failure to discriminate the grades
of reflux in the pelvicalyceal system [7,28,29]. Recently, VUS using the intravesical application of an US contrast medium has been shown to have very high sensitivity and specificity in the diagnosis of VUR [30]. The number of VCUGs has significantly been reduced as a result of the implementation of VUS as part of the routine diagnostic imaging modality for VUR. However, it has some drawbacks such as little functional information, less accurate grading, equipment or operator dependency, insufficient anatomical evaluation of the ureters, the urethra or some diverticula (e.g. those that fill and appear only during voiding) [31].

If reflux is identified, prophylactic treatment is initiated until reflux disappears, or in selected cases, surgical correction is chosen. However, VUR may occur intermittently, and for this reason, cyclic VCUG is currently used [9,17,18,32,33]. All reports concerning VCUG examination, including limited-cycle VCUG examinations, in contrast to our study, have been performed with fluoroscopy. Jequier and Jequier [17] in a study of 207 children, including 164 followed for urinary tract infection, have reported a significant difference in VUR grade between successive cycles. Paltiel et al. [32] reported in a study of 142 children, including 112 with a prior history of urinary tract infection, that after a negative first filling, the second filling showed 16 new VUR in various grades. Franchi-Abella et al. [33] reported in a study of 234 children, including 139 cases with three fillings, that the presence of new VUR or an increase in VUR grade for the second and third cycles were statistically significant (16 new VUR, 20 changing VUR grade). Papadopoulou et al. [18] in a study of 275 children who underwent only two-cycle examinations, reported that intermittent VUR occurred
in up to 23% of the children. In our study, as in the literature, we found that VUR occurs intermittently and it can show downgrading or upgrading in a statistically significant number among successive cycles.

In our study, the negative predictive value of the first cycle for all the children was 96.2% considering the second cycle as the standard of reference, and for the second cycle it was 93.7% considering the third cycle as the standard of reference, which was statistically acceptable as a diagnostic method. However, it will be unacceptable for a clinician to miss reflux, even in one child undergoing VCUG who should have been on prophylactic treatment.

Evaluation of the reliability of VCUG faces many problems, merely because of the intermittent nature of VUR and the absence of a true gold standard for comparison. Cyclic VCUG increases the reliability of this method. An argument against VCUG is the radiation dose related to this procedure. Although it increases diagnostic reliability, it is inevitable that the cyclic VCUG examination necessitates much more radiation exposure than the standard VCUG. Studies on reducing the radiation dose in children by using various fluoroscopic methods in VCUG examination have been undertaken [5–10]. However, there is not a standardized fluoroscopic method in the evaluation of VCUG in the literature. In all of these studies, the radiation dose arising from fluoroscopy is the subject of controversy regarding how much they decrease or increase the radiation dose. It is obvious that VCUG examination performed with fluoroscopic monitoring, whatever the method of fluoroscopy is, possesses a much higher radiation dose than performing VCUG examination without fluoroscopic monitoring. Generally, fluoroscopic dose is estimated as 80% of the whole radiation dose in a VCUG examination [5]. Our study showed that VCUG examinations could be performed without using fluoroscopic monitoring (avoiding the unnecessary 80% of the dose), because our overall prevalence of VUR was approximately the same as the results of the previously performed studies that used fluoroscopic monitoring. Both the cyclic nature of this study and the results that were
comparable with the literature indicate that this method could be used for the children suspected with VUR. On the other hand, one can argue that VCUG examinations performed without using fluoroscopic monitoring could be problematic, especially in grading its cyclic nature. However, the results of this study were similar to VCUG studies in the literature that had been performed with fluoroscopic monitoring. In addition, performing some of the cycles of the cyclic VCUG examination with fluoroscopic monitoring and some without fluoroscopic monitoring in the same patient, thereby decreasing the radiation dose, could be the objective of future studies. One can also argue that differentiation low pressure reflux from high pressure reflux or diagnosis of functional disturbances is cumbersome with this method. However, In addition to classical VCUG protocols, adapted protocols allow for additional evaluation of functional aspects (modified VCUG) with accuracy similar to manometry. Using adapted protocols, VCUG offers functional information in addition to the excellent anatomic survey. Most sophisticated application of VCUG is the combination of fluoroscopy with urodynamic testing, called video-urodynamics, which has become the generally accepted state of the art procedure for evaluating and monitoring functional abnormalities [35]. We think that not to use fluoroscopic monitoring in some cycles of the VCUG will not affect the adopted VCUG in cycles where fluoroscopic monitoring is used. Visualization of the urethra, functional disturbances such as spinning top urethra, structural disturbances such as trabeculation or diverticula of the bladder, and VUR during the filling phase are all important in a VCUG examination [34]. We visualized not only the entire
urethra perfectly in all patients during each cycle, which can be difficult considering the short length of the urethra in children, but also the associated findings in the bladder and ureter in prevoiding and postvoiding radiographs. In conclusion, we believe that although fluoroscopic monitoring is mandatory, VCUG examination could also be performed without the use of fluoroscopic monitoring where adequate fluoroscopic examination is not possible. However, the responsibility of pediatric radiologist always must also include the task to provide proper equipment for imaging children with suspected VUR.

References


